BACTERIAL SKIN INFECTIONS

CHI Formulary Indication Review

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM – January 2024

To the CHI Original Bacterial Skin Infections - Issued April 2020

Contents

Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

List of Tables

List of Figures

Abbreviations

AAST - American Association for the Surgery of Trauma

ABSSSI - Acute Bacterial Skin and Skin Structure Infection

bd - Twice a day

BID - Twice a day (from the Latin "bis in die")

BPM - Beats Per Minute

CADTH - Canadian Agency for Drugs and Technologies in Health

CA-MRSA - Community-Acquired Methicillin-Resistant Staphylococcus Aureus

CHI - Council of Health Insurance

CPGs - Clinical Practice Guidelines

CrCl - Creatinine Clearance

DS - Double Strength

EMA - European Medicines Agency

ENT - Ear, Nose, and Throat

FBC - Full Blood Count

FDA - Food and Drug Administration

GAIS - Global Alliance for Infections in Surgery

HAS - Haute Autorité de Santé (French: High Authority of Health)

HD - Hemodialysis

hib - Haemophilus influenzae type b

HITH - Hospital in the Home

HTA - Health Technology Assessment

I and D - Incision and Drainage

ID - Infectious Diseases

IDF - CHI Drug Formulary

IQWIG - Institute for Quality and Efficiency in Health Care (German: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen)

IV - Intravenous

IVIG - Intravenous Immunoglobulin

MRSA - Methicillin-Resistant Staphylococcus Aureus

MSF - Médecins Sans Frontières (Doctors Without Borders)

MSSA - Methicillin-Sensitive Staphylococcus Aureus

N/A - Not Applicable or Not Available

NHS - National Health Service

NICE - National Institute for Health and Care Excellence

NSAIDS - Nonsteroidal Anti-Inflammatory Drugs

NSTI - Necrotizing Soft Tissue Infection

PBAC - Pharmaceutical Benefits Advisory Committee

PD - Pharmacodynamics

PK - Pharmacokinetics

PO - Per os (by mouth)

QID - Four times a day

RCH - Royal Children's Hospital

SFDA - Saudi Food and Drug Authority

SHC – Standford Health Care

SIRS - Systemic Inflammatory Response Syndrome

SIS-E - Surgical Infection Society-Europe

SS – Single Strength

SSSS - Staphylococcal Scalded Skin Syndrome

SSTI - Skin and Soft Tissue Infection

tds - Three times a day

TID - Three times a day

TMP-SMX - Trimethoprim-Sulfamethoxazole

WSES - World Society of Emergency Surgery

WSIS - World Surgical Infection Society

Executive Summary

Skin infections occur when bacteria infect the skin and sometimes the deep tissue beneath the skin. Bacterial skin infections can be classified as skin and soft-tissue infections (SSTI) and acute bacterial skin and skin structure infections (ABSSSI)[1].

SSTIs include carbuncles, ecthyma, erythrasma, folliculitis, furuncles, impetigo, lymphadenitis, and minor cutaneous abscesses[1].

ABSSSIs are complex bacterial skin infections. They include, cellulitis, erysipelas, lymphangitis, major cutaneous abscesses (> 75 cm^2 including edema, erythema, and induration), necrotizing soft-tissue infection, and wound infections[1].

In general, patients with bacterial skin infections can develop symptoms gradually or suddenly[2]. These symptoms include skin redness, pain, tenderness, warmth, swelling, and/or pus-filled abscess. SSTIs can be associated with serious complications such as gangrene, osteomyelitis, bacteremia, and sepsis[2].

Factors that increase the risk of bacterial skin infections include injury to the skin, chronic swelling of the legs or arms, obesity, diabetes, and skin conditions such as athlete's foot or eczema[2].

Bacterial skin diseases represented 3.3% of the total prevalence of skin disease in the Kingdom of Saudi Arabia (KSA)[3]. Several studies have investigated the economic implications of SSTIs. According to findings by Lee and colleagues, the overall cost of SSTIs in the United States amounted to $13.8 billion in 2012. Hospitalizations played a significant role in driving these costs, with an average expenditure of $22,706 per individual[4].

Mainstay treatments of bacterial skin infections include antibiotics and drainage of abscesses[1]. An antibiotic ointment is used if a minor skin infection develops. Oral or parenteral antibiotics are needed if a large area of skin is infected[1].

CHI issued Bacterial Skin Infections clinical guidance after thorough review of renowned international and national clinical guidelines in April 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI Bacterial Skin Infections clinical guidance and seeks to offer guidance for the effective management of Bacterial Skin Infections. It provides an **update on the Bacterial Skin Infections Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, being **the issuance of new guidelines that are added to this report** such as the Cellulitis and other bacterial

skin infections - The Royal Children's Hospital (RCH) Clinical Practice Guidelines **2020**, Impetigo – Medecins Sans Frontieres MSF medical guidelines **2023**, Furuncles and carbuncles - MSF medical guidelines **2023**, Erysipelas and cellulitis - MSF medical guidelines **2023**, Stanford Health Care (SHC) Clinical Guideline: Outpatient Management of Skin and Soft Tissue Infections **2022**, C.S Mott Children's Hospital Michigan Medicine **2023** - Empiric antibiotic guidelines for skin and soft tissue infections in patients on pediatric services, WSES/GAIS/WSIS/SIS-E/AAST global clinical pathways for patients with skin and soft tissue infections **2022**, the NHS Foundation Trust Guideline for skin and soft tissue infection including diabetic foot ulcer **2022,** Cellulitis and erysipelas: antimicrobial prescribing **NICE guideline 2019**, and the **Saudi 2018 National Antimicrobial Therapy Guidelines** for Community and Hospital Acquired Infections in Adults**.**

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is important to note that it is recommended to **add Azithromycin, Cefuroxime, Minocycline, Tigecycline, Telavancin, and Teicoplanin** on the CHI formulary. Additionally, it is also recommended to **delist Benzylpenicillin and Clavulanic acid** from the Bacterial Skin Infections CHI formulary. Furthermore, there have been **updates** regarding certain previously mentioned drugs in terms of drug information and prescribing edits since April 2020.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in the therapeutic management of Bacterial Skin Infections.

Below is a table summarizing the major changes based on the different Bacterial Skin Infections treatment guidelines used to issue this report:

Table 1. General Recommendations for the Management of Bacterial Skin Infections

Management of Bacterial Skin Infections		
General Recommendations	**Level of Evidence/ Grade of Recommendation**	**Reference**
Please refer to section 1.0 for antibiotic options and dosing regimens.		
<u>Treatment recommendations of impetigo</u>: • Localized non bullous impetigo (max. 5 lesions in a single skin area): 2% mupirocin ointment: one application 3 times daily for 7 days. Reassess after 3	Not graded	MSF medical guidelines 2023[5]

days. If there is no response, switch to oral antibiotic therapy. • Extensive non bullous impetigo (more than 5 lesions or impetigo involving more than one skin area), bullous impetigo, ecthyma, impetigo with abscess; immunocompromised patient; topical treatment failure: oral antibiotic therapy recommended. • Note: in newborns with lesions located around the umbilicus, administer cloxacilllin IV.		
Treatment of simple abscess: • Incision and drainage • Oral antibiotic therapy is recommended only in selected patients. • Target pathogens: S.aureus and streptococci. • In cases of recurrent skin abscess, it is necessary to look for the presence of foreign materials and identify and correct local factors that may cause recurring infection.	Not graded	WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines[6]
<u>Treatment recommendations of furuncles and carbuncles</u>: • Furuncle on the face, multiple furuncles, carbuncles or in immunocompromised patients: oral antibiotic therapy is recommended.	Not graded	MSF medical guidelines 2023[7]
<u>Treatment recommendations of erysipelas and cellulitis</u>: • Administer antibiotics: either orally or IV depending on severity. • Treat portal of entry and comorbidities. • Check and/or catch-up tetanus vaccination. • Target Pathogens: S. aureus and streptococci, CA- MRSA is unusual.	Not graded	MSF medical guidelines 2023[8] WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines [6]

• In case of necrotizing fasciitis, septic arthritis, or osteomyelitis: urgent transfer to a surgical center, initiate IV antibiotic treatment while awaiting transfer.		
• Hospitalize for the following: children younger than 3 months, critically ill appearing patient, local complications, debilitated patient (chronic conditions, the elderly) or if there is a risk of non-compliance with or failure of outpatient treatment. Treat other patients as outpatients.	Not graded	MSF medical guidelines 2023[8]
In minor skin infections, localized impetigo (non-bullous or bullous), secondarily infected skin lesions such eczema, ulcers, or lacerations, or folliculitis (small follicular abscess in epidermis): • Topical therapy: Generally preferred over oral therapy. • Oral therapy: Indicated instead of topical therapy for patients with numerous impetigo lesions or in outbreak settings to reduce transmission. • Target Pathogens: Staphylococcus aureus, group A Streptococcus • If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX).	Not graded	C.S Mott Children's Hospital Michigan 2023[9]
For cellulitis, review antibiotics at day 5, can extend if not fully resolved. The choice of antimicrobial therapy may be guided by: • History of presenting complaint: o Acute or chronic o Circumstances surrounding the development of the SSTI	Not graded	NHS 2022 Guidelines[10]

• Significant past medical history:
  ○ Diabetes
  ○ Immunocompromised state
  ○ Similar presentation with SSTI previously, etc.
• Recent antimicrobial history within the last one month
• Previous or recent positive microbiology results		

<u>In non-purulent cellulitis</u>: • Target Pathogens: Group A Streptococcus, Staphylococcus aureus (the role of community-acquired MRSA is unknown) • Cephalexin and cefazolin provide coverage for group A Streptococcus and MSSA. TMP-SMX provides adequate coverage for group A Streptococcus, MSSA, and MRSA. • If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX or linezolid).	Not graded	C.S Mott Children's Hospital Michigan 2023[9]
<u>In purulent cellulitis or abscesses including folliculitis, furuncles, carbuncles</u>: • Target Pathogen: Staphylococcus aureus (including CA- MRSA). • Cultures and susceptibilities are recommended when I&D is performed. Blood cultures are also recommended for patients with fever, rapidly progressive cellulitis, and systemic illness. • In neutropenic and immunocompromised patients, Gram-negative bacteria should be considered. • When to Consider Admission	Not graded	C.S Mott Children's Hospital Michigan 2023[9] WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines [6] SHC 2022 Guidelines [11]

• ≥2 SIRS criteria* (*fever ≥38 or <36 C, tachycardia >90 bpm, RR> 20 bpm leukocytosis >12k cells/μL) • Hypotension • Rapid disease progression • Clinical signs of deeper infection (bullae, skin sloughing, organ dysfunction)		
Treatment of perianal and perirectal abscesses: • Incision and drainage + antibiotic therapy in selected patients. • Target Pathogen: Gram-positive and Gram-negative • Outpatient therapy (oral antibiotic) or inpatient therapy (IV medications) depending on severity	Not graded	WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines[6]
Treatment of bite wounds (animal and human bites): • Irrigation of the wound and debridement of necrotic tissue • Antibiotic prophylaxis as principle is not recommended. It is recommended in select patients. • Tetanus prophylaxis in bite wounds	Not graded	WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines[6]
Treatment of burn wounds: • Early initiation of dressings and effective topical antimicrobial therapy • Daily inspection of the wounds by a qualified surgeon or wound care expert • Early excision of all full thickness and deep partial thickness burns • Systemic antibiotic for infected wounds • Graft and coverage options • Target Pathogen: Gram-positive	Not graded	WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines[6]

and Gram-negative • Outpatient therapy (oral antibiotic) or inpatient therapy (IV medications) depending on severity		
<u>In Staphylococcal Scalded Skin Syndrome (SSSS)</u>: • This results in loss of keratinocyte cell adhesion and leads to blistering of the upper layer of the skin. • Pediatric Infectious Diseases consultation is recommended. Consider Dermatology consult if diagnosis is unclear or specific skin care recommendations are needed. • Common pathogens: Staphylococcus aureus (MSSA predominantly reported in the literature) • Consider discontinuing linezolid when patient is clinically stable (e.g., vital signs within normal limits, no vasopressor requirements) for 24-48 hours and rash no longer progressing (usual duration of 3-5 days).	Not graded	C.S Mott Children's Hospital Michigan 2023[9]
<u>In necrotizing fasciitis cases</u>: • Urgent referral to surgical team for debridement, seeking specialist advice for antibiotics, and considering IVIg are recommended. • Early and aggressive surgical exploration (within 6 hours after admission) and debridement is critical. Emergent surgical consultation and ID consult are strongly recommended. • Common pathogens: Group A β-hemolytic Streptococcus, S. aureus, E. coli, Pseudomonas spp., Enterobacter spp., Klebsiella spp.,	Not graded	RCH 2020 Clinical Practice Guidelines for pediatrics[12], C.S Mott Children's Hospital Michigan Medicine 2023[9] NHS 2022 Guidelines [10] WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines [6]

Proteus spp., Bacteroides spp., Clostridia spp., Peptostreptococcus spp.
• Empiric antibiotics should be continued until the following criteria are met:
  o Debridement no longer needed,
  o Clinical improvement, and
  o Minimum of 48-72 hours after completion of surgical debridement
• Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs.
• Clindamycin is initiated for anti-toxin activity for Streptococcal and Staphylococcal infections and can be stopped after 24-72 hours if infection has improved and patient is stable.		

<u>Traumatic wound infections WITHOUT water exposure</u>: • Usually polymicrobial from environmental contamination. • Target pathogens: Staphylococcus aureus, Clostridia spp., Bacteroides spp., Prevotella spp., Porphyromonas spp., and Peptostreptococcus spp. • Consider Pediatric ID consult for infections that are deep, extensive or respond slowly. • Debridement of devitalized tissues and contaminating debris is critical to source control and successful healing. • Empiric therapy should take into account site of wound and prior	Not graded	C.S Mott Children's Hospital Michigan 2023[9]

cultures and colonization.		
<u>Traumatic wound infections WITH water exposure</u>: • Usually polymicrobial from environmental contamination. • Target pathogens: Staphylococcus aureus, Clostridia spp., Bacteroides spp., Prevotella spp., Porphyromonas spp., and Peptostreptococcus spp. • Consider Aeromonas and Pseudomonas spp., other gram negatives if significant water exposure • Vibrio vulnificus wound infections require extensive debridement and mortality can be high. Consider combination therapy with ceftazidime and doxycycline.	Not graded	WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines [6]
<u>Fournier's gangrene</u>: • Surgical source control as soon as possible. Re-explorations should be repeated until the time when very little or no debridement is required. • Diverting colostomy or rectal diversion devices • Antibiotic therapy • Supportive measures • The initial empirical antibiotic regimen should comprise broad-spectrum drugs, including anti-MRSA and anti-Gram-negative coverage. Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs.	Not graded	WSES/GAIS/WSIS/SIS-E/AAST 2022 Guidelines [6]
<u>Treatment of gas gangrene</u>: • The infection is rapidly progressive,	Not graded	WSES/GAIS/WSIS/SIS-E/AAST 2022

it is important to treat patients aggressively, by early surgical debridement, antibiotics. and intravenous fluid resuscitation.		Guidelines [6]
Pediatrics		
• Manage sepsis if features present • Manage source if identifiable — i.e. remove foreign body, drain abscess Antimicrobial recommendations may vary according to local antimicrobial susceptibility patterns.	Not graded	RCH 2020 Clinical Practice Guidelines for pediatrics [12]
In cases of moderate cellulitis, if oral antibiotics are not tolerated or no improvement after 48 hours, manage as per severe cellulitis. When improving, switch to oral antibiotics as per mild cellulitis.	Not graded	RCH 2020 Clinical Practice Guidelines for pediatrics [12]
In established animal/human bites, seeking specialist advice is recommended first. Indications for prophylactic antibiotics in an animal/human bite • Presentation delayed by > 8 hours • Puncture wound unable to be adequately debrided • Bite on hands, feet, face • Involves deep tissues (e.g. bones, joints, tendons) • Involves an open fracture • Immunocompromised patient • Cat bites	Not graded	RCH 2020 Clinical Practice Guidelines for pediatrics [12]
In waterborne skin infections – seawater or fresh water, it is recommended to clean and debride wound as needed. Prophylactic antibiotics are not recommended.	Not graded	RCH 2020 Clinical Practice Guidelines for pediatrics [12]
In severe cellulitis or Staphylococcal scalded skin syndrome, consider early	Not graded	RCH 2020 Clinical Practice Guidelines

discharge to HITH once stable. When improving, switch to oral antibiotics as per mild cellulitis.		for pediatrics [12]
Consider consultation with local pediatric team when • No improvement or deterioration after 24–48 hours of therapy • Deep abscess or necrotizing fasciitis suspected — consider surgical opinion	Not graded	RCH 2020 Clinical Practice Guidelines for pediatrics [12]
Adults and pediatrics		
Duration of therapy depends on the type and severity of the infection and patient's clinical response to treatment.	Not graded	RCH 2020 [12], MSF 2023[5,7,8], SHC 2022[11], C.S Mott Children's Michigan Medicine 2023[9], WSES/GAIS/WSIS/SIS-E/AAST 2022[6], NHS 2022[10]
Low-risk allergies include pruritus without rash, remote (>10 years) unknown reaction, patient denies allergy but is on record, mild rash with no other symptoms (mild rash: non-urticarial rash that resolves without medical intervention).	Not graded	C.S Mott Children's Hospital Michigan Medicine 2023[9]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Bacterial Skin Infections clinical and therapeutic management.** Additionally, **appendices** are provided for treatment algorithms and further information on the topic.

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Bacterial Skin Infections report, while the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This section contains the **updated versions** of the guidelines mentioned in the April 2020 CHI Bacterial Skin Infections Report and the corresponding recommendations:

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
Infectious Diseases Society of America (**IDSA**) Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections (**2014**)	Not available
National Institute for Health and Care Excellence (**NICE**) Antimicrobial Prescribing for Impetigo (**2020**)	Not available

1.1.1 Infectious Diseases Society of America (IDSA) Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections (2014)

*Please refer to **section 1.0** of the previous Bacterial Skin Infections CHI report.*

1.1.2 National Institute for Health and Care Excellence (NICE) Antimicrobial Prescribing for Impetigo (2020)

*Please refer to **section 1.0** of the previous Bacterial Skin Infections CHI report.*

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Bacterial Skin Infections report, along with their recommendations.

Table 3. List of Additional Guidelines

Additional Guidelines	
Saudi National Antimicrobial Therapy Guidelines for Community and Hospital Acquired Infections in Adults (**2018**)	
Royal Children's Hospital (RCH) Clinical Practice Guidelines for Cellulitis and Other Bacterial Skin Infections (**2020**)	
Médecins Sans Frontières (MSF) Medical Guidelines	Impetigo (**2023**)
	Furuncles and Carbuncles (**2023**)
	Erysipelas and Cellulitis (**2023**)
Stanford Health Care (SHC) Clinical Guideline: Outpatient Management of Skin and Soft Tissue Infections (**2022**)	
C.S Mott Children's Hospital Michigan Medicine – Empiric Antibiotic Guidelines for Skin and Soft Tissue Infections in Patients on Pediatric Services (**2023**)	
WSES/GAIS/WSIS/SIS-E/AAST Global Clinical Pathways for Patients with Skin and Soft Tissue Infections (**2022**)	
NHS Foundation Trust Guideline for Skin and Soft Tissue Infection Including Diabetic Foot Ulcer (**2022**)	
National Institute for Health and Care Excellence (NICE) Antimicrobial Prescribing Guideline for Cellulitis and Erysipelas (**2019**)	

1.2.1 Saudi National Antimicrobial Therapy Guidelines for Community and Hospital Acquired Infections in Adults (2018)

The 2018 edition of the antimicrobial guidelines, prepared by the Antimicrobial Stewardship Technical Subcommittee under the National Antimicrobial Resistance Committee (AMR), is designed to assist physicians across various levels of healthcare acuity. Its primary focus is on aiding in the selection of suitable empirical antibiotics for the treatment of prevalent community and healthcare-associated infections[13].

The table below outlines the recommendations regarding community-acquired infections in adults[13]:

Table 4. Saudi National Antimicrobial Therapy 2018 Recommendations for Community-Acquired Infections in Adults

Therapy for Purulent Skin and Soft Tissue Infections (Furuncle/Carbuncle/Abscess)	Empiric therapy	Duration
Mild	Incision and drainage only or with antibiotics in some cases (similarly to moderate cases)	7–10 days
Moderate	Incision and drainage with: - Trimethoprim-sulfamethoxazole PO160/800 mg [DS] q12h - Doxycycline PO 100mg q12h	
Severe	Incision and drainage with: - Vancomycin IV 15mg/kg q12h **OR** - Linezoild PO 600mg q12hr **OR** - Daptomycin IV 4mg/kg q24h	
Therapy for non-purulent Skin and Soft Tissue Infections (Necrotizing infection/Cellulitis/Erysipelas)	**Empiric Therapy**	**Duration**
Mild	Cloxacillin or Flucloxacillin 500mg PO q6h **OR** Cephalexin 500mg PO q6h (if non-immediate-type or non-severe hypersensitivity reaction to penicillin) **OR** Clindamycin PO 300-450 mg q6hr (if immediate-type or severe hypersensitivity reaction to beta-lactam)	7–10 days

Moderate	Penicillin G 2-4 million units IV q4-6h **OR** Cefazolin 1g IV q8h (if non-immediate-type or non-severe hypersensitivity reaction to penicillin) **OR** Clindamycin 600mg IV q8h (if immediate-type or severe hypersensitivity reaction to beta-lactam)	
Severe	Vancomycin IV 15mg/kg q12hr **PLUS** Piperacillin-tazobactam IV 4.5g q6-8hr **OR** Vancomycin IV 15mg/kg q12h **PLUS** Imipenem-cilastatin IV 500mg q6hr **OR** Vancomycin IV 15mg/kg q12h **PLUS** Meropenem IV 1000mg q8hr **OR** Vancomycin IV 15mg/kg q12h **PLUS** Ciprofloxacin PO 500-750mg **OR** Ciprofloxacin IV 400mg q12h **PLUS** Metronidazole PO/IV 500mg q8h **<u>If necrotizing fasciitis, also add</u>** Clindamycin 600-900mg IV q8h	
Animal bite & Human bite	**Therapy (dosing interval)**	**Duration**
Animal or human bite	Amoxicillin-clavulanic acid 1000mg PO q12h **OR** Cefuroxime axetil 500mg PO q12h **PLUS** Metronidazole 500mg PO q8h **OR** Doxycycline 100mg PO q12h	7 days

1.2.2 Royal Children's Hospital (RCH) Clinical Practice Guidelines for Cellulitis and Other Bacterial Skin Infections (2020)

The below recommendations (ungraded) are published by the Royal Children's Hospital (RCH) Clinical Practice Guidelines 2020, for the management of cellulitis and other bacterial skin infections[12]:

- Manage sepsis if features present
- Manage source if identifiable — ie remove foreign body, drain abscess
- Antimicrobial recommendations may vary according to local antimicrobial susceptibility patterns
- Cellulitis frequently looks worse after 24 hours of treatment; consider waiting 48 hours to change therapies
- Young, unvaccinated children are at risk of *Haemophilus influenzae* type B (Hib).

Table 5. Suggested Antibiotic Therapy Regimens for Bacterial Skin Infections (RCH 2020 Recommendations)

Diagnosis	Antibiotic	Total duration	Comments
Impetigo	Topical Mupirocin 2% ointment or cream to crusted areas tds **OR** Cefalexin 33 mg/kg (max 500 mg) oral bd if widespread or large lesions	5 days	
Mild cellulitis	Cefalexin 33 mg/kg (max 500 mg) oral tds	5 days	
Moderate cellulitis	A trial of high-dose oral antibiotics with close review may be considered: Cefalexin 33 mg/kg (max 1 g) oral tds Consider Ambulatory/Hospital-in-the-Home (HITH) if available: Ceftriaxone 50 mg/kg (max 2g)	5–10 days	If oral antibiotics not tolerated or no improvement after 48 hours, manage as per severe cellulitis When improving, switch to oral antibiotics as per mild cellulitis

	IV daily Cefazolin 50 mg/kg (max 2g) IV bd		
Severe cellulitis or Staphylococcal scalded skin syndrome	Flucloxacillin 50 mg/kg (max 2 g) IV 6H (if rapidly progressive consider adding Clindamycin 10 mg/kg (max 600 mg) IV 6H)	5–10 days	Consider early discharge to HITH once stable. When improving, switch to oral antibiotics as per mild cellulitis
Necrotising Fasciitis	Vancomycin and Meropenem 20 mg/kg IV (max 1 g) 8H **AND** Clindamycin 10 mg/kg (max 600 mg) IV 6H		Urgent referral to surgical team for debridement Seek specialist advice for antibiotics Consider IVIg
Mammalian bites (uninfected / prophylactic)	Often do **not** need prophylactic antibiotics. When indicated*: Amoxicillin/Clavulanate **80 mg/mL amoxicillin oral liquid (7:1)** 22.5 mg/kg (max 875 mg) oral bd	5 days	
Animal/human bites (established infection)	Amoxicillin/Clavulanate **80 mg/mL amoxicillin oral liquid (7:1)** 22.5 mg/kg (max 875 mg) oral bd If unable to tolerate oral antibiotics: 25 mg/kg (max 1g) IV 6–8H	5 days (extend if severe, penetrating, involving deep tissues)	Seek specialist advice
Waterborne skin infections – seawater or fresh water	Cefalexin 33 mg/kg (max 1 g) oral tds and Ciprofloxacin 10 mg/kg (max 500 mg) oral bd **OR** Trimethoprim/sulfamethoxazole 8/40 mg/kg (max 320/1600 mg) oral bd	5–10 days	Clean and debride wound as needed Prophylactic antibiotics are not recommended

*Indications for prophylactic antibiotics in an animal/human bite

- Presentation delayed by > 8 hours
- Puncture wound unable to be adequately debrided
- Bite on hands, feet, face
- Involves deep tissues (eg bones, joints, tendons)
- Involves an open fracture
- Immunocompromised patient
- Cat bites

Table 6 lists the suggested antibiotic therapy where MRSA is suspected:

Table 6. Suggested Antibiotic Therapy where MRSA is Suspected (RCH 2020 Recommendations)

Diagnosis	Antibiotic	Total duration	Comments
Mild cellulitis	Trimethoprim/sulfamethoxazole 8/40 mg/kg (max 320/1600 mg) oral bd **OR** Clindamycin 10 mg/kg (max 450 mg) oral qid	5 days	
Moderate cellulitis	A trial of oral antibiotics with close review may be considered **OR** Vancomycin IV		When improving, switch to oral antibiotics as per mild cellulitis
Severe cellulitis or Staphylococcal scalded skin syndrome	Vancomycin IV **OR** Clindamycin 10 mg/kg (max 600 mg) IV 6H	When improving, switch to oral antibiotics as per mild cellulitis	

Risk factors for MRSA infection

- Residence in an area with high prevalence of MRSA, eg Northern Territory, remote communities in northern Queensland
- Previous colonization or infection with MRSA (particularly recent)

Consider consultation with local pediatric team when:

- No improvement or deterioration after 24–48 hours of therapy
- Deep abscess or necrotizing fasciitis suspected — consider surgical opinion

1.2.3 Médecins Sans Frontières (MSF) Medical Guidelines

1.2.3.1 Impetigo (2023)

Impetigo is a benign, contagious infection of the epidermis due to group A ß-haemolytic streptococcus and *Staphylococcus aureus*. Co-infection is common. Transmission is by direct contact. Lack of water, and poor hygiene, increase spread.

Primary infections are most common in children. Secondary infections complicating preexisting pruritic dermatoses (lice, scabies, eczema, herpes, chickenpox, etc.) are more common in adults [5].

Treatment recommendations of impetigo:

- **Localized non bullous impetigo** (max. 5 lesions in a single skin area):
    - Clean with soap and water and dry before applying mupirocin.
    - **2% mupirocin** ointment: one application 3 times daily for 7 days. Reassess after 3 days. If there is no response, switch to oral antibiotic therapy (see below).
    - Keep fingernails short. Avoid touching the lesions, keep them covered with gauze if possible.
- **Extensive non bullous impetigo** (more than 5 lesions or impetigo involving more than one skin area), bullous impetigo, ecthyma, impetigo with abscess; immunocompromised patient; topical treatment failure:
    - Clean with soap and water and dry 2 to 3 times daily.
    - Keep fingernails short. Avoid touching the lesions, keep them covered with gauze if possible.
    - Incise abscesses if present.
    - Administer oral antibiotic therapy[a]:
        - **Cefalexin** PO for 7 days

          Neonates under 7 days: 25 mg/kg 2 times daily

          Neonates 7 to 28 days: 25 mg/kg 3 times daily

          Children 1 month to 12 years: 25 mg/kg 2 times daily

          Children 12 years and over and adults: 1 g 2 times daily

Or

- **Cloxacillin** PO for 7 days

  Children over 10 years: 15 mg/kg 3 times daily (max. 3 g daily)

  Adults: 1 g 3 times daily

Note: in newborns with lesions located around the umbilicus, administer cloxacilllin IV.

(a): **In penicillin-allergic patients only** (resistance to macrolides is common), azithromycin PO for 3 days (children: 10 mg/kg once daily; adults: 500 mg once daily).

- **For all patients**
  - Quarantine from school (children can return to school after 24 to 48 hours of antibiotic therapy).
  - Look for and treat any underlying dermatosis: lice, scabies, eczema, herpes, scalp ringworm, or an ENT infection.
  - Trace and treat contacts.
  - Check for proteinuria (use urine dipstick) 3 weeks after the infection.

1.2.3.2 Furuncles and Carbuncles (2023)

Necrotising perifollicular infection, usually due to *Staphylococcus aureus*. Risk factors include nasal carriage of *S. aureus*, maceration, breaks in the skin, poor hygiene; diabetes mellitus, malnutrition, iron deficiency or immunodeficiency[7].

Treatment recommendations of furuncles and carbuncles:

- **Single furuncle:**
  - Clean with soap and water 2 times daily and cover with a dry dressing.
  - Apply warm moist compresses to the furuncle in order to encourage it to drain.
  - After drainage, clean and apply a dry dressing until the lesion has healed.
- **Furuncle on the face, multiple furuncles, carbuncles or in immunocompromised patients:**
  - Same local care.
  - Add systematically an antibiotic for 7 days [a]: (a): For penicillin-allergic patients: clindamycin PO (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily)

- **Cefalexin** PO

  Neonates under 7 days: 25 mg/kg 2 times daily

  Neonates 7 to 28 days: 25 mg/kg 3 times daily

  Children 1 month to 12 years: 25 mg/kg 2 times daily Children 12 years and over and adults: 1 g 2 times daily

  Or

- **Amoxicillin/clavulanic acid** (co-amoxiclav) PO. Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin:

  Children < 40 kg: 25 mg/kg 2 times daily

  Children ≥ 40 kg and adults:

  Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)

  Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

- **In all cases**: wash hand frequently, wash bedding.

1.2.3.3 Erysipelas and Cellulitis (2023)

Erysipelas is a superficial infection (affecting the dermis and superficial lymph vessels), while cellulitis affects the deeper tissues (deep dermis layers and subcutaneous fat)[8].

Treatment recommendations of erysipelas and cellulitis:

- **In all cases:**
  - Outline the area of erythema with a pen in order to follow the infection. The erythema will regress if the treatment is effective. If the erythema spreads consider a treatment failure (MRSA or a necrotizing infection).
  - Bed rest, elevation of affected area (e.g. leg).
  - Treatment of pain. Avoid NSAIDs that may increase the risk of necrotizing fasciitis.
  - Administer antibiotics: either orally or IV depending on severity.
  - Treat portal of entry and comorbidities.
  - Check and/or catch up tetanus vaccination.
  - In case of necrotizing fasciitis, septic arthritis or osteomyelitis: urgent transfer to a surgical center, initiate IV antibiotic treatment while awaiting transfer.

- Hospitalize for the following: children younger than 3 months, critically ill appearing patient, local complications, debilitated patient (chronic conditions, the elderly) or if there is a risk of non-compliance with or failure of outpatient treatment. Treat other patients as outpatients.
    - Critically ill appearing child: weak grunting or crying, drowsy and difficult to arouse, does not smile, disconjugate or anxious gaze, pallor or cyanosis, general hypotonia.
- Outpatient antibiotherapy:
    - **Cefalexin** PO for 7 to 10 days
    - Children 1 month to under 12 years: 25 mg/kg 2 times daily
    - Children 12 years and over and adults: 1 g 2 times daily

      Or
    - **Amoxicillin/clavulanic acid** (co-amoxiclav) PO for 7 to 10 days.
    - Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin:

      Children < 40 kg: 25 mg/kg 2 times daily

      Children ≥ 40 kg and adults:

      Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)

      Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)
    - **For penicillin-allergic patients**, clindamycin PO for 7 to 10 days (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily).
- In the event of worsening clinical signs after 48 hours of antibiotic treatment, consider IV route.
- Inpatient antibiotherapy:
    - First line therapy:
        - **Cloxacillin** IV infusion over 60 minutes:
        - Cloxacillin powder for injection should be reconstituted in 4 ml of water for injection. Then dilute each dose of cloxacillin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

          Children 1 month to under 12 years: 12.5 to 25 mg/kg every 6 hours

          Children 12 years and over and adults: 1 g every 6 hours

Or

- **Amoxicillin/clavulanic acid** (co-amoxiclav) by slow IV injection (3 minutes) or IV infusion (30 minutes). The dose is expressed in amoxicillin:

  Children under 3 months: 30 mg/kg every 12 hours

  Children 3 months and over: 20 to 30 mg/kg every 8 hours (max. 3 g daily)

  Adults: 1 g every 8 hours

- If there is clinical improvement after 48 hours (afebrile and erythema and oedema have improved) switch to cefalexin or amoxicillin/clavulanic acid PO at the doses indicated above to complete 7 to 10 days of treatment.
- **For penicillin-allergic patients, clindamycin** IV infusion (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily).

- If there is no clinical improvement after 48 hours, consider MRSA:
  - Clindamycin IV infusion over 30 minutes: Dilute each dose of clindamycin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

    Children 1 month and over: 10 mg/kg every 8 hours

    Adults: 600 mg every 8 hours

  - After 48 hours, change to clindamycin PO at the doses indicated above to complete 7 to 10 days of treatment.

1.2.4 Stanford Health Care (SHC) Clinical Guideline: Outpatient Management of Skin and Soft Tissue Infections (2022)

Table 7 summarizes the 2022 recommendations by the Stanford Health Care (SHC) clinical guideline for the outpatient management of bacterial skin and soft tissue infections, and table 8 details dosing in renal impairment[11]:

Table 7. Outpatient Empiric Antibiotic Guidelines for Acute Bacterial Skin and Soft Tissue Infections (SSTI) (SHC 2022 Guideline)

Clinical Syndrome	Most Common Organism	Treatment Options	Duration	Comments
NON-PURULENT INFECTIONS Acutely spreading, poorly demarcated skin changes: dolor (pain), calor (heat), rubor (erythema), and tumor (swelling) **Erysipelas:** Superficial sharply demarcated infection of the upper dermis without focus of purulence (drainage, exudate, or abscess) **Cellulitis:** Deeper infection of the dermis & subcutaneous fat without focus of purulence (drainage, exudate, or abscess)	***B-hemolytic Streptococci*** 1. Group A (S. pyogenes) 2. Other Streptococcus groups: B,C,G	**Preferred**: **Cephalexin** 500mg PO q6h **OR** 1g PO q8h **Alternative for β-lactam Allergy[#]:** **Clindamycin** 450mg PO q8h **or TMP-SMX** 1-2 DS tab PO BID *Combination therapy is not recommended*	5 Days	When to Consider Cellulitis Mimics[†] 1. Inconsistent presentation (bilateral distribution, well demarcated chronic to subacute progression, etc.) 2. Symptoms improved with leg elevation without use of antibiotics 3. Symptoms not improved with antibiotics Patient Instructions • Elevate infected area above the level of the heart to reduce redness & swelling • Keep infected area clean & dry • Call your doctor if symptoms have not improved after 72h OR if fever or other symptoms develop
PURULENT INFECTIONS **Furuncle**	Staphylococcus aureus	I&D + Antibiotics Preferred:	5 Days After I&D	1. Tailor antibiotic therapy to results of gram stain, culture

Infection of a hair follicle extending to dermis with small 'boil' **Carbuncle** Infection of several follicles leading to coalescing mass **Abscess** Cutaneous collection of pus within dermis and deeper skin layers	MSSA & MRSA	TMP-SMX 1-2 DS tab PO BID OR Doxycycline 100mg PO BID Clindamycin is not preferred therapy due to decreased susceptibility rates		and susceptibilities from I&D 2. S. aureus susceptibility rates are 99% for TMP-SMX and 93% for doxycycline <u>When to Consider Admission</u> • ≥2 SIRS criteria* • Hypotension • Rapid disease progression • Clinical signs of deeper infection (bullae, skin sloughing, organ dysfunction)
*fever ≥38 or <36 C, tachycardia >90 bpm, RR> 20 bpm leukocytosis >12k cells/μL †Consider Dermatology Consult for evaluation of cellulitis mimics such as stasis dermatitis, lipodermatosclerosis, contact dermatitis, lymphedema # Clinically significant IgE or T lymphocyte mediated β-lactam allergies are extremely rare (<5%)				

Table 8. Antimicrobial Drug Dosing in Renal Impairment (SHC 2022 Guideline)

Antimicrobial Drug	CrCl > 30 mL/min*	CrCl 15-30 mL/min*	CrCl < 15 mL/min*	Intermittent Hemodialysis (thrice weekly dialysis)
Cephalexin (PO)	500mg q6h OR 1g q8h	500mg q8-12h	500mg q24h	500mg q24h (dosed after HD on HD days)
Clindamycin (PO)	450mg q6h	450mg q6h	450mg q6h	450mg q6h
TMP-SMX (PO) **SS = single strength (80mg of TMP)** **DS = double strength (160mg of TMP)**	1-2 DS tablets BID	Administer 50% of recommended dose	Administer 25-50% of usual dose - Use with caution and close monitoring	Administer 25-50% of recommended dose
Doxycycline (PO)	100mg q12h	100mg q12h	100mg q12h	100mg q12h
*Creatinine clearance (CrCl) is calculated via the Cockcroft-Gault Method				

1.2.5 C.S Mott Children's Hospital Michigan Medicine– Empiric Antibiotic Guidelines for Skin and Soft Tissue Infections in Patients on Pediatric Services (2023)

This guideline is designed to provide guidance in pediatric patients with a primary skin and soft tissue infection (SSTI). Management of skin and soft tissue infections in patients < 2 months of age or those presenting with sepsis or septic shock not related to necrotizing fasciitis is beyond the scope of these guidelines[9].

Table 9 summarizes all treatment recommendations:

Table 9. Empiric Antibiotic Recommendations for Skin and Soft Tissue Infections in Pediatric Population

Setting	Empiric Therapy	Duration/Comments
Minor Skin Infections • Localized impetigo (non-bullous or bullous) • Secondarily infected skin lesions such eczema, ulcers, or lacerations • Folliculitis (small follicular abscess in epidermis) Topical therapy: Generally preferred over oral therapy *Oral therapy:* Indicated instead of topical therapy for patients with numerous impetigo lesions or in outbreak settings to reduce transmission *Target Pathogens*: *Staphylococcus aureus, group A Streptococcus*	Topical Therapy **Mupirocin** 2% topical ointment applied BID Oral Therapy *1st line:* **Cephalexin** 25 mg/kg/DOSE PO TID (max: 1 g/DOSE) *If MRSA risk factors present[1] or allergy that precludes cephalexin use:* **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) Alternative to TMP-SMX if sulfa allergy: **Clindamycin** 10 mg/kg/DOSE PO TID (max: 450 mg/DOSE)	Duration: 5 days S. aureus isolates from impetigo are commonly methicillin susceptible (MSSA). Michigan Medicine S. aureus resistance rates are low for TMP-SMX (2%), compared to clindamycin (19% for MSSA and 25% for methicillin-resistant S. aureus [MRSA] in 2022). If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX).
Non-Purulent Cellulitis Absence of purulent drainage or exudate, ulceration, and no associated abscess. Includes erysipelas. *Target Pathogens: Group A Streptococcus, Staphylococcus aureus (the role of community-acquired MRSA is unknown)*	Outpatient or Step-down (from IV to PO) Therapy: *1st line:* **Cephalexin** 25 mg/kg/DOSE PO TID (max: 1 g/DOSE) *If MRSA risk factors present[1] or allergy that precludes cephalexin use*: **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) Alternative to TMP-SMX if sulfa allergy: **Clindamycin**	Duration: 5 days May extend therapy up to 7-10 days if lack of symptom resolution at 5 days. Cephalexin and cefazolin provide coverage for group A Streptococcus and MSSA. TMP-SMX provides adequate coverage for group A Streptococcus, MSSA, and MRSA. If worsening or not improving after 48 hours of oral cephalexin therapy,

	10 mg/kg/DOSE PO TID (max: 450 mg/DOSE) **OR** **Linezolid** PO: ▪ <12 years: 10 mg/kg/DOSE TID (max: 600 mg/DOSE) ▪ ≥12 years: 10 mg/kg/DOSE BID (max: 600 mg/DOSE) <u>Inpatient (IV) Therapy</u> *1st Line*: **Cefazolin** 33 mg/kg/DOSE IV q8h (max: 2 g/DOSE) *Alternative if MRSA risk factors present1or allergy that precludes cefazolin use* **Vancomycin** IV	consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX or linezolid). Linezolid suspension may not be readily available at all community pharmacies. Some insurance companies (including state Medicaid) may require prior authorization.
<u>Purulent Cellulitis or Abscesses including Folliculitis, Furuncles, Carbuncles</u> *Abscess*: Collection of pus within the dermis and deeper skin tissues *Furuncle*: Infection of the hair follicle with suppuration extending through the dermis into subcutaneous tissue *Carbuncle*: Confluence of furuncles with wider infiltration *Target Pathogen:* *Staphylococcus aureus (including MRSA)*	<u>Incision and drainage (I&D) is recommended as primary management for abscesses. Antibiotics** are (at a minimum) recommended if patient meets one of the following criteria:</u> • Substantial surrounding cellulitis • Abscess >2 cm in diameter; >1 cm in infants and young children • Inability to adequately drain the abscess • Signs or symptoms of systemic illness (e.g., fever ≥38°C)	Duration: 5 days May extend therapy up to 7-10 days if lack of symptom resolution at 5 days. Cultures and susceptibilities are recommended when I&D is performed. Blood cultures are also recommended for patients with fever, rapidly progressive cellulitis, and systemic illness. Michigan Medicine S. aureus resistance rates are low for TMP-SMX (2%) and doxycycline (3%), compared to clindamycin (19% for

	• Immunodeficiency • Multiple sites <u>Outpatient Therapy or Step-down (from IV to PO) Therapy</u> *1st Line:* **TMP-SMX**, 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) *Alternative for sulfa allergy:* **Doxycycline** 2.2 mg/kg/DOSE PO BID (max: 100 mg/DOSE) <u>Inpatient (IV) Therapy</u> *1st Line:* **Vancomycin** IV *Alternative for vancomycin allergy (not vancomycin infusion reaction):* **Linezolid** PO/IV (PO preferred): ▪ <12 years: 10 mg/kg/DOSE TID (max: 600 mg/DOSE) ▪ ≥12 years: 10 mg/kg/DOSE BID (max: 600 mg/DOSE)	methicillin-susceptible S. aureus [MSSA] and 25% for methicillin-resistant S. aureus [MRSA] in 2022). Tailor antibiotic therapy to results of Gram stain, culture, and sensitivities. **Although ~70% of abscesses may resolve with I&D alone, an additional 10% are more likely to resolve with the addition of antibiotics. Clinical context should be taken into account when deciding if antibiotics are appropriate. Linezolid suspension may not be readily available at all community pharmacies. Some insurance companies (state Medicaid) may require prior authorization.
<u>Staphylococcal Scalded Skin Syndrome (SSSS)</u> Results in loss of keratinocyte cell adhesion and leads to blistering of upper layer of the skin. Pediatric Infectious Diseases consultation is recommended. Consider	<u>1st Line:</u> **Cefazolin** 33 mg/kg/DOSE IV q8h (max: 2 g/DOSE) + **Linezolid** PO/IV (PO preferred): ▪ <12 years: 10 mg/kg/DOSE TID (max: 600 mg/DOSE) ▪ ≥12 years: 10	Duration: 10 days Consider discontinuing linezolid when patient is clinically stable (e.g., vital signs within normal limits, no vasopressor requirements) for 24-48 hours and rash no longer progressing (usual duration

Dermatology consult if diagnosis is unclear or specific skin care recommendations are needed *Common pathogens: Staphylococcus aureus (MSSA predominantly reported in the literature)*	mg/kg/DOSE BID (max: 600 mg/DOSE Step-down (from IV to PO) Therapy *1st Line*: **Cephalexin** 25 mg/kg/DOSE PO TID (max: 1 g/DOSE) *Alternative if MRSA risk factors present or allergy that precludes cephalexin use*: **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE)	of 3-5 days). Staphylococcal Scalded Skin Syndrome (SSSS) is usually diagnosed in children <5 years of age.
Necrotizing Fasciitis Early and aggressive surgical exploration and debridement is critical. Emergent surgical consultation and ID consult are strongly recommended. *Common pathogens: Group A β-hemolytic Streptococcus, S. aureus, E. coli, Pseudomonas spp., Enterobacter spp., Klebsiella spp., Proteus spp., Bacteroides spp., Clostridia spp., Peptostreptococcus spp.*	1st Line: **Piperacillin-tazobactam** 75 mg of piperacillin/kg/DOSE IV q6h (max: 4 g piperacillin/DOSE) extended infusion + **Vancomycin** IV + **Clindamycin** 13 mg/kg/DOSE IV q8h (max: 900 mg/DOSE) Alternative for low-risk allergy to penicillins: **Cefepime** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) extended infusion + **Vancomycin** IV + **Clindamycin** 13 mg/kg/DOSE IV q8h (max: 900 mg/DOSE) **ADD Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) TID (max: 500 mg/DOSE) if perineum or groin involved	Duration: Empiric antibiotics should be continued until the following criteria are met: ▪ Debridement no longer needed, ▪ Clinical improvement, and ▪ Minimum of 48-72 hours after completion of surgical debridement Clindamycin is initiated for anti-toxin activity for Streptococcal and Staphylococcal infections and can be stopped after 24-72 hours if infection has improved and patient is stable. Tailor antibiotic therapy to results of deep tissue Gram stain, culture, and

	Alternative for allergy that precludes use of both piperacillin-tazobactam and cefepime: REPLACE cefepime with **Aztreonam** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) <u>Alternative for vancomycin allergy (not vancomycin infusion reaction):</u> **Piperacillin-tazobactam** 75 mg of piperacillin/kg/DOSE IV q6h (max: 4 g piperacillin/DOSE) extended infusion + **Linezolid** PO/IV (PO preferred): ▪ <12 years: 10 mg/kg/DOSE TID (max: 600 mg/DOSE) ▪ ≥12 years: 10 mg/kg/DOSE BID (max: 600 mg/DOSE)	sensitivities. Linezolid has in-vitro data that demonstrates suppression of toxin production with S. aureus and group A streptococcus. Clinical success against toxic shock syndrome is reported in case reports.
Traumatic Wound Infections WITHOUT Water Exposure Usually polymicrobial from environmental contamination. See section above if concern for necrotizing fasciitis. For animal/human bites, refer to Animal Bite Guidelines on antimicrobial stewardship webpage. Evaluate tetanus immunization status, and if indicated, administer tetanus immunization +/-	Traumatic wounds without evidence of local infection or systemic signs of infection typically do not need antimicrobial therapy. <u>Outpatient (PO) Therapy</u> *1st Line*: **Amoxicillin-clavulanate** 25 mg amoxicillin/kg/DOSE PO BID (max: 875 mg amoxicillin/DOSE) ▪ 7:1 formulation is recommended (400/57/ 5ml or 200/28.5/5 ml) If MRSA risk factors present[1]	Duration: 7 days Therapy may need to be extended based on severity of infection and response to treatment. Consider Pediatric ID consult for infections that are deep, extensive or respond slowly Debridement of devitalized tissues and contaminating debris is critical to source control and successful healing. Empiric therapy should take

tetanus immune globulin. Target pathogens: Staphylococcus aureus, Clostridia spp., Bacteroides spp., Prevotella spp., Porphyromonas spp., Peptostreptococcus spp.	ADD **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) *Alternative for low-risk allergy[5] to penicillins*: **Cephalexin** 25 mg/kg/DOSE PO TID (max: 1 g/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO TID (max: 500 mg/DOSE) *Alternative for allergy that precludes use of both amoxicillin-clavulanate and cephalexin:* **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO TID (max: 500 mg/DOSE) <u>Inpatient (IV) Therapy</u> *1st Line:* **Ampicillin-sulbactam** 50 mg of ampicillin/kg/DOSE IV q6h (max: 2 g ampicillin/DOSE) *Alternative for low-risk allergy[5] to penicillins*: **Cefazolin** 33 mg/kg/DOSE IV q8h (max: 2 g/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) TID (max: 500 mg/DOSE)	into account site of wound and prior cultures and colonization. Tailor antibiotic therapy to results of deep tissue Gram stain, culture, and sensitivities.

	Alternative if MRSA risk factors present[1], or allergy that precludes use of both ampicillin-sulbactam and cefazolin: **Vancomycin** IV + **Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) q8h (max: 500 mg/DOSE)	
<u>Traumatic Wound Infections WITH Water Exposure</u> Usually polymicrobial from environmental contamination. See section above if concern for necrotizing fasciitis. For animal/human bites, refer to Animal Bite Guidelines on antimicrobial stewardship webpage. Evaluate tetanus immunization status, and if indicated, administer tetanus immunization ± tetanus immune globulin. *Target pathogens:* *Staphylococcus aureus,* *Clostridia spp.,* *Bacteroides spp.,* *Prevotella spp.,* *Porphyromonas spp.,* *Peptostreptococcus spp.* Consider Aeromonas and Pseudomonas spp., other	<u>Outpatient (PO) Therapy:</u> **Levofloxacin** PO: ▪ <5 years: 10 mg/kg/DOSE PO BID (max: 375 mg/DOSE) ▪ ≥5 years: 10 mg/kg/DOSE PO daily (max: 750 mg/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO TID (max: 500 mg/dose) If MRSA risk factors present[1] ADD **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) <u>Inpatient (IV) Therapy</u>: *1st Line:* **Cefepime** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) extended infusion + **Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) q8h (max: 500 mg/DOSE) If MRSA risk factors present[1] ADD **Vancomycin** IV	Duration: 7 days Therapy may need to be extended based on severity of infection and response to treatment. Consider Pediatric ID consult for infections that are deep, extensive or respond slowly Debridement of devitalized tissues and contaminating debris is critical to source control and successful healing. Empiric therapy should take into account site of wound and prior cultures and colonization. Vibrio vulnificus wound infections require extensive debridement and mortality can be high. Consider combination therapy with ceftazidime and doxycycline. Tailor antibiotic therapy to

gram negatives if significant water exposure	*Alternative for allergy that precludes cefepime use:* **Levofloxacin** IV/PO (PO preferred): ▪ <5 years: 10 mg/kg/DOSE PO BID (max: 375 mg/DOSE) ▪ ≥5 years: 10 mg/kg/DOSE PO daily (max: 750 mg/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO/IV TID (PO preferred) (max: 500 mg/DOSE) If MRSA risk factors present1 ADD **Vancomycin** IV	results of deep tissue Gram stain, culture, and sensitivities.

[1] Consider MRSA coverage if any of the following are present: severe sepsis or septic shock, immunocompromised status, personal or household contact with MRSA infection, or colonization in the past 12 months.

[5] Low-risk allergies include: pruritus without rash, remote (>10 years) unknown reaction, patient denies allergy but is on record, mild rash with no other symptoms (mild rash: non-urticarial rash that resolves without medical intervention).

1.2.6 WSES/GAIS/WSIS/SIS-E/AAST Global Clinical Pathways for Patients with Skin and Soft Tissue Infections (2022)

The World Society of Emergency Surgery (WSES), the Global Alliance for Infections in Surgery (GAIS), the Surgical Infection Society-Europe (SIS-E), The World Surgical Infection Society (WSIS), and the American Association for the Surgery of Trauma (AAST) have jointly completed an international multi-society document to promote global standards of care in SSTIs guiding clinicians by describing reasonable approaches to the management of SSTIs[6].

- SSTIs were divided in four classes:
    - Class 1 patients with SSTI, but no signs or symptoms of systemic toxicity or co-morbidities.
    - Class 2 patients are either systemically unwell with stable co-morbidities or systemically well, but with comorbidity (e.g., diabetes, obesity) that may complicate or delay resolution.
    - Class 3 patients appear toxic and unwell (fever, tachycardia, tachypnoea, and/or hypotension).
    - Class 4 patients have sepsis syndrome and life-threatening infection: for example, necrotizing fasciitis.
- Antibiotics recommended for MRSA infections are listed below.
    - Oral options:
        - Minocycline 100 mg every 12 h
        - Trimethoprim and sulfamethoxazole 160/800 or320/1600 every 12 h
        - Doxycycline 100 mg every 12 h
        - Clindamycin 300–450 mg every 8 h (high resistance rate)
        - Linezolid 600 mg every 12 h
        - Tedizolid 200 mg every 24 h
    - Intravenous options:
        - Clindamycin 600–900 mg every 8 h
        - Trimethoprim and sulfamethoxazole 320/1600 every 12 h
        - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h
        - Tigecycline 100 mg IV as a single dose, then 50 mg IV every 12 h

        - Linezolid 600 mg every 12 h
        - Daptomycin 6 mg/kg every 24 h
        - Ceftaroline 600 mg every 12 h
        - Dalbavancin 1000 mg once followed by 500 mg after 1 week or 1500 mg one dose
        - Tedizolid 200 mg every 24 h
        - Telavancin 10 mg/kg every 24 h

- Treatment of simple abscess:
    - Incision and drainage
    - Antibiotic therapy only in selected patients for 5 days. You may extend therapy up to 7–10 days if lack of symptom resolution at 5 days.
    - **Empiric antibiotic regimens. Normal renal function - Target Pathogens: S.aureus and streptococci - One of the following oral antibiotics**
        - Amoxicillin-clavulanate 1 g every 8 h
        - Cephalexin 500 mg every 6 h
        - In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to firstline therapy add one of the following oral antibiotics
            - Minocycline 100 mg every 12 h
            - Doxycycline 100 mg every 12 h
            - Trimethoprim and Sulfamethoxazole 160/800 mg every 12 h

          Or
        - **In patients with beta-lactam allergy:** Clindamycin 300 mg every 8 h
    - A recurrent abscess at a site of previous infection may be caused by local causes such as a pilonidal cyst, hidradenitis suppurativa, or foreign material. Therefore, it always requires research of a local cause.
    - In cases of recurrent skin abscess, it is necessary to look for the presence of foreign materials and identify and correct local factors that may cause recurring infection.

- For recurrent skin abscess bacterial culture testing should be performed to verify the causative bacteria and antibiotics susceptibility to define a targeted therapy. If an abscess is treated with prolonged antibiotics without drainage, it can lead to formation of sterile pus surrounded by thick fibrous tissue. It makes a hard lump that sometimes mimics malignancy. The treatment is surgical drainage with excision of fibrous wall.

- Treatment of erysipelas:
  - Erysipelas is distinguished clinically from cellulitis by the following two features:
    - In erysipelas the lesions are raised above the level of the surrounding skin, and
    - Erysipelas is characterized by a clear line of demarcation between involved and uninvolved tissue.
  - Streptococci are the primary cause. The role of S. aureus, and specifically MRSA, remains controversial.
  - Treatment is with antibiotic therapy for 5 days. Duration may be extended up to 10 days if lack of symptom resolution at 5 days.
  - Use intravenous antibiotics if signs of systemic inflammation.
  - **Empiric antibiotic regimens. Normal renal function - Target Pathogens: S. aureus and streptococci, CA- MRSA is unusual -** Outpatient therapy or step down, One of the following oral antibiotics:
    - Amoxicillin-clavulanate 1 g every 8 h
    - Cephalexin 500 mg every 6 h
    - In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to firstline therapy add one of the following oral antibiotics
      - Trimethoprim and sulfamethoxazole 160/800– 320/1600 mg every 12 h
      - Minocycline 100 mg every 12 h
      - Doxycycline 100 mg every 12 h

Or

- **In patients with beta-lactam allergy:** Clindamycin 300 mg every 8 h

- **Inpatient therapy -** One of following intravenous antibiotics
  - Cefazolin 2 g every 8 h
  - Amoxicillin-clavulanate 1.2/2.2 gr every 8 h
- **In patients at risk for CA-MRSA including critically ill and immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to first-line therapy add one of following intravenous antibiotics**
  - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h
  - Linezolid 600 mg every 12 h

- Treatment of cellulitis:
  - Treatment with antibiotic therapy for 5 days. Duration may be extended up to 7-10 days if lack of symptoms resolution at 5 days.
  - Incision and drainage in purulent cellulitis
  - **Typical (non-purulent) cellulitis - Empiric antibiotic regimens. Normal renal function –** Target Pathogens: S. aureus and streptococci, CA-MRSA is unusual – Outpatient therapy or step-down, one of the following oral antibiotics:
    - Amoxicillin-clavulanate 1 g every 8 h
    - Cephalexin 500 mg every 6 h
    - In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days, with cellulitis associated with penetrating trauma especially from illicit drug use or who do not respond to first-line therapy add one of the following oral antibiotics:
      - Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h
      - Minocycline 100 mg every 12 h

- Doxycycline 100 mg every 12 h

Or

- **In patients with beta-lactam allergy:** Clindamycin 300 mg every 8 h

- **Inpatient therapy,** one of following intravenous antibiotics:
  - Cefazolin 2 g every 8 h
  - Amoxicillin-clavulanate 1.2/2.2 gr every 8 h
- **In patients at risk for CA-MRSA including critically ill and immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days, with cellulitis associated with penetrating trauma especially from illicit drug use or who do not respond to first-line therapy one of the following intravenous antibiotics**
  - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h
  - Linezolid 600 mg every 12 h
- **In patients at risk for Gram-negative infections or severe forms who do not respond to first-line therapy**
  - Consider Piperacillin/tazobactam 4,5 g every 6 h.

- Purulent cellulitis
  - Incision and drainage are recommended as primary management for abscesses with associated cellulitis. In these cases, antibiotics is generally suggested.
  - **Empiric antibiotic regimens. Normal renal function - Target Pathogen: S. aureus including CA-MRSA - Outpatient therapy or step-down, one of the following oral antibiotics**
    - Amoxicillin-clavulanate 1 g every 8 h
    - Cephalexin 500 mg every 6 h

    Or
  - **In a region or a population with a high prevalence of CA-MRSA, where > 10% of clinical S. aureus isolates are MRSA isolates or in patients at high risk for CA-MRSA**
    - Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h

        - Minocycline 100 mg every 12 h
        - Doxycycline 100 mg every 12 h

      Or

    - **Inpatient therapy,** one of the following intravenous antibiotics
        - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h
        - Linezolid 600 mg every 12 h
    - **In patients at risk for Gram-negative infections or severe forms who do not respond to first-line therapy**
        - Consider Piperacillin/tazobactam 4,5 g every 6 h.
    - In neutropenic and immunocompromised patients, Gram-negative bacteria should be considered.

- Treatment of perianal and perirectal abscesses:
    - Incision and drainage + antibiotic therapy for 5 days in selected patients. You may extend therapy up to 7–10 days if lack of symptom resolution at 5 days.
    - In perianal and perirectal abscesses identification of eventual fistula tract, and either proceed with primary fistulotomy to prevent recurrence (only in cases of low fistula not involving the sphincter muscle) or place a draining seton for future consideration. Fistulotomy can risk continence if too extensive and placement of seton should only be performed if the tract and openings are very clear, as there is risk of creating a false internal orifice and complicating the condition.
    - **Empiric antibiotic regimens. Normal renal function - Target Pathogen: Gram-positive and Gram-negative - Outpatient therapy or step-down, one of the following antibiotics**
        - Amoxicillin/clavulanate 1 g every 8 h

      Or

    - **In patients with beta-lactam allergy**
        - Ciprofloxacin 500 mg every 8 h + Metronidazole 500 mg every 8 h
    - **In patients at risk for CA-MRSA or who do not respond to first-line therapy add one of following oral antibiotics**
        - Minocycline 100 mg every 12 h

        - Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h
        - Doxycycline 100 mg every 12 h

    Or

    - **Inpatient therapy -** One of following intravenous antibiotics
        - Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h
        - Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h
        - Piperacillin/tazobactam 4,5 g every 6 h

    Or

    - **In patients with beta-lactam allergy**
        - Ciprofloxacin 400 mg every 8 h + Metronidazole 500 mg every 8 h
    - **In patients at risk for CA-MRSA or who do not respond to first-line therapy add one of following intravenous antibiotics**
        - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h
        - Linezolid 600 mg every 12 h
- Treatment of bite wounds (animal and human bites)
    - Irrigation of the wound and debridement of necrotic tissue
    - Antibiotic prophylaxis as principle is not recommended. It is recommended in selected patients.
    - Antibiotic therapy in selected patients for 5 days. The duration may be extended up to 7–10 days if there is a lack of symptom resolution at 5 days.
    - Tetanus prophylaxis in bite wounds
- Treatment of pressure ulcers:
    - Prevention by pressure redistribution devices such as high-specification foam mattresses or cushions, or both and by frequent patient repositioning
    - Debridement of devitalized tissue and biofilm and abscess drainage
    - Appropriate selection of dressings and topical agents
    - Routine use of systemic antibiotics is not currently recommended for the treatment of uninfected pressure ulcers. Systemic antibiotics

should be administered only when there are systemic signs of inflammation (serious infection), spreading cellulitis (deep skin infection) or underlying osteomyelitis.

- Medical and nutritional patient optimization.

- Treatment of burn wounds:
  - Early initiation of dressings and effective topical antimicrobial therapy
  - Daily inspection of the wounds by a qualified surgeon or wound care expert
  - Early excision of all full thickness and deep partial thickness burns
  - Systemic antibiotic for infected wounds
  - Graft and coverage options
  - **Empiric antibiotic regimens. Normal renal function - Target Pathogen: Gram-positive and Gram-negative - Outpatient therapy or step-down, one of the following antibiotics**
    - Amoxicillin/clavulanate 1 g every 8 h

    Or
  - **In patients with beta-lactam allergy**
    - Ciprofloxacin 500 mg every 12 h + Metronidazole 500 mg every 8 h
  - *First-generation cephalosporins, such as cephalexin, penicillinase-resistant penicillins, macrolides such as erythromycin, and clindamycin, all have poor in vitro activity against Pasteurella multocida and should be avoided in animal bites.*
  - **In patients at risk for CA-MRSA or who do not respond to first-line therapy add - One of following oral antibiotics**
    - Minocycline 100 mg every 12 h
    - Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h
    - Doxycycline 100 mg every 12 h

    Or
  - **Inpatient therapy, one of following intravenous antibiotics**
    - Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h
    - Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h

        - Piperacillin/tazobactam 4,5 g every 6 h

    Or

    - **In patients with beta-lactam allergy**
        - Ciprofloxacin 200 mg every 8 h + Metronidazole 500 mg every 8 h
    - **In patients at risk for CA-MRSA or who do not respond to first-line therapy add**
        - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h
        - Linezolid 600 mg every 12 h

- Treatment of necrotizing fasciitis:
    - Surgical source control as soon as possible within 6 h after admission. Delay in early surgical increases mortality.
    - Appropriate and effective debridement techniques. Skin-sparing debridement techniques focusing on tissue directly involved in necrosis.
    - Re-explorations should be repeated until the time when very little or no debridement is required.
    - Empiric antibiotic therapy optimizing Pharmacokinetics (PK) and Pharmacodynamics (PD) targets.
    - Deep samples collected at the interface between healthy and necrotized tissues during initial debridement and blood cultures allow the identification of causative pathogens in most cases.
    - De-escalation of antibiotic therapy be based on clinical improvement, cultured pathogens, and results of rapid diagnostic tests where available.
    - (Organ) supportive measures
    - Hyperbaric oxygen therapy where it is available.
    - Intravenous immunoglobulin (IVIG) in patients with streptococcal NSTIs
- Wound management after source control:
    - Empiric antibiotic regimens. Normal renal function - The initial empirical antibiotic regimen should comprise broad-spectrum drugs, including anti-MRSA and anti-Gram-negative coverage. Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs.

- **In stable patients,** one of the following antibiotics
    - Amoxicillin/clavulanate 1.2/2.2 g every 8 h
    - Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h
    - Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h

      +
    - Clindamycin 600–900 mg every 8 h
- **In unstable patients,** one of the following antibiotics
    - Piperacillin/tazobactam 4.5 g every 6 h
    - Meropenem 1 g every 8 h
    - Imipenem/Cilastatin 500 mg every 6 h

      + One of the following antibiotics
    - Linezolid 600 mg every 12 h
    - Tedizolid 200 mg every 24 h

      Or another anti-MRSA-antibiotic as
    - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 8 h
    - Daptomycin 6–8 mg/kg every 24 h *
    - Telavancin 10 mg/kg every 24 h

      +
    - Clindamycin 600–900 mg every 8 h

      *Approved at the dosage of 4–6 mg/kg/24 h, it is currently used at higher dosages.

- Fournier's gangrene:
    - Surgical source control as soon as possible. Re-explorations should be repeated until the time when very little or no debridement is required.
    - Diverting colostomy or rectal diversion devices
    - Antibiotic therapy
    - (Organ) supportive measures
    - The initial empirical antibiotic regimen should comprise broad-spectrum drugs, including anti-MRSA and anti-Gram-negative coverage. Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs.

- **In stable patients, one of the following antibiotics**
  - Amoxicillin/clavulanate 1.2/2.2 g every 8 h
  - Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h
  - Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h

    +
  - Clindamycin 600–900 mg every 8 h
- **In unstable patients, one of the following antibiotics**
  - Piperacillin/tazobactam 4.5 g every 6 h
  - Meropenem 1 g every 8 h
  - Imipenem/Cilastatin 500 mg every 6 h

    + One of the following antibiotics
  - Linezolid 600 mg every 12 h
  - Tedizolid 200 mg every 24 h

    Or another anti-MRSA-antibiotic as
  - Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 8 h
  - Teicoplanin LD 12 mg/kg 12-hourly for 3 doses, then 6 mg/kg every 12 h
  - Daptomycin 6–8 mg/kg every 24 h *
  - Telavancin 10 mg/kg every 24 h

    +
  - Clindamycin 600–900 mg every 8 h

    *Approved at the dosage of 4 mg/kg/24 h, it is currently used at higher dosages.

- Water and soil-borne necrotizing fasciitis:
  - Most cases of A. hydrophila wound infection occur in healthy people. In particular, A. hydrophila wound infection is reported following natural disasters, such as the tsunami and hurricane. The wound infections due to A. hydrophila can progress rapidly to NSTIs.
  - Patients with a presumptive diagnosis of V. vulnificus should be treated immediately by antibiotics and managed aggressively by a prompt debridement and resuscitation in an intensive care unit to minimize

the possible consequences of hypotension, septic shock, and the risk of multiorgan system failure.

- Treatment of gas gangrene:
    - Because the infection is rapidly progressive, it is important to treat patients aggressively, by early surgical debridement, antibiotics, and intravenous fluid resuscitation.
- New agents to treat NSTIs:
    - Reltecimod (previously known as AB103 or p2TA), a peptide derived from the T-cell receptor CD28, modulates the host immune response by targeting the costimulatory pathway, which is essential for the induction of multiple pro-inflammatory cytokines.
    - Consequently, reltecimod has demonstrated beneficial effects against different bacterial infections such as NSTIs.
    - A randomized, double-blind, placebo-controlled trial of single dose reltecimod (0.5 mg/kg) administered within 6 h of NSTI diagnosis was recently published.
    - Reltecimod was associated with improved resolution of organ dysfunction and hospital discharge status.
    - Further studies are warranted to establish the real efficacy in clinical practice.
- Mesh infection:
    - The usual causative micro-organisms associated mesh infection are S. aureus including MRSA, S. epidermidis and streptococci and Gram-negative bacteria including Enterobacteriaceae.
    - The aim of the infection prevention and control strategies including surgical antibiotic prophylaxis is to minimize bacterial count in the wound and decrease adherence to the mesh preventing biofilm production; thereby blocking the key step for mesh infection.
    - The management of mesh infections is challenging and always requires an individualized approach combining medical and surgical approaches.
    - Although, several studies have demonstrated that in certain instances, non-operative strategies with conservative (non-surgical) management have been successful for salvaging a mesh in many cases complete surgical removal of the mesh is suggested to reduce the risk of infection recurrence or severe complications, such as visceral adhesions and fistulae.

- After removing the infected mesh, the intra-operative options are (a) no implant of a new mesh, (b) re-implantation of a new synthetic lightweight, microporous mesh, and (c) replacement of the infected synthetic by a biological mesh.

1.2.7 NHS Foundation Trust Guideline for Skin and Soft Tissue Infection Including Diabetic Foot Ulcer (2022)

The below recommendations (ungraded) are published by the NHS Foundation Trust Guideline 2022 for the management of bacterial skin and soft tissue infections[10]:

Management of cellulitis

- Mark area of redness on skin (this will help with review of clinical progress)
- Start empirical antibiotic as stated in table below.
- Consider switching to oral antibiotic with good clinical response.
- Review antibiotics at day 5, can extend if not fully resolved.
- The choice of antimicrobial therapy may be guided by:
    - History of presenting complaint
        - Acute or chronic
        - Circumstances surrounding the development of the skin & soft tissue infection (SSTI)
    - Significant past medical history:
        - Diabetes
        - Immunocompromised state
        - Similar presentation with SSTI previously, etc.
    - Recent antimicrobial history within the last one month
    - Previous or recent positive microbiology results

Management of necrotizing fasciitis

- Necrotizing fasciitis can be categorized into 2 groups:
    - **Type 1** is a mixed infection including anaerobes, gram negative organisms and gram-positive organisms. Mostly occurs in immunocompromised individuals. Typically occurs in the perineum and trunk, and

    - **Type 2** is mainly due to Group A streptococcus with or without Staphylococcus aureus. This is less common than the type 1. Typically occurs in the limbs and affects healthy individuals, with often associated history of trauma (usually minor).
- If necrotizing fasciitis is suspected the patient must be referred for IMMEDIATE review by a senior clinician, as this is a rapidly progressing, life threatening infection.
- Surgical exploration is essential to definitively establish the diagnosis from other entities, also in obtaining samples for culture to identify the pathogen involved and as part of treatment, which consist of wide debridement of skin, subcutaneous tissue, fascia, and any necrotic muscle, and may require multiple debridements. The use of antibiotics without debridement is associated with mortality rate approaching 100%.
- Discuss with microbiologist if the region involved includes the perineum, scrotum (as in Fournier's gangrene) or if there is risk of polymicrobial involvement.
- Blood cultures are positive in about 60% and 20% of type 2 and type 1 necrotizing fasciitis respectively.
- The table below lists the empirical antibiotic guide for skin and soft tissue infection:

Table 10. Empirical Antibiotic Guide for Skin and Soft Tissue Infection (NHS 2022 Guideline)

CLINICAL CONDITION	FIRST LINE	PENICILLIN ALLERGY	MRSA	Duration
Mild to moderate cellulitis	Oral Flucloxacillin 500mg -1g, 6 hourly	Oral Clarithromycin 500mg 12 hourly	**Use options in Penicillin allergy.** **If resistant** to Clarithromycin and Clindamycin, use: IV Vancomycin (refer to Trust policy for dosing) **OR** Oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring)	5-7 days **OR** until full resolution, whichever is later.
Moderate to severe cellulitis	IV Flucloxacillin 1-2g, 6 hourly	IV Clindamycin 600mg - 1.2g, 6 hourly		
Erysipelas and impetigo	Oral Flucloxacillin 500mg -1g, 6 hourly (consider IV if severe)	Oral Clarithromycin 500mg 12 hourly		
Necrotising fasciitis: Type 1	IV Piperacillin/tazobactam 4.5g 8 hourly **AND** IV Clindamycin 1.2g 6 hourly	IV Meropenem 1g 8 hourly **AND** IV Clindamycin 1.2g 6 hourly	**If resistant** to Clindamycin use: IV Meropenem 1g 8 hourly **AND** IV Linezolid 600mg 12 hourly	5-7 days **OR** until full resolution, whichever is later.
Necrotising fasciitis: Type 2	IV Benzylpenicillin 1.2 -2.4 gm 6 hourly **AND** IV Clindamycin 1.2g 6 hourly	**Non-severe allergy:** IV Ceftriaxone 1 - 2g 12 hourly **AND** IV Clindamycin 1.2g 6	**If resistant** to Clindamycin use: IV Ceftriaxone 1 – 2g 12 hourly **AND**	

		hourly **Penicillin anaphylaxis:** IV Ciprofloxacin 400mg 8 - 12 hourly **AND** IV Clindamycin 1.2g 6 hourly	IV Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring)	
	Consider administering IVIG for patients with Type 2 infections who are critically unwell			
Cellulitis associated with bite (e.g. Human, dog, cat)	IV Co-amoxiclav 1.2g, 8 hourly **OR** Oral Co-amoxiclav 625mg, 8 hourly if mild to moderate	Oral Ciprofloxacin 500mg, 12 hourly **AND** Oral Clindamycin 300mg-450mg, 6 hourly	**If resistant** to Clindamycin and Ciprofloxacin: Add oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring)	10 days
Cutaneous abscess (including Intravenous Drug Abuser)	IV Flucloxacillin 1-2g, 6 hourly **AND** Oral Metronidazole 400mg 8 hourly **OR** Oral Flucloxacillin 500mg-1g, 6 hourly **AND** Oral Metronidazole 400mg 8 hourly	**Non-severe allergy**: IV Cefuroxime 750mg -1.5g 8hrly **AND** Oral Metronidazole 400mg 8hrly **Penicillin anaphylaxis:** Oral Clindamycin 450mg 6hrly	Oral Clindamycin 450mg 6 hourly **If resistant to Clindamycin use:** Oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring)	5-7 days **OR** until full resolution, whichever is later.

			AND Oral Metronidazole 400mg 8 hourly	
Cellulitis associated with sea or fresh water contact	Oral Doxycycline 100mg 12 hourly **AND** IV Ceftazidime 2g 8 hourly	Oral Doxycycline 100mg 12 hourly **AND** Oral Ciprofloxacin 500mg, 12 hourly	**If resistant** to Doxycycline then use: Oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring) **AND** Oral Ciprofloxacin 500mg 12 hourly	5-7 days **OR** until full resolution, whichever is later.
Cellulitis associated with fish tank water exposure	Contact Microbiologist			
Orbital cellulitis	IV Ceftriaxone 1-2g, 12 hourly **AND** Oral Metronidazole 400mg 8 hourly	Contact Microbiologist	Add Linezolid 600mg 12 hourly IV/PO (Ensure no drug interactions. Requires weekly FBC monitoring)	10 days
Mild to moderate infected foot ulcer	IV Flucloxacillin 1-2g 6 hourly **AND** oral Metronidazole 400mg 8 hourly	IV Clindamycin 600mg 6 hourly (monotherapy) **OR** Oral Clarithromycin 500mg 12 hourly **AND** oral Metronidazole		5-7 days OR until full resolution, whichever is later Review antimicrobial

		400mg 8 hourly		choice with culture results. Surgical debridement is essential
Severe infected foot ulcer	IV Co-amoxiclav 1.2g 8 hourly **OR** Oral Co-amoxiclav 625mg 8 hourly **OR** treat according to culture and sensitivity	IV Clindamycin 600mg - 1.2gm 6 hourly **OR** Oral Clindamycin 450mg 6 hourly **OR** Treat according to culture and sensitivity		
Clinical evidence of osteomyelitis at site of foot ulcer (in mild to severe foot ulcer)	IV Flucloxacillin 1-2g 6 hourly **AND** oral Fusidic acid 500mg 8 hourly **OR** treat according to culture and sensitivity	IV Clindamycin 600mg – 1.2g 6 hourly **AND** oral Fusidic acid 500mg 8 hourly **OR** Treat according to culture and sensitivity		4-6 weeks
History of positive MRSA from foot ulcer swab/tissue sample (in mild to severe cases)	Oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring) **AND** Oral Metronidazole 400mg 8 hourly	Discuss with Microbiologist if patient cannot have any of first line treatment.		5-7 days **OR** until full resolution, whichever is later

➔ NOTE: Never use Fusidic acid on its own

1.2.8 National Institute for Health and Care Excellence (NICE) Antimicrobial Prescribing Guideline for Cellulitis and Erysipelas (2019)

This guideline sets out an antimicrobial prescribing strategy for adults, young people, children, and babies aged 72 hours and over with cellulitis and erysipelas[14].

The recommendations are listed below[14]:

- Offer an antibiotic for people with cellulitis or erysipelas. When choosing an antibiotic (see the recommendations on choice of antibiotic), take account of:
    - The severity of symptoms
    - The site of infection (for example, near the eyes or nose)
    - The risk of uncommon pathogens (for example, from a penetrating injury, after exposure to water-borne organisms, or an infection acquired outside the country)
    - Previous microbiological results from a swab
    - The person's methicillin-resistant Staphylococcus aureus (MRSA) status if known.
- Give oral antibiotics first line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.
- If intravenous antibiotics are given, review by 48 hours and consider switching to oral antibiotics if possible.
- Manage any underlying condition that may predispose to cellulitis or erysipelas.
- The tables below outline the antibiotic choice for cellulitis and erysipelas for adult and pediatric populations:

Table 11. Antibiotic Recommendations for Cellulitis and Erysipelas for Adults Aged 18 Years and Over (NICE 2019 Guideline)

Treatment	Antibiotic, dosage, and course length
First-choice antibiotic (give orally unless person unable to take oral or severely unwell)	**Flucloxacillin** (5 to 7 days): 500 mg to 1 g four times a day orally **or** 1 g to 2 g four times a day intravenously
Alternative first-choice antibiotics for penicillin allergy or if flucloxacillin is unsuitable (give orally unless person	**Clarithromycin** (5 to 7 days): 500 mg twice a day orally **or** 500 mg twice a day intravenously

unable to take oral or severely unwell)	**Erythromycin** (in pregnancy; 5 to 7 days): 500 mg four times a day orally **Doxycycline** (5 to 7 days in total): 200 mg on the first day then 100 mg once a day orally
First-choice antibiotic if infection is near the eyes or nose (consider seeking specialist advice; give orally unless person unable to take oral or severely unwell)	**Co-amoxiclav** (7 days): 500/125 mg three times a day orally **or** 1.2 g three times a day intravenously
Alternative first-choice antibiotics if infection is near the eyes or nose for penicillin allergy or if co-amoxiclav is unsuitable (consider seeking specialist advice; give orally unless person unable to take oral or severely unwell)	**Clarithromycin** (7 days): 500 mg twice a day orally **or** 500 mg twice a day intravenously **with Metronidazole** (7 days): 400 mg three times a day orally **or** 500 mg three times a day intravenously
Alternative choice antibiotics for severe infection	**Co-amoxiclav** (7 days): 500/125 mg three times a day orally **or** 1.2 g three times a day intravenously **Cefuroxime** (7 days): 750 mg to 1.5 g three or four times a day intravenously **Clindamycin** (7 days): 150 mg to 300 mg four times a day (can be increased to 450 mg four times a day) orally **or** 600 mg to 2.7 g daily intravenously in two to four divided doses, increased if necessary in life-threatening infection to 4.8 g daily (maximum per dose 1.2 g) **Ceftriaxone** (7 days; only for ambulatory care; other antibiotics may be appropriate based on microbiological results and specialist advice): 2 g once a day intravenously
Antibiotics to be added if methicillin-**resistant Staphylococcus aureus infection is suspected or confirmed (combination therapy with an antibiotic listed above; other antibiotics may be appropriate based**	**Vancomycin**: 15 mg/kg to 20 mg/kg two or three times a day intravenously (maximum 2 g per dose), adjusted according to serum vancomycin concentration **Teicoplanin**: Initially 6 mg/kg every 12

on microbiological results and specialist advice)	hours for three doses, then 6 mg/kg once a day intravenously **Linezolid** (if vancomycin or teicoplanin cannot be used; specialist use only): 600 mg twice a day orally or 600 mg twice a day intravenously
• A longer course length (up to 14 days in total) may be needed based on clinical assessment. However, skin does take some time to return to normal, and full resolution of symptoms at 5 to 7 days is not expected. • Infection around the eyes or the nose (the triangle from the bridge of the nose to the corners of the mouth, or immediately around the eyes including periorbital cellulitis) is of more concern because of risk of a serious intracranial complication. • Erythromycin is preferred if a macrolide is needed in pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms.	

Table 12. Antibiotic Recommendations for Cellulitis and Erysipelas for Children and Young People Under 18 Years (NICE 2019 Guideline)

Treatment	Antibiotic, dosage, and course length
Children under 1 month	Antibiotic choice based on specialist advice.
First-choice antibiotic for children aged 1 month and over (give orally unless person unable to take oral or severely unwell)	**Flucloxacillin** (5 to 7 days): 1 month to 1 year, 62.5 mg to 125 mg four times a day orally 2 years to 9 years, 125 mg to 250 mg four times a day orally 10 years to 17 years, 250 mg to 500 mg four times a day orally **or** 1 month to 17 years, 12.5 mg/kg to 25 mg/ kg four times a day intravenously (maximum 1 g four times a day)
Alternative first-choice antibiotics for penicillin allergy or if flucloxacillin unsuitable (give orally unless person unable to take oral or severely unwell)	**Co-amoxiclav** (not in penicillin allergy; 5 to 7 days): 1 month to 11 months, 0.25 ml/kg of 125/31 suspension three times a day orally (dose doubled in severe infection)

	1 year to 5 years, 0.25 ml/kg or 5 ml of 125/31 suspension three times a day orally (dose doubled in severe infection) 6 years to 11 years, 0.15 ml/kg or 5 ml of 250/ 62 suspension three times a day orally (dose doubled in severe infection) 12 years to 17 years, 250/125 mg or 500/125 mg three times a day orally **or** 1 month to 2 months, 30 mg/kg twice a day intravenously 3 months to 17 years, 30 mg/kg three times a day intravenously (maximum 1.2 g three times a day) **Clarithromycin** (5 to 7 days): 1 month to 11 years: under 8 kg, 7.5 mg/kg twice a day orally 8 kg to 11 kg, 62.5 mg twice a day orally 12 kg to 19 kg, 125 mg twice a day orally 20 kg to 29 kg, 187.5 mg twice a day orally 30 kg to 40 kg, 250 mg twice a day orally 12 years to 17 years, 250 mg to 500 mg twice a day orally **or** 1 month to 11 years, 7.5 mg/kg twice a day intravenously (maximum 500 mg per dose) 12 years to 17 years, 500 mg twice a day intravenously **Erythromycin** (in pregnancy; 5 to 7 days): 8 years to 17 years, 250 mg to 500 mg four times a day orally
First-choice antibiotic if infection near the eyes or nose (consider seeking specialist advice; give orally unless person unable to take oral or severely unwell)	**Co-amoxiclav** (7 days): 1 month to 11 months, 0.25 ml/kg of 125/31 suspension three times a day orally (dose doubled in severe infection) 1 year to 5 years, 0.25 ml/kg or 5 ml of 125/31 suspension three times a day orally (dose doubled in severe infection) 6 years to 11 years, 0.15 ml/kg or 5 ml of 250/ 62 suspension three times a day

	orally (dose doubled in severe infection) 12 years to 17 years, 250/125 mg or 500/ 125 mg three times a day orally **or** 1 month to 2 months, 30 mg/kg twice a day intravenously 3 months to 17 years, 30 mg/kg three times a day intravenously (maximum 1.2 g three times a day)
Alternative first-choice antibiotics if infection near the eyes or nose for penicillin allergy or if co-amoxiclav unsuitable (consider seeking specialist advice; give orally unless person unable to take oral or severely unwell)	Clarithromycin (7 days): 1 month to 11 years: under 8 kg, 7.5 mg/kg twice a day orally 8 kg to 11 kg, 62.5 mg twice a day orally 12 kg to 19 kg, 125 mg twice a day orally 20 kg to 29 kg, 187.5 mg twice a day orally 30 kg to 40 kg, 250 mg twice a day orally 12 years to 17 years, 250 mg to 500 mg twice a day orally **or** 1 month to 11 years, 7.5 mg/kg twice a day intravenously (maximum 500 mg per dose) 12 years to 17 years, 500 mg twice a day intravenously **with** (if anaerobes suspected) **Metronidazole** (7 days): 1 month, 7.5 mg/kg twice a day orally 2 months to 11 years, 7.5 mg/kg three times a day orally (maximum per dose 400 mg) 12 years to 17 years, 400 mg three times a day orally **or** 1 month, loading dose 15 mg/kg, then (after 8 hours) 7.5 mg/kg three times a day intravenously 2 months to 17 years, 7.5 mg/kg three times a day intravenously (maximum per dose 500 mg)
Alternative choice antibiotics for severe infection (other antibiotics may	**Co-amoxiclav** (7 days): 1 month to 11 months, 0.25 ml/kg of 125/31

be appropriate based on microbiological results and specialist advice)	suspension three times a day orally (dose can be doubled) 1 year to 5 years, 0.25 ml/kg or 5 ml of 125/31 suspension three times a day orally (dose can be doubled) 6 years to 11 years, 0.15 ml/kg or 5 ml of 250/ 62 suspension three times a day orally (dose can be doubled) 12 years to 17 years, 250/125 mg or 500/ 125 mg three times a day orally **or** 1 month to 2 months, 30 mg/kg twice a day intravenously 3 months to 17 years, 30 mg/kg three times a day intravenously (maximum 1.2 g three times a day) **Cefuroxime** (7 days): 1 month to 17 years, 20 mg/kg three times a day intravenously (maximum 750 mg per dose), can be increased to 50 mg/kg to 60 mg/kg three or four times a day intravenously (maximum 1.5 g per dose) **Clindamycin** (7 days): 1 month to 17 years, 3 mg/kg to 6 mg/kg four times a day orally (maximum per dose 450 mg) **or** 1 month to 17 years, 3.75 mg/kg to 6.25 mg/ kg four times a day intravenously, increased if necessary, in life-threatening infection to 10 mg/kg four times a day intravenously (maximum per dose 1.2 g); total daily dose may alternatively be given in three divided doses (maximum per dose 1.2 g)
Antibiotics to be added if methicillin resistant **Staphylococcus aureus infection is suspected or confirmed (combination therapy with an**	**Vancomycin**: 1 month to 11 years, 10 mg/kg to 15 mg/kg four times a day intravenously, adjusted according to serum vancomycin

antibiotic listed above; other antibiotics may be appropriate based on microbiological results and specialist advice)	concentration 12 years to 17 years, 15 mg/kg to 20 mg/kg two or three times a day intravenously (maximum 2 g per dose), adjusted according to serum vancomycin concentration **Teicoplanin**: 1 month, initially 16 mg/kg for one dose, then (after 24 hours) 8 mg/kg once a day intravenously 2 months to 11 years, initially 10 mg/kg every 12 hours for three doses, then 6 mg/kg to 10 mg/kg once a day intravenously 12 years to 17 years, initially 6 mg/kg every 12 hours for three doses, then 6 mg/kg once a day intravenously **Linezolid** (if vancomycin or teicoplanin cannot be used; specialist use only): 1 month to 11 years, 10 mg/kg three times a day orally (maximum 600 mg per dose) 12 years to 17 years, 600 mg twice a day orally or 1 month to 11 years, 10 mg/kg three times a day intravenously (maximum 600 mg per dose) 12 years to 17 years, 600 mg twice a day intravenously. In September 2019, the use of linezolid in children and young people under 18 years was off label.

- Give oral antibiotics first line if the person can take oral medicines, and the severity of their symptoms does not warrant intravenous antibiotics. If intravenous antibiotics are given, review by 48 hours and consider switching to oral antibiotics, if possible.
- A longer course length (up to 14 days in total) may be needed based on clinical assessment. However, skin does take some time to return to normal, and full resolution of symptoms at 5 to 7 days is not expected.
- If flucloxacillin oral solution is not tolerated because of poor palatability, consider capsules.

- Co-amoxiclav 400/57 suspension may also be considered to allow twice daily dosing.
- Infection around the eyes or the nose (the triangle from the bridge of the nose to the corners of the mouth, or immediately around the eyes including periorbital cellulitis) is of more concern because of risk of a serious intracranial complication.
- Erythromycin is preferred if a macrolide is needed in pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms

- Preventing recurrent cellulitis or erysipelas:
    - Do not routinely offer antibiotic prophylaxis to prevent recurrent cellulitis or erysipelas.
    - For adults who have had treatment in hospital, or under specialist advice, for at least 2 separate episodes of cellulitis or erysipelas in the previous 12 months, specialists may consider a trial of antibiotic prophylaxis. Involve the person in a shared decision by discussing and taking account of:
        - The severity and frequency of previous symptoms
        - The risk of developing complications
        - Underlying conditions (such as oedema, diabetes, or venous insufficiency) and their management
        - The risk of resistance with long-term antibiotic use
        - The person's preference for antibiotic use.
    - When choosing an antibiotic for prophylaxis, take account of any previous microbiological results and previous antibiotic use.
    - Review antibiotic prophylaxis for recurrent cellulitis or erysipelas at least every 6 months. The review should include:
        - Assessing the success of prophylaxis
        - Discussing continuing, stopping, or changing prophylaxis (taking into account the person's preferences for antibiotic use and the risk of antimicrobial resistance)
        - Stop or change the prophylactic antibiotic to an alternative if cellulitis or erysipelas recurs
    - The table below outlines the choice of antibiotic prophylaxis for adults 18 years and over:

Table 13. Choice of Antibiotic Prophylaxis for Adults 18 Years and Over (NICE 2019 Guideline)

Prophylaxis	Antibiotic and dosage
First choice Choose antibiotics according to recent microbiological results when possible, and avoid using the same antibiotic for treatment and prophylaxis	**Phenoxymethylpenicillin**: 250 mg orally twice a day
Alternative first choice for penicillin allergy Choose antibiotics according to recent microbiological results when possible, and avoid using the same antibiotic for treatment and prophylaxis	**Erythromycin**: 250 mg orally twice a day

Section 2.0 Drug Therapy in Bacterial Skin Infections

This section comprises three subsections: the first one contains the newly recommended drugs, the second one covers drug modifications, and the third one outlines the drugs that have been withdrawn from the market.

2.1 Additions

Table 14 lists the added SFDA-registered drugs to the Bacterial Skin Infections drug summary spreadsheet. These drugs are recommended by the previously mentioned guidelines for the treatment of Bacterial Skin Infections.

Table 14. List of Added SFDA-Registered Drugs to the Bacterial Skin Infections Drug Summary Spreadsheet

Drug	Recommendation and Prescribing Edits
Azithromycin	**ST**: In extensive non bullous impetigo (more than 5 lesions or impetigo involving more than one skin area), bullous impetigo, ecthyma, impetigo with abscess; immunocompromised patient; or topical treatment failure AND In penicillin-allergic patients only (resistance to macrolides is common), azithromycin PO for 3 days (children: 10 mg/kg once daily; adults: 500 mg once daily).
Cefuroxime	In Cutaneous abscess (including Intravenous Drug Abuser) and non-severe allergy IV cefuroxime is recommended in combination with oral metronidazole
Minocycline	One of the oral option for MRSA infected SSTIs: In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to first-line therapy or in a region or a population with a high prevalence of CA-MRSA, where > 10% of clinical S. aureus isolates are MRSA isolates
Tigecycline	One of the intravenous options for MRSA infected SSTIs: In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to first-line

	therapy or in a region or a population with a high prevalence of CA-MRSA, where > 10% of clinical S. aureus isolates are MRSA isolates
Telavancin	One of the intravenous options for MRSA infected SSTIs
Teicoplanin	One of the intravenous/intramuscular options for MRSA infected SSTIs

2.2 Modifications

Below are the modifications made to the list of Bacterial Skin Infections drugs since the CHI report in April 2020, reflecting the changes and updates:

Table 15. Prescribing Edits (PE) Modifications of Certain Bacterial Skin Infections Drugs

Drugs	PE Modifications
Amoxicillin/ Clavulanic acid	**ST**: oral antibiotic therapy; treatment for ecthyma should be an oral antimicrobial, but the treatment of bullous and non-bullous impetigo should be with either mupirocin or retapamulin topically for patients with limited number of lesions, oral therapy is recommended only for patients with numerous lesions or in outbreaks affecting several people. indicated as first line outpatient therapy in mammalian bites (infected/prophylactic), and animal/human bites. can also be used as preferred systemic therapy for simple abscess, furuncle of the face, multiple furuncles, carbuncles or in immunocompromised patients or outpatient therapy for children with erysipelas and mild cellulitis, along with cefalexin. This drug is also recommended as inpatient therapy for the treatment of erysipelas and cellulitis, along with cloxacillin and cefazolin. It is also the preferred outpatient therapy for treatment of perianal and perirectal abscesses and burn wounds. amox/clav is indicated as one of the preferred line therapies along with clindamycin for stable patients with fournier's gangrene. **CU**: amox/clav is indicated as one of the preferred line therapies along with clindamycin for stable patients with fournier's gangrene. it can also be used with other antibiotics in case of risk of CA-MRSA or who do not respond to first-line

	therapy.
Ampicillin/ sulbactam	**PA and CU were removed** **ST**: ampicillin/sulbactam is recommended as first line IV therapy for traumatic wound infections without water exposure
Benzathine penicillin	**ST:** This drug is recommended as a first line therapy in necrotizing fasciitis type 2 (based on NHS guidelines 2022), in combination with clindamycin for patients who do not have penicillin energy **CU:** This drug is recommended in combination with clindamycin for necrotizing fasciitis type 2 management
Cefalexin	**ST:** this drug is recommended as the preferred line of therapy for simple abscess impetigo, erysipelas, and cellulitis (non-purulent and purulent) in adults. it is recommended as one of the preferred oral therapies for extensive non bullous impetigo, for furuncle on the face, multiple furuncles, carbuncles or in immunocompromised patients. it is also recommended as first line therapy when step down therapy (from IV to PO) is recommended in Staphylococcal Scalded Skin Syndrome. Cephalexin is recommended as an alternative to amox/clav and in combination with Metronidazole in patients with low-risk allergy to penicillins and Traumatic Wound Infections WITHOUT Water Exposure. **CU:** this drug can be used in combination with ciprofloxacin for the management of waterborne skin infections - seawater or fresh water. Cephalexin is recommended as an alternative to amox/clav and in combination with Metronidazole in patients with low-risk allergy to penicillins and Traumatic Wound Infections WITHOUT Water Exposure.
Cefazolin	**ST:** it is recommended as the first line IV therapy for cellulitis. It is recommended as one of the preferred options for ambulatory/hospital in the home if available. This drug is also recommended as first line therapy for Staphylococcal Scalded Skin Syndrome in combination with linezolid. Cefazolin is recommended as the preferred alternative for low-risk allergy to penicllins patients with Traumatic Wound Infections WITHOUT Water Exposure, in combination with metronidazole. **CU:** this drug is recommended for Staphylococcal Scalded Skin Syndrome in combination with linezolid. Additionally, Cefazolin

	is recommended for low-risk allergy to penicllins patients with Traumatic Wound Infections without Water Exposure in combination with metronidazole
Cefepime	**PA was removed** **ST:** In necrotizing fasciitis, it is recommended as an alternative to first line therapy, for patients with low-risk allergy to penicillins, in combination with other antibiotics. Nevertheless, it is also recommended as 1st line IV therapy for inpatient traumatic wound infections with water exposure, in combination with other antibiotics. **CU:** ST: in necrotizing fasciitis, it is recommended as an alternative to first line therapy, for patients with low-risk allergy to penicillins, in combination with other antibiotics. Nevertheless, it is also recommended as 1st line IV therapy for inpatient Traumatic Wound Infections WITH Water Exposure, in combination with other antibiotics. On another note, cefepime is recommended in combination with metronidazole in traumatic wound infections with water Exposure. Vancomycin can also be added in case of MRSA risk factors.
Cefotaxime	**ST:** recommended as one of the preferred intravenous antibiotics for the inpatient treatment of perianal and perirectal abscesses, burn wounds, wound management after source control, and Fournier's gangrene, in combination with other antibiotics **CU:** this drug is not given monotherapy; it is recommended in combination with metronidazole for the indication previously mentioned.
Ceftaroline	**ST removed** One of the intravenous options for MRSA infected SSTIs
Ceftazidime	**PA was removed** **CU:** ceftazidime is recommended in combination with doxycycline in Vibrio vulnificus wound infections and in Cellulitis associated with sea or freshwater contact
Ertapenem	**PA and CU were removed** Note: For patients with select surgical site infections (intestinal, GU tract), necrotizing infections, or patients with or at risk for pathogens resistant to other agents
Mupirocin topical	**ST:** this topical drug is recommended as a first line option (along with cefalexin) for the treatment of localized non bullous

	impetigo, secondarily infected skin lesions such eczema, ulcers, or lacerations, folliculitis (small follicular abscess in epidermis)
Flucloxacillin	**ST:** oral preferred therapy for mild to moderate cellulitis, staphylococcal scalded skin syndrome, erysipelas, and impetigo **CU:** oral flucloxacillin can be used in combination with metronidazole for cutaneous abscess
Levofloxacin	**PA was removed** **CU:** given in combination with metronidazole for the management of traumatic wound infections with water exposure (both outpatient and inpatient therapy but PO is preferred) **ST:** preferred outpatient therapy, in combination with metronidazole, for the management of traumatic wound infections with water exposure. It is also recommended in combination with metronidazole, as the alternative option, to the first line (cefepime) in inpatient therapy. if MRSA risk factors are present, TMP-SMX (outpatient) or vancomycin (inpatient therapy) should be added.
Daptomycin	**PA and ST were removed** **AGE**: The manufacturer recommends avoiding use in patients <12 months due to musculoskeletal, neuromuscular, and nervous system adverse effects observed in neonatal canine models. Approved ages and uses for generic products may vary; consult labeling for specific information. **CU**: one of the IV options where MRSA coverage is needed. can be used in combination with other antibiotic therapy (such as clindamycin)
Imipenem/ cilastatin	**PA was removed** **CU:** recommended in combination with anti-MRSA antibiotics for wound management after source control
Clarithromycin	**ST:** used as alternative to first line therapy, for patients with penicillin allergy (mild to moderate cellulitis, erysipelas, and impetigo, mild to moderate infected foot ulcer) **CU:** it is also recommended in combination with metronidazole for the management of mild to moderate infected ulcer.
Linezolid	**QL:** The maximum treatment duration is 28 days. The safety and effectiveness of linezolid when administered for periods longer than 28 days have not been established. Consider

	discontinuing linezolid when patient is clinically stable (e.g., vital signs within normal limits, no vasopressor requirements) for 24-48 hours and rash no longer progressing. maximum dose in adults is 1200 mg/day, maximum dose: 600 mg/dose FOR Infants and Children <12 years. **ST:** If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., linezolid) for the management of non-purulent cellulitis. used as an alternative to vancomycin for anti-MRSA activity. It is also recommended as first line therapy, in combination with cefazolin for staphylococcal scalded skin syndrome. **CU:** it is recommended (for an anti-MRSA effect) in combination with other antibiotic therapy
Piperacillin/tazobactam	**PA was removed** **QL:** adult 13.5 for usual coverage, for pseudomonas coverage: maximum dose 18 G / DAY. for peds: maximum dose of 16g/day **ST:** recommended as first line therapy in necrotizing fasciitis management (in combination with other antibiotics for full coverage). Also, recommended as an alternative to vancomycin when MRSA activity is needed, and vancomycin allergy is present. recommended as subsequent line of therapy when patients do not respond to first line therapy or in unstable patients (non-purulent and purulent cellulitis, perianal and perirectal abscesses, burn wounds, wound management, fournier's gangrene) **CU:** recommended in combination with other antibiotic for full coverage (such as vancomycin, linezolid, tedizolid, clindamycin) for necrotizing fasciitis management
Metronidazole	**CU:** metronidazole is always used in combination with other antibiotics metronidazole should not be used as monotherapy or in the routine treatment of diabetic foot infections, unless cultures in the diabetic foot against facultative and obligate anaerobes, then can be added to the therapeutic regimen, as it is effective against anaerobic bacteria **QL:** adult maximum dose is 2 g/day, peds: oral: maximum daily dose: 2,250 mg/day, IV: maximum daily dose: 4,000 mg/day.
Clindamycin	**CU:** it is recommended in combination with other antibiotic therapy to treat rapidly progressing infections

	ST: recommended as the preferred therapy in mild cellulitis where MRSA is suspected or as an alternative to vancomycin in severe cellulitis or staphylococcal scalded skin syndrome where MRSA is suspected. it is also recommended in cases of penicillin allergic patients or alternative to TMP-SMX for patients with sulfa allergy **QL:** for peds: Impetigo, ecthyma (if MRSA is suspected or confirmed): Oral: maximum dose: 400 mg/dose. Cellulitis, erysipelas, purulent/fluctuant SSTI: IV: maximum dose: 600 mg/dose. Oral: Methicillin-susceptible Staphylococcus aureus (MSSA) infection: Oral: maximum dose: 450 mg/dose. MRSA infection: Oral: maximum dose: 450 mg/dose. Necrotizing soft tissue infections: IV: maximum dose: 900 mg/dose.
Vancomycin	**PA was removed** **ST:** recommended first line therapy when MRSA is suspected, for inpatient therapy **CU:** used as monotherapy or given in combination with other antibiotic therapy in severe bacterial skin infections **QL:** adult maximum daily dose is 2g/day
Trimethoprim/Sulfamethoxazole	**ST:** one of the preferred oral/intravenous therapy options for management of waterborne skin infections, mild cellulitis (where MRSA is suspected) **CU:** can be used as monotherapy or in combination with other antibiotic therapy **QL:** for peds. Cellulitis, purulent/fluctuant SSTI: Oral, IV: maximum dose: 320 mg TMP/dose
Cloxacillin	**ST:** It is recommended as the 1st line therapy for erysipelas and cellulitis inpatient management **QL:** maximum dose 2g/day for adults and peds
Ceftriaxone	**PA was removed** **QL:** maximum dose is 2g/day for adult and peds **ST:** recommended as one of the preferred IV options for perianal and perirectal abscesses, burn wounds, wound management after source control, Fournier's gangrene, and orbital cellulitis. can also be used as subsequent line of therapy in necrotizing fasciitis type 2 (refer to report for the types of necrotizing fasciitis) in patients with non-severe penicillin allergy, **CU:** can be used in combination with metronidazole or

	clindamycin
Meropenem	**PA was removed** **CU:** it is to be given in combination with other antibiotic therapy such as clindamycin in necrotizing fasciitis or anti-MRSA drugs where MRSA is suspected **QL:** adult maximum dose: 3g/day, for peds: maximum dose 1 g/day
Ciprofloxacin	**PA was removed** **CU**: preferred treatment option with cefalexin for waterborne skin infections. Preferred in beta-lactam allergy, in combination with metronidazole, for perianal and perirectal abscesses, burn wounds. It is also recommended in combination with clindamycin in penicillin anaphylaxis for necrotizing fasciitis type 2 or in combination with doxycycline in penicillin allergy patients with cellulitis associated with sea or freshwater contact **QL**: adult maximum dose of 750 mg per dose
Doxycycline	**PA was removed** **ST:** recommended as the preferred option for purulent infections, especially for patients with sulfa allergy (who cannot take TMP-SMX). one of the preferred options for oral therapy where MRSA is suspected (along with TMP/SMX or minocycline). **CU:** can be given with IV ceftazidime (preferred option) or with ciprofloxacin (in penicillin allergy) in cellulitis associated with sea or freshwater contact**.** **QL:** adult maximum dose per day is 200 mg. for peds: maximum dose is 100 mg/dose
Amoxicillin	**QL:** for adults, maximum dose is 1500 mg/day. For peds, maximum is 500 mg per dose

2.3 Delisting

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is recommended to delist the following drugs from the CHI formulary:

Table 16. Delisted Drugs

Drug	Reason	SFDA-registered Alternative
Benzylpenicillin	Not SFDA-registered	Benzathine penicillin
Clavulanic acid		Amoxicillin/clavulanic acid

2.4 Other Drugs

The drugs detailed in table 17 are **not SFDA registered**. However, they have been recommended for the treatment of bacterial skin infections.

Table 17. Non-SFDA Approved Drugs for the Management of Bacterial Skin Infections

Drug	Approval	Indication	Dosing Regimen
Tedizolid	FDA approved in 2014[15] EMA approved in 2015[16]	Indicated in adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria. To reduce the development of drug-resistant bacteria and maintain the effectiveness of this drug, Tedizolid should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria[15,16].	Note: Reserve for patients with or at risk for MRSA infection who cannot receive preferred agents[17]. **Oral, IV**: 200 mg once daily. Total duration of therapy is ≥5 days; may extend up to 14 days depending on severity and clinical response.[17]
Dalbavancin	FDA approved in 2014[18] EMA approved in 2015[19]	Indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults and pediatric patients aged 3 months and older[18,19].	Note: Reserve for patients with or at risk for MRSA infection who cannot receive preferred agents[17]. **IV**: 1.5 g as a single dose or 1 g as a single dose initially, followed by 500 mg as a single dose 1 week later; the single dose has been shown to be as effective as the two-dose regimen[17].

Section 3.0 Key Recommendations Synthesis

- Treatment recommendations of impetigo[5]:
    - Localized non bullous impetigo (max. 5 lesions in a single skin area): 2% mupirocin ointment: one application 3 times daily for 7 days. Reassess after 3 days. If there is no response, switch to oral antibiotic therapy.
    - Extensive non bullous impetigo (more than 5 lesions or impetigo involving more than one skin area), bullous impetigo, ecthyma, impetigo with abscess; immunocompromised patient; topical treatment failure: oral antibiotic therapy recommended.
    - Note: in newborns with lesions located around the umbilicus, administer cloxacilllin IV.
- Treatment of simple abscess[6]:
    - Incision and drainage
    - Oral antibiotic therapy is recommended only in selected patients.
    - Target pathogens: S.aureus and streptococci
    - In cases of recurrent skin abscess, it is necessary to look for the presence of foreign materials and identify and correct local factors that may cause recurring infection.
- Treatment recommendations of furuncles and carbuncles[7]:
    - Furuncle on the face, multiple furuncles, carbuncles or in immunocompromised patients: oral antibiotic therapy is recommended.
- Treatment recommendations of erysipelas and cellulitis[6,8]:
    - Administer antibiotics: either orally or IV depending on severity.
    - Treat portal of entry and comorbidities.
    - Check and/or catch-up tetanus vaccination.
    - Target Pathogens: S. aureus and streptococci, CA- MRSA is unusual.
    - In case of necrotizing fasciitis, septic arthritis, or osteomyelitis: urgent transfer to a surgical center, initiate IV antibiotic treatment while awaiting transfer.
- Hospitalize for the following: children younger than 3 months, critically ill appearing patient, local complications, debilitated patient (chronic conditions, the elderly) or if there is a risk of non-compliance with or failure of outpatient treatment. Treat other patients as outpatients[8].

- In minor skin infections, localized impetigo (non-bullous or bullous), secondarily infected skin lesions such eczema, ulcers, or lacerations, or folliculitis (small follicular abscess in epidermis)[9]:
    - Topical therapy: Generally preferred over oral therapy.
    - Oral therapy: Indicated instead of topical therapy for patients with numerous impetigo lesions or in outbreak settings to reduce transmission.
    - Target Pathogens: Staphylococcus aureus, group A Streptococcus
    - If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX).
- For cellulitis, review antibiotics at day 5, can extend if not fully resolved[10].
- The choice of antimicrobial therapy may be guided by[10]:
    - History of presenting complaint:
        - Acute or chronic
        - Circumstances surrounding the development of the skin & soft tissue infection (SSTI)
    - Significant past medical history:
        - Diabetes
        - Immunocompromised state
        - Similar presentation with SSTI previously, etc.
    - Recent antimicrobial history within the last one month
    - Previous or recent positive microbiology results
- In non-purulent cellulitis[9]:
    - Target Pathogens: Group A Streptococcus, Staphylococcus aureus (the role of community-acquired MRSA is unknown)
    - Cephalexin and cefazolin provide coverage for group A Streptococcus and MSSA. TMP-SMX provides adequate coverage for group A Streptococcus, MSSA, and MRSA.
    - If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX or linezolid).
- In cases of moderate cellulitis, if oral antibiotics are not tolerated or no improvement after 48 hours, manage as per severe cellulitis. When improving, switch to oral antibiotics as per mild cellulitis.[12]

- In Purulent Cellulitis or Abscesses including Folliculitis, Furuncles, Carbuncles[6,9,11]:
    - Target Pathogen: Staphylococcus aureus (including CA- MRSA)
    - Cultures and susceptibilities are recommended when I&D is performed. Blood cultures are also recommended for patients with fever, rapidly progressive cellulitis, and systemic illness.
    - In neutropenic and immunocompromised patients, Gram-negative bacteria should be considered.
    - When to Consider Admission
        - ≥2 SIRS criteria* (*fever ≥38 or <36 C, tachycardia >90 bpm, RR> 20 bpm leukocytosis >12k cells/μL)
        - Hypotension
        - Rapid disease progression
        - Clinical signs of deeper infection (bullae, skin sloughing, organ dysfunction)
- Treatment of perianal and perirectal abscesses[6]:
    - Incision and drainage + antibiotic therapy in selected patients.
    - Target Pathogen: Gram-positive and Gram-negative
    - Outpatient therapy (oral antibiotic) or inpatient therapy (IV medications) depending on severity
- Treatment of bite wounds (animal and human bites)[6]
    - Irrigation of the wound and debridement of necrotic tissue
    - Antibiotic prophylaxis as principle is not recommended. It is recommended in selected patients.
    - Tetanus prophylaxis in bite wounds
- Treatment of burn wounds[6]:
    - Early initiation of dressings and effective topical antimicrobial therapy
    - Daily inspection of the wounds by a qualified surgeon or wound care expert
    - Early excision of all full thickness and deep partial thickness burns
    - Systemic antibiotic for infected wounds
    - Graft and coverage options
    - Target Pathogen: Gram-positive and Gram-negative

    - Outpatient therapy (oral antibiotic) or inpatient therapy (IV medications) depending on severity

- In Staphylococcal Scalded Skin Syndrome (SSSS) [9]
    - Results in loss of keratinocyte cell adhesion and leads to blistering of upper layer of the skin.
    - Pediatric Infectious Diseases consultation is recommended. Consider Dermatology consult if diagnosis is unclear or specific skin care recommendations are needed
    - Common pathogens: Staphylococcus aureus (MSSA predominantly reported in the literature)
    - Consider discontinuing linezolid when patient is clinically stable (e.g., vital signs within normal limits, no vasopressor requirements) for 24-48 hours and rash no longer progressing (usual duration of 3-5 days).
- In necrotizing fasciitis cases[6,9,10,12]:
    - Urgent referral to surgical team for debridement, seeking specialist advice for antibiotics, and considering IVIg are recommended
    - Early and aggressive surgical exploration (within 6 hours after admission) and debridement is critical. Emergent surgical consultation and ID consult are strongly recommended.
    - Common pathogens: Group A β-hemolytic Streptococcus, S. aureus, E. coli, Pseudomonas spp., Enterobacter spp., Klebsiella spp., Proteus spp., Bacteroides spp., Clostridia spp., Peptostreptococcus spp.
    - Empiric antibiotics should be continued until the following criteria are met:
        - Debridement no longer needed,
        - Clinical improvement, and
        - Minimum of 48-72 hours after completion of surgical debridement
    - Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs.
    - Clindamycin is initiated for anti-toxin activity for Streptococcal and Staphylococcal infections and can be stopped after 24-72 hours if infection has improved and patient is stable.
- Traumatic Wound Infections WITHOUT Water Exposure[9]:
    - Usually polymicrobial from environmental contamination.

    - Target pathogens: Staphylococcus aureus, Clostridia spp., Bacteroides spp., Prevotella spp., Porphyromonas spp., and Peptostreptococcus spp.
    - Consider Pediatric ID consult for infections that are deep, extensive or respond slowly
    - Debridement of devitalized tissues and contaminating debris is critical to source control and successful healing.
    - Empiric therapy should take into account site of wound and prior cultures and colonization.
- Traumatic Wound Infections WITH Water Exposure[6]
    - Usually polymicrobial from environmental contamination.
    - Target pathogens: Staphylococcus aureus, Clostridia spp., Bacteroides spp., Prevotella spp., Porphyromonas spp., and Peptostreptococcus spp.
    - Consider Aeromonas and Pseudomonas spp., other gram negatives if significant water exposure
    - Vibrio vulnificus wound infections require extensive debridement and mortality can be high. Consider combination therapy with ceftazidime and doxycycline.
- Fournier's gangrene[6]:
    - Surgical source control as soon as possible. Re-explorations should be repeated until the time when very little or no debridement is required.
    - Diverting colostomy or rectal diversion devices
    - Antibiotic therapy
    - Supportive measures
    - The initial empirical antibiotic regimen should comprise broad-spectrum drugs, including anti-MRSA and anti-Gram-negative coverage. Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs.
- Treatment of gas gangrene[6]:
    - The infection is rapidly progressive, it is important to treat patients aggressively, by early surgical debridement, antibiotics and intravenous fluid resuscitation.

➔ PEDIATRICS:

- Manage sepsis if features present[12]
- Manage source if identifiable — i.e. remove foreign body, drain abscess [12]

- Antimicrobial recommendations may vary according to local antimicrobial susceptibility patterns [12]
- In cases of moderate cellulitis, if oral antibiotics not tolerated or no improvement after 48 hours, manage as per severe cellulitis. When improving, switch to oral antibiotics as per mild cellulitis.[12]
- In established animal/human bites, seeking specialist advice is recommended first. Indications for prophylactic antibiotics in an animal/human bite[12]:
    - Presentation delayed by >8 hours
    - Puncture wound unable to be adequately debrided
    - Bite on hands, feet, face
    - Involves deep tissues (eg bones, joints, tendons)
    - Involves an open fracture
    - Immunocompromised patient
    - Cat bites
- In waterborne skin infections – seawater or fresh water, it is recommended to clean and debride wound as needed. Prophylactic antibiotics are not recommended [12]
- In Severe cellulitis or Staphylococcal scalded skin syndrome, consider early discharge to HITH once stable. When improving, switch to oral antibiotics as per mild cellulitis.[12]
- Consider consultation with local pediatric team when [12]:
    - No improvement or deterioration after 24–48 hours of therapy
    - Deep abscess or necrotizing fasciitis suspected — consider surgical opinion

➔ ADULTS AND PEDIATRICS:

- Duration of therapy depends on the type and severity of the infection and patient's clinical response to treatment.[5–12]
- Low-risk allergies include: pruritus without rash, remote (>10 years) unknown reaction, patient denies allergy but is on record, mild rash with no other symptoms (mild rash: non-urticarial rash that resolves without medical intervention).[9]

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Bacterial Skin Infections report** and aims to provide recommendations to aid in the management of Bacterial Skin Infections. These recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Bacterial Skin Infections. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses, and sequence of therapy

Appendix B. Bacterial Skin Infections Scope

<table>
<tr><th>Section</th><th>Rationale/Updates</th></tr>
<tr><td>Section 1.1.1
Cellulitis and other bacterial skin infections - The Royal Children’s Hospital (RCH) Clinical Practice Guidelines 2020</td><td>

Manage sepsis if features present
Manage source if identifiable — ie remove foreign body, drain abscess
Antimicrobial recommendations may vary according to local antimicrobial susceptibility patterns
Cellulitis frequently looks worse after 24 hours of treatment; consider waiting 48 hours to change therapies
Young, unvaccinated children are at risk of Haemophilus influenzae type B (Hib)

<table>
<tr><th>Diagnosis</th><th>Antibiotic</th><th>Total duration</th><th>Comments</th></tr>
<tr><td>Impetigo</td><td>Topical Mupirocin 2% ointment or cream to crusted areas tds OR
Cefalexin 33 mg/kg (max 500 mg) oral bd if widespread or large lesions</td><td>5 days</td><td></td></tr>
<tr><td>Mild cellulitis</td><td>Cefalexin 33 mg/kg (max 500 mg) oral tds</td><td>5 days</td><td></td></tr>
<tr><td>Moderate cellulitis</td><td>A trial of high-dose oral antibiotics with close review may be considered:

Cefalexin 33 mg/kg (max 1 g) oral tds

Consider Ambulatory/Hospital-in-the-Home (HITH) if available:</td><td>5–10 days</td><td>If oral antibiotics not tolerated or no improvement after 48 hours, manage as per severe cellulitis
When improving,</td></tr>
</table>
</td></tr>
</table>

		Ceftriaxone 50 mg/kg (max 2g) IV daily Cefazolin 50 mg/kg (max 2g) IV bd		switch to oral antibiotics as per mild cellulitis
	Severe cellulitis or Staphylococcal scalded skin syndrome	Flucloxacillin 50 mg/kg (max 2 g) IV 6H (if rapidly progressive consider adding Clindamycin 10 mg/kg (max 600 mg) IV 6H)	5–10 days	Consider early discharge to HITH once stable. When improving, switch to oral antibiotics as per mild cellulitis
	Necrotising Fasciitis	Vancomycin and Meropenem 20 mg/kg IV (max 1 g) 8H **AND** Clindamycin 10 mg/kg (max 600 mg) IV 6H		Urgent referral to surgical team for debridement Seek specialist advice for antibiotics Consider IVIg
	Mammalian bites (uninfected / prophylactic)	Often do **not** need prophylactic antibiotics. When indicated*: Amoxicillin/Clavulanate **80 mg/mL amoxicillin oral liquid (7:1)** 22.5 mg/kg (max 875 mg) oral bd	5 days	
	Animal/human bites (established	Amoxicillin/Clavulanate **80 mg/mL amoxicillin oral liquid (7:1)**	5 days (extend if severe,	Seek specialist advice

infection)	22.5 mg/kg (max 875 mg) oral bd If unable to tolerate oral antibiotics: 25 mg/kg (max 1g) IV 6–8H	penetrating, involving deep tissues)	
Waterborne skin infections – seawater or fresh water	Cefalexin 33 mg/kg (max 1 g) oral tds and Ciprofloxacin 10 mg/kg (max 500 mg) oral bd **OR** Trimethoprim/sulfamethoxazole 8/40 mg/kg (max 320/1600 mg) oral bd	5–10 days	Clean and debride wound as needed Prophylactic antibiotics are not recommended

*Indications for prophylactic antibiotics in a animal/human bite

- Presentation delayed by >8 hours
- Puncture wound unable to be adequately debrided
- Bite on hands, feet, face
- Involves deep tissues (eg bones, joints, tendons)
- Involves an open fracture
- Immunocompromised patient
- Cat bites

➔ Suggested antibiotic therapy where MRSA is suspected:

Diagnosis	Antibiotic	Total duration	Comments
Mild cellulitis	Trimethoprim/sulfamethoxazole 8/40 mg/kg (max 320/1600 mg) oral bd **OR** Clindamycin 10 mg/kg (max 450 mg) oral qid	5 days	
Moderate	A trial of oral antibiotics with close		When

<table>
<tr><td></td><td>
<table>
<tr><td>cellulitis</td><td>review may be considered
OR
<u>Vancomycin</u> IV</td><td></td><td>improving, switch to oral antibiotics as per mild cellulitis</td></tr>
<tr><td>Severe cellulitis or Staphylococcal scalded skin syndrome</td><td><u>Vancomycin</u> IV
OR
Clindamycin 10 mg/kg (max 600 mg) IV 6H</td><td>When improving, switch to oral antibiotics as per mild cellulitis</td><td></td></tr>
</table>
➔ Risk factors for MRSA infection
• Residence in an area with high prevalence of MRSA, eg Northern Territory, remote communities in northern Queensland
• Previous colonization or infection with MRSA (particularly recent)

➔ Consider consultation with local pediatric team when
• No improvement or deterioration after 24–48 hours of therapy
• Deep abscess or necrotizing fasciitis suspected — consider surgical opinion
</td></tr>
<tr><td>Section 1.1.2
Impetigo - MSF medical guidelines 2023</td><td>Treatment recommendations of impetigo:
• Localized non bullous impetigo (max. 5 lesions in a single skin area):
  ○ Clean with soap and water and dry before applying mupirocin.
  ○ 2% mupirocin ointment: one application 3 times daily for 7 days. Reassess after 3 days. If there is no response, switch to oral antibiotic therapy (see below).
  ○ Keep fingernails short. Avoid touching the lesions, keep them covered with gauze if possible.
• Extensive non bullous impetigo (more than 5 lesions or impetigo involving more</td></tr>
</table>

	than one skin area), bullous impetigo, ecthyma, impetigo with abscess; immunocompromised patient; topical treatment failure: o Clean with soap and water and dry 2 to 3 times daily. o Keep fingernails short. Avoid touching the lesions, keep them covered with gauze if possible. o Incise abscesses if present. o Administer oral antibiotic therapy [a]: ▪ **Cefalexin** PO for 7 days Neonates under 7 days: 25 mg/kg 2 times daily Neonates 7 to 28 days: 25 mg/kg 3 times daily Children 1 month to 12 years: 25 mg/kg 2 times daily Children 12 years and over and adults: 1 g 2 times daily **Or** ▪ **Cloxacillin** PO for 7 days Children over 10 years: 15 mg/kg 3 times daily (max. 3 g daily) Adults: 1 g 3 times daily Note: in newborns with lesions located around the umbilicus, administer cloxacilllin IV. (a): **In penicillin-allergic patients only** (resistance to macrolides is common), azithromycin PO for 3 days (children: 10 mg/kg once daily; adults: 500 mg once daily). • **For all patients:** • Quarantine from school (children can return to school after 24 to 48 hours of antibiotic therapy). • Look for and treat any underlying dermatosis: lice, scabies, eczema, herpes, scalp ringworm, or an ENT infection. • Trace and treat contacts. • Check for proteinuria (use urine dipstick) 3 weeks after the infection.
Section 1.1.3	Treatment recommendations of furuncles and carbuncles:

Furuncles and carbuncles - MSF medical guidelines 2023	• **Single furuncle:**
	  o Clean with soap and water 2 times daily and cover with a dry dressing.
	  o Apply warm moist compresses to the furuncle in order to encourage it to drain.
	  o After drainage, clean and apply a dry dressing until the lesion has healed.
	
	• **Furuncle on the face, multiple furuncles, carbuncles or in immunocompromised patients:**
	  o Same local care.
	  o Add systematically an antibiotic for 7 days [a]:
	  ▪ **Cefalexin** PO
	  Neonates under 7 days: 25 mg/kg 2 times daily
	  Neonates 7 to 28 days: 25 mg/kg 3 times daily
	  Children 1 month to 12 years: 25 mg/kg 2 times daily Children 12 years and over and adults: 1 g 2 times daily
	  Or
	  ▪ Amoxicillin/clavulanic acid (co-amoxiclav) PO. Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin:
	  Children < 40 kg: 25 mg/kg 2 times daily
	  Children ≥ 40 kg and adults:
	  Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
	  Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)
	• **In all cases**: wash hand frequently, wash bedding.
	• **(a)**: For penicillin-allergic patients: **clindamycin** PO (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily)

Section 1.1.4 **Erysipelas and cellulitis - MSF medical guidelines**	Treatment recommendations of erysipelas and cellulitis: • **In all cases:** o Outline the area of erythema with a pen in order to follow the infection. The erythema will regress if the treatment is effective. If the erythema spreads

2023	consider a treatment failure (MRSA or a necrotizing infection). o Bed rest, elevation of affected area (e.g. leg). o Treatment of pain. Avoid NSAIDs that may increase the risk of necrotizing fasciitis. o Administer antibiotics: either orally or IV depending on severity. o Treat portal of entry and comorbidities. o Check and/or catch up tetanus vaccination. o In case of necrotizing fasciitis, septic arthritis or osteomyelitis: urgent transfer to a surgical center, initiate IV antibiotic treatment while awaiting transfer. • Hospitalize for the following: children younger than 3 months, critically ill appearing patient, local complications, debilitated patient (chronic conditions, the elderly) or if there is a risk of non-compliance with or failure of outpatient treatment. Treat other patients as outpatients. o Critically ill appearing child: weak grunting or crying, drowsy and difficult to arouse, does not smile, disconjugate or anxious gaze, pallor or cyanosis, general hypotonia. • Outpatient antibiotherapy: ▪ **Cefalexin** PO for 7 to 10 days ▪ Children 1 month to under 12 years: 25 mg/kg 2 times daily ▪ Children 12 years and over and adults: 1 g 2 times daily Or ▪ **Amoxicillin/clavulanic acid** (co-amoxiclav) PO for 7 to 10 days. ▪ Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin: Children < 40 kg: 25 mg/kg 2 times daily Children ≥ 40 kg and adults: Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily) Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily) ▪ **For penicillin-allergic patients**, clindamycin PO for 7 to 10 days (children: 10

	mg/kg 3 times daily; adults: 600 mg 3 times daily). • In the event of worsening clinical signs after 48 hours of antibiotic treatment, consider IV route. • Inpatient antibiotherapy: o First line therapy: ▪ **Cloxacillin** IV infusion over 60 minutes: ▪ Cloxacillin powder for injection should be reconstituted in 4 ml of water for injection. Then dilute each dose of cloxacillin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults. Children 1 month to under 12 years: 12.5 to 25 mg/kg every 6 hours Children 12 years and over and adults: 1 g every 6 hours **Or** ▪ **Amoxicillin/clavulanic acid** (co-amoxiclav) by slow IV injection (3 minutes) or IV infusion (30 minutes). The dose is expressed in amoxicillin: Children under 3 months: 30 mg/kg every 12 hours Children 3 months and over: 20 to 30 mg/kg every 8 hours (max. 3 g daily) Adults: 1 g every 8 hours ▪ If there is clinical improvement after 48 hours (afebrile and erythema and oedema have improved) switch to cefalexin or amoxicillin/clavulanic acid PO at the doses indicated above to complete 7 to 10 days of treatment. ▪ **For penicillin-allergic patients, clindamycin** IV infusion (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily). o If there is no clinical improvement after 48 hours, consider MRSA: ▪ Clindamycin IV infusion over 30 minutes: Dilute each dose of clindamycin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults. Children 1 month and over: 10 mg/kg every 8 hours

<table>
<tr><td></td><td>Adults: 600 mg every 8 hours
▪ After 48 hours, change to clindamycin PO at the doses indicated above to complete 7 to 10 days of treatment.</td></tr>
<tr><td>Section 1.1.5
Stanford Health Care (SHC) Clinical Guideline: Outpatient Management of Skin and Soft Tissue Infections 2022</td><td>SHC Clinical Guideline: Outpatient Management of Skin and Soft Tissue Infections:
• The below table showcases the Stanford Outpatient Empiric Antibiotic Guidelines for Acute Bacterial Skin and Soft Tissue Infections (SSTI):
<table>
<tr><th>Clinical Syndrome</th><th>Most Common Organism</th><th>Treatment Options</th><th>Duration</th><th>Comments</th></tr>
<tr><td><u>NON-PURULENT INFECTIONS</u>
Acutely spreading, poorly demarcated skin changes: dolor (pain), calor (heat), rubor (erythema), and tumor (swelling)
Erysipelas:
Superficial sharply demarcated infection of the upper dermis without focus of purulence</td><td>B-hemolytic Streptococci
3. Group A (S. pyogenes)
4. Other Streptococcus groups: B,C,G</td><td>Preferred:
Cephalexin
500mg PO q6h
OR 1g PO q8h

Alternative for β-lactam Allergy[#]:
Clindamycin
450mg PO q8h
or TMP-SMX 1-2 DS tab PO BID

Combination therapy is not recommended</td><td>5 Days</td><td><u>When to Consider Cellulitis Mimics[†]</u>
4. Inconsistent presentation (bilateral distribution, well demarcated chronic to subacute progression, etc.)
5. Symptoms improved with leg elevation without use of antibiotics
6. Symptoms not improved with antibiotics
<u>Patient</u></td></tr>
</table></td></tr>
</table>

	(drainage, exudate, or abscess) **Cellulitis:** Deeper infection of the dermis & subcutaneous fat without focus of purulence (drainage, exudate, or abscess)				<u>Instructions</u> • Elevate infected area above the level of the heart to reduce redness & swelling • Keep infected area clean & dry • Call your doctor if symptoms have not improved after 72h OR if fever or other symptoms develop
	PURULENT INFECTIONS **Furuncle Infection of a hair follicle extending to dermis with small 'boil'** **Carbuncle Infection of**	Staphylococcus aureus MSSA & MRSA	I&D + Antibiotics Preferred: TMP-SMX 1-2 DS tab PO BID OR Doxycycline 100mg PO BID Clindamycin is not preferred therapy due to decreased	5 Days After I&D	3. Tailor antibiotic therapy to results of gram stain, culture and susceptibilities from I&D 4. S. aureus susceptibility rates are 99%

	several follicles leading to coalescing mass Abscess Cutaneous collection of pus within dermis and deeper skin layers		susceptibility rates		for TMP-SMX and 93% for doxycycline When to Consider Admission • ≥2 SIRS criteria* • Hypotension • Rapid disease progression • Clinical signs of deeper infection (bullae, skin sloughing, organ dysfunction)

***fever ≥38 or <36 C, tachycardia >90 bpm, RR> 20 bpm leukocytosis >12k cells/μL**
†Consider Dermatology Consult for evaluation of cellulitis mimics such as stasis dermatitis, lipodermatosclerosis, contact dermatitis, lymphedema
 # Clinically significant IgE or T lymphocyte mediated β-lactam allergies are extremely rare (<5%)

- The table below showcases the antimicrobial Drug Dosing in Renal Impairment:

Antimicrobial Drug	CrCl > 30 mL/min*	CrCl 15-30 mL/min*	CrCl < 15 mL/min*	Intermittent Hemodialysis (thrice weekly dialysis)
Cephalexin (PO)	500mg	500mg q8-12h	500mg q24h	500mg q24h

		q6h OR 1g q8h			(dosed after HD on HD days)
	Clindamycin (PO)	450mg q6h	450mg q6h	450mg q6h	450mg q6h
	TMP-SMX (PO) **SS = single strength (80mg of TMP)** **DS = double strength (160mg of TMP)**	1-2 DS tablets BID	Administer 50% of recommended dose	Administer 25-50% of usual dose - Use with caution and close monitoring	Administer 25-50% of recommended dose
	Doxycycline (PO)	100mg q12h	100mg q12h	100mg q12h	100mg q12h
	***Creatinine clearance (CrCl) is calculated via the Cockcroft-Gault Method**				

Section 1.1.6

C.S Mott Children's Hospital Michigan Medicine 2023 - Empiric antibiotic guidelines for skin and soft tissue infections in patients on pediatric services

This guideline is designed to provide guidance in pediatric patients with a primary skin and soft tissue infection (SSTI). Management of skin and soft tissue infections in patients <2 months of age or those presenting with sepsis or septic shock not related to necrotizing fasciitis is beyond the scope of these guidelines.

➔ The below table showcases all treatment recommendations:

Setting	Empiric Therapy	Duration/Comments
Minor Skin Infections • **Localized impetigo (non-bullous or bullous)** • **Secondarily infected skin**	Topical Therapy **Mupirocin** 2% topical ointment applied BID Oral Therapy *1st line:* **Cephalexin** 25 mg/kg/DOSE PO TID (max: 1 g/DOSE)	Duration: 5 days S. aureus isolates from impetigo are commonly methicillin susceptible (MSSA). Michigan Medicine S. aureus resistance rates are low for TMP-

	lesions such eczema, ulcers, or lacerations • **Folliculitis (small follicular abscess in epidermis)** **Topical therapy: Generally preferred over oral therapy** ***Oral therapy:*** **Indicated instead of topical therapy for patients with numerous impetigo lesions or in outbreak settings to reduce transmission** ***Target Pathogens*:** ***Staphylococcus aureus, group A Streptococcus***	*If MRSA risk factors present[1] or allergy that precludes cephalexin use:* **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) Alternative to TMP-SMX if sulfa allergy: **Clindamycin** 10 mg/kg/DOSE PO TID (max: 450 mg/DOSE)	SMX (2%), compared to clindamycin (19% for MSSA and 25% for methicillin-resistant S. aureus [MRSA] in 2022). If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX).
	Non-Purulent Cellulitis **Absence of purulent drainage or exudate, ulceration, and no associated abscess. Includes erysipelas.** ***Target Pathogens:***	Outpatient or Step-down (from IV to PO) Therapy: *1st line:* **Cephalexin** 25 mg/kg/DOSE PO TID (max: 1 g/DOSE) *If MRSA risk factors present[1] or allergy that precludes*	Duration: 5 days May extend therapy up to 7-10 days if lack of symptom resolution at 5 days. Cephalexin and cefazolin provide coverage for group A Streptococcus and MSSA. TMP-SMX provides adequate

	Group A Streptococcus, Staphylococcus aureus (the role of community-acquired MRSA is unknown)	*cephalexin use*: **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) <u>Alternative to TMP-SMX if sulfa allergy</u>: **Clindamycin** 10 mg/kg/DOSE PO TID (max: 450 mg/DOSE) **OR** **Linezolid** PO: ▪ <12 years: 10 mg/kg/DOSE TID (max: 600 mg/DOSE) ▪ ≥12 years: 10 mg/kg/DOSE BID (max: 600 mg/DOSE) <u>Inpatient (IV) Therapy</u> *1st Line*: **Cefazolin** 33 mg/kg/DOSE IV q8h (max: 2 g/DOSE) *Alternative if MRSA risk factors present1or allergy that precludes cefazolin use* **Vancomycin** IV	coverage for group A Streptococcus, MSSA, and MRSA. If worsening or not improving after 48 hours of oral cephalexin therapy, consider changing to an agent with anti-MRSA activity (i.e., TMP-SMX or linezolid). Linezolid suspension may not be readily available at all community pharmacies. Some insurance companies (including state Medicaid) may require prior authorization.

		Purulent Cellulitis or Abscesses including Folliculitis, Furuncles, Carbuncles ***Abscess*:** Collection of pus within the dermis and deeper skin tissues ***Furuncle*:** Infection of the hair follicle with suppuration extending through the dermis into subcutaneous tissue ***Carbuncle*:** Confluence of furuncles with wider infiltration *Target Pathogen: Staphylococcus aureus (including MRSA)*	Incision and drainage (I&D) is recommended as primary management for abscesses. Antibiotics** are (at a minimum) recommended if patient meets one of the following criteria: • Substantial surrounding cellulitis • Abscess >2 cm in diameter; >1 cm in infants and young children • Inability to adequately drain the abscess • Signs or symptoms of systemic illness (e.g., fever ≥38°C) • Immunodeficiency • Multiple sites Outpatient Therapy or Step-down (from IV to PO) Therapy *1st Line:* **TMP-SMX**, 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) *Alternative for sulfa allergy:* **Doxycycline** 2.2 mg/kg/DOSE	Duration: 5 days . May extend therapy up to 7-10 days if lack of symptom resolution at 5 days. Cultures and susceptibilities are recommended when I&D is performed. Blood cultures are also recommended for patients with fever, rapidly progressive cellulitis, and systemic illness. Michigan Medicine S. aureus resistance rates are low for TMP-SMX2 (2%) and doxycycline (3%), compared to clindamycin (19% for methicillin-susceptible S. aureus [MSSA] and 25% for methicillin-resistant S. aureus [MRSA] in 2022). Tailor antibiotic therapy to results of Gram stain, culture, and sensitivities. **Although ~70% of abscesses may resolve with I&D alone, an additional 10% are more likely to resolve with the addition of antibiotics. Clinical context should be taken into account

		PO BID (max: 100 mg/DOSE) <u>Inpatient (IV) Therapy</u> *1st Line:* **Vancomycin** IV *Alternative for vancomycin allergy (not vancomycin infusion reaction):* **Linezolid** PO/IV (PO preferred): ▪ <12 years: 10 mg/kg/DOSE TID (max: 600 mg/DOSE) ▪ ≥12 years: 10 mg/kg/DOSE BID (max: 600 mg/DOSE)	when deciding if antibiotics are appropriate. Linezolid suspension may not be readily available at all community pharmacies. Some insurance companies (state Medicaid) may require prior authorization.
	<u>Staphylococcal Scalded Skin Syndrome (SSSS)</u> Results in loss of keratinocyte cell adhesion and leads to blistering of upper layer of the skin**.** Pediatric Infectious Diseases consultation	<u>1st Line:</u> **Cefazolin** 33 mg/kg/DOSE IV q8h (max: 2 g/DOSE) + **Linezolid** PO/IV (PO preferred): ▪ <12 years: 10 mg/kg/DOSE TID (max: 600 mg/DOSE) ▪ ≥12 years: 10	Duration: 10 days Consider discontinuing linezolid when patient is clinically stable (e.g., vital signs within normal limits, no vasopressor requirements) for 24-48 hours and rash no longer progressing (usual duration of 3-5 days). Staphylococcal Scalded Skin Syndrome (SSSS) is usually

	is recommended. Consider Dermatology consult if diagnosis is unclear or specific skin care recommendations are needed *Common pathogens: Staphylococcus aureus (MSSA predominantly reported in the literature)*	mg/kg/DOSE BID (max: 600 mg/DOSE <u>Step-down (from IV to PO) Therapy</u> *1st Line*: **Cephalexin** 25 mg/kg/DOSE PO TID (max: 1 g/DOSE) *Alternative if MRSA risk factors present or allergy that precludes cephalexin use*: **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE)	diagnosed in children <5 years of age.
	<u>Necrotizing Fasciitis</u> Early and aggressive surgical exploration and debridement is critical. Emergent surgical consultation and ID consult are strongly recommended. *Common pathogens: Group A β-hemolytic Streptococcus, S. aureus, E. coli,*	<u>1st Line:</u> **Piperacillin-tazobactam** 75 mg of piperacillin/kg/DOSE IV q6h (max: 4 g piperacillin/DOSE) extended infusion + **Vancomycin** IV + **Clindamycin** 13 mg/kg/DOSE IV q8h (max: 900 mg/DOSE) <u>Alternative for low-risk allergy to penicillins</u>: **Cefepime** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) extended infusion +	<u>Duration</u>: Empiric antibiotics should be continued until the following criteria are met: ▪ Debridement no longer needed, ▪ Clinical improvement, and ▪ Minimum of 48-72 hours after completion of surgical debridement Clindamycin is initiated for anti-

		Pseudomonas spp., Enterobacter spp., Klebsiella spp., Proteus spp., Bacteroides spp., Clostridia spp., Peptostreptococcus spp.	**Vancomycin** IV + **Clindamycin** 13 mg/kg/DOSE IV q8h (max: 900 mg/DOSE) **ADD Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) TID (max: 500 mg/DOSE) if perineum or groin involved *Alternative for allergy that precludes use of both piperacillin-tazobactam and cefepime:* REPLACE cefepime with **Aztreonam** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) <u>Alternative for vancomycin allergy (not vancomycin infusion reaction):</u> **Piperacillin-tazobactam** 75 mg of piperacillin/kg/DOSE IV q6h (max: 4 g piperacillin/DOSE) extended infusion + **Linezolid** PO/IV (PO preferred): ▪ <12 years: 10 mg/kg/DOSE TID (max: 600	toxin activity for Streptococcal and Staphylococcal infections and can be stopped after 24-72 hours if infection has improved and patient is stable. Tailor antibiotic therapy to results of deep tissue Gram stain, culture, and sensitivities. Linezolid has in-vitro data that demonstrates suppression of toxin production with S. aureus and group A streptococcus. Clinical success against toxic shock syndrome is reported in case reports.

		mg/DOSE) ▪ ≥12 years: 10 mg/kg/DOSE BID (max: 600 mg/DOSE)	
	Traumatic Wound Infections WITHOUT Water Exposure **Usually polymicrobial from environmental contamination.** **See section above if concern for necrotizing fasciitis.** **For animal/human bites, refer to Animal Bite Guidelines on antimicrobial stewardship webpage.** **Evaluate tetanus immunization status, and if indicated, administer tetanus immunization +/- tetanus immune globulin.** **Target pathogens: Staphylococcus**	Traumatic wounds without evidence of local infection or systemic signs of infection typically do not need antimicrobial therapy. <u>Outpatient (PO) Therapy</u> *1st Line*: **Amoxicillin-clavulanate** 25 mg amoxicillin/kg/DOSE PO BID (max: 875 mg amoxicillin/DOSE) ▪ 7:1 formulation is recommended (400/57/ 5ml or 200/28.5/5 ml) If MRSA risk factors present[1] ADD **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) *Alternative for low-risk allergy[5] to penicillins*: **Cephalexin** 25 mg/kg/DOSE	Duration: 7 days Therapy may need to be extended based on severity of infection and response to treatment. Consider Pediatric ID consult for infections that are deep, extensive or respond slowly Debridement of devitalized tissues and contaminating debris is critical to source control and successful healing. Empiric therapy should take into account site of wound and prior cultures and colonization. Tailor antibiotic therapy to results of deep tissue Gram stain, culture, and sensitivities.

	aureus, Clostridia spp., Bacteroides spp., Prevotella spp., Porphyromonas spp., Peptostreptococcus spp.	PO TID (max: 1 g/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO TID (max: 500 mg/DOSE) *Alternative for allergy that precludes use of both amoxicillin-clavulanate and cephalexin:* **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max: 320 mg TMP/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO TID (max: 500 mg/DOSE) <u>Inpatient (IV) Therapy</u> *1st Line:* **Ampicillin-sulbactam** 50 mg of ampicillin/kg/DOSE IV q6h (max: 2 g ampicillin/DOSE) *Alternative for low-risk allergy[5] to penicillins*: **Cefazolin** 33 mg/kg/DOSE IV q8h (max: 2 g/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) TID (max: 500	

		mg/DOSE) *Alternative if MRSA risk factors present[1], or allergy that precludes use of both ampicillin-sulbactam and cefazolin:* **Vancomycin** IV + **Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) q8h (max: 500 mg/DOSE)	
	<u>Traumatic Wound Infections WITH Water Exposure</u> Usually polymicrobial from environmental contamination. See section above if concern for necrotizing fasciitis. **For animal/human bites, refer to Animal Bite Guidelines on antimicrobial stewardship webpage.**	<u>Outpatient (PO) Therapy:</u> **Levofloxacin** PO: ▪ <5 years: 10 mg/kg/DOSE PO BID (max: 375 mg/DOSE) ▪ ≥5 years: 10 mg/kg/DOSE PO daily (max: 750 mg/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO TID (max: 500 mg/dose) If MRSA risk factors present[1] ADD **TMP-SMX** 6 mg of TMP/kg/DOSE PO BID (max:	Duration: 7 days Therapy may need to be extended based on severity of infection and response to treatment. Consider Pediatric ID consult for infections that are deep, extensive or respond slowly Debridement of devitalized tissues and contaminating debris is critical to source control and successful healing. Empiric therapy should take into account site of wound and prior

		Evaluate tetanus immunization status, and if indicated, administer tetanus immunization ± tetanus immune globulin. ***Target pathogens:*** ***Staphylococcus aureus,*** ***Clostridia spp.,*** ***Bacteroides spp.,*** ***Prevotella spp.,*** ***Porphyromonas spp.,*** *Peptostreptococcus spp.* Consider Aeromonas and Pseudomonas spp., other gram negatives if significant water exposure	320 mg TMP/DOSE) <u>Inpatient (IV) Therapy</u>: *1st Line:* **Cefepime** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) extended infusion + **Metronidazole** 10 mg/kg/DOSE PO/IV (PO preferred) q8h (max: 500 mg/DOSE) If MRSA risk factors present[1] ADD **Vancomycin** IV *Alternative for allergy that precludes cefepime use:* **Levofloxacin** IV/PO (PO preferred): ▪ <5 years: 10 mg/kg/DOSE PO BID (max: 375 mg/DOSE) ▪ ≥5 years: 10 mg/kg/DOSE PO daily (max: 750 mg/DOSE) + **Metronidazole** 10 mg/kg/DOSE PO/IV TID (PO	cultures and colonization. Vibrio vulnificus wound infections require extensive debridement and mortality can be high. Consider combination therapy with ceftazidime and doxycycline. Tailor antibiotic therapy to results of deep tissue Gram stain, culture, and sensitivities.

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If MRSA risk factors present1 ADD Vancomycin IV</td><td></td></tr>
<tr><td colspan="3">[1] Consider MRSA coverage if any of the following are present: severe sepsis or septic shock, immunocompromised status, personal or household contact with MRSA infection, or colonization in the past 12 months
[5] Low-risk allergies include: pruritus without rash, remote (>10 years) unknown reaction, patient denies allergy but is on record, mild rash with no other symptoms (mild rash: non-urticarial rash that resolves without medical intervention).</td></tr>
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<tr><td>Section 1.1.7
WSES/GAIS/WSIS/SIS-E/AAST global clinical pathways for patients with skin and soft tissue infections 2022</td><td>

SSTIs were divided in four classes:

Class 1 patients with SSTI, but no signs or symptoms of systemic toxicity or co-morbidities.
Class 2 patients are either systemically unwell with stable co-morbidities or systemically well, but with comorbidity (e.g., diabetes, obesity) that may complicate or delay resolution.
Class 3 patients appear toxic and unwell (fever, tachycardia, tachypnoea, and/or hypotension).
Class 4 patients have sepsis syndrome and life-threatening infection; for example, necrotizing fasciitis.

Antibiotics recommended for MRSA infections are listed below.

Oral options:

Minocycline 100 mg every 12 h
Trimethoprim and sulfamethoxazole 160/800 or320/1600 every 12 h
Doxycycline 100 mg every 12 h
Clindamycin 300–450 mg every 8 h (high resistance rate)
Linezolid 600 mg every 12 h

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	▪ Tedizolid 200 mg every 24 h o Intravenous options: ▪ Clindamycin 600–900 mg every 8 h ▪ Trimethoprim and sulfamethoxazole 320/1600 every 12 h ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h ▪ Tigecycline 100 mg IV as a single dose, then 50 mg IV every 12 h ▪ Linezolid 600 mg every 12 h ▪ Daptomycin 6 mg/kg every 24 h ▪ Ceftaroline 600 mg every 12 h ▪ Dalbavancin 1000 mg once followed by 500 mg after 1 week or 1500 mg one dose ▪ Tedizolid 200 mg every 24 h ▪ Telavancin 10 mg/kg every 24 h • Treatment of simple abscess: o Incision and drainage o Antibiotic therapy only in selected patients for 5 days. You may extend therapy up to 7–10 days if lack of symptom resolution at 5 days. o **Empiric antibiotic regimens. Normal renal function - Target Pathogens: S.aureus and streptococci - One of the following oral antibiotics** ▪ Amoxicillin-clavulanate 1 g every 8 h ▪ Cephalexin 500 mg every 6 h ▪ In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to firstline therapy add one of the following oral antibiotics ▪ Minocycline 100 mg every 12 h ▪ Doxycycline 100 mg every 12 h ▪ Trimethoprim and Sulfamethoxazole 160/800 mg every 12 h Or

	○ **In patients with beta-lactam allergy** ▪ Clindamycin 300 mg every 8 h ○ A recurrent abscess at a site of previous infection may be caused by local causes such as a pilonidal cyst, hidradenitis suppurativa, or foreign material. Therefore, it always requires research of a local cause. ○ In cases of recurrent skin abscess, it is necessary to look for the presence of foreign materials and identify and correct local factors that may cause recurring infection. ○ For recurrent skin abscess bacterial culture testing should be performed to verify the causative bacteria and antibiotics susceptibility to define a targeted therapy. If an abscess is treated with prolonged antibiotics without drainage, it can lead to formation of sterile pus surrounded by thick fibrous tissue. It makes a hard lump that sometimes mimics malignancy. The treatment is surgical drainage with excision of fibrous wall. • Treatment of erysipelas: ○ Erysipelas is distinguished clinically from cellulitis by the following two features: ▪ In erysipelas the lesions are raised above the level of the surrounding skin, and ▪ Erysipelas is characterized by a clear line of demarcation between involved and uninvolved tissue. ○ Streptococci are the primary cause. The role of S. aureus, and specifically MRSA, remains controversial. ○ Treatment is with antibiotic therapy for 5 days. Duration may be extended up to 10 days if lack of symptom resolution at 5 days ○ Use intravenous antibiotics if signs of systemic inflammation ○ **Empiric antibiotic regimens. Normal renal function - Target Pathogens: S. aureus and streptococci, CA- MRSA is unusual -** Outpatient therapy or step down, One of the following oral antibiotics: ▪ Amoxicillin-clavulanate 1 g every 8 h

	▪ Cephalexin 500 mg every 6 h ▪ In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to firstline therapy add one of the following oral antibiotics ▪ Trimethoprim and sulfamethoxazole 160/800– 320/1600 mg every 12 h ▪ Minocycline 100 mg every 12 h ▪ Doxycycline 100 mg every 12 h Or o **In patients with beta-lactam allergy** ▪ Clindamycin 300 mg every 8 h Or o **Inpatient therapy -** One of following intravenous antibiotics ▪ Cefazolin 2 g every 8 h ▪ Amoxicillin-clavulanate 1.2/2.2 gr every 8 h Or o **In patients at risk for CA-MRSA including critically ill and immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days or who do not respond to first-line therapy add one of following intravenous antibiotics** ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h ▪ Linezolid 600 mg every 12 h • Treatment of cellulitis: o Treatment with antibiotic therapy for 5 days. Duration may be extended up to 7-10 days if lack of symptoms resolution at 5 days. o Incision and drainage in purulent cellulitis • **Typical (non-purulent) cellulitis - Empiric antibiotic regimens. Normal renal**

	function - Target Pathogens: S. aureus and streptococci, CA-MRSA is unusual - Outpatient therapy or step-down, one of the following oral antibiotics ▪ Amoxicillin-clavulanate 1 g every 8 h ▪ Cephalexin 500 mg every 6 h ▪ In patients at risk for CA-MRSA including immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days, with cellulitis associated with penetrating trauma especially from illicit drug use or who do not respond to first-line therapy add one of the following oral antibiotics ▪ Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h ▪ Minocycline 100 mg every 12 h ▪ Doxycycline 100 mg every 12 h Or o **In patients with beta-lactam allergy** ▪ Clindamycin 300 mg every 8 h Or o **Inpatient therapy,** one of following intravenous antibiotics ▪ Cefazolin 2 g every 8 h ▪ Amoxicillin-clavulanate 1.2/2.2 gr every 8 h Or o **In patients at risk for CA-MRSA including critically ill and immunocompromised status, personal or household contact with MRSA infection or colonization in the past 12 months, with prior antibiotic use for 5 days during the last 90 days, with cellulitis associated with penetrating trauma especially from illicit drug use or who do not respond to first-line therapy one of the following intravenous antibiotics** ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h ▪ Linezolid 600 mg every 12 h o **In patients at risk for Gram-negative infections or severe forms who do not**

	respond to first-line therapy ▪ Consider Piperacillin/tazobactam 4,5 g every 6 h. • Purulent cellulitis o Incision and drainage are recommended as primary management for abscesses with associated cellulitis. In these cases, antibiotics is generally suggested. o **Empiric antibiotic regimens. Normal renal function - Target Pathogen: S. aureus including CA-MRSA - Outpatient therapy or step-down, one of the following oral antibiotics** ▪ Amoxicillin-clavulanate 1 g every 8 h ▪ Cephalexin 500 mg every 6 h Or o **In a region or a population with a high prevalence of CA-MRSA, where > 10% of clinical S. aureus isolates are MRSA isolates or in patients at high risk for CA-MRSA** ▪ Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h ▪ Minocycline 100 mg every 12 h ▪ Doxycycline 100 mg every 12 h Or o **Inpatient therapy,** one of the following intravenous antibiotics ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h ▪ Linezolid 600 mg every 12 h o **In patients at risk for Gram-negative infections or severe forms who do not respond to first-line therapy** ▪ Consider Piperacillin/tazobactam 4,5 g every 6 h. • In neutropenic and immunocompromised patients, Gram-negative bacteria should be considered. • Treatment of perianal and perirectal abscesses:

	○ Incision and drainage + antibiotic therapy for 5 days in selected patients. You may extend therapy up to 7–10 days if lack of symptom resolution at 5 days. ○ In perianal and perirectal abscesses identification of eventual fistula tract, and either proceed with primary fistulotomy to prevent recurrence (only in cases of low fistula not involving the sphincter muscle) or place a draining seton for future consideration. Fistulotomy can risk continence if too extensive and placement of seton should only be performed if the tract and openings are very clear, as there is risk of creating a false internal orifice and complicating the condition. ○ **Empiric antibiotic regimens. Normal renal function - Target Pathogen: Gram-positive and Gram-negative - Outpatient therapy or step-down, one of the following antibiotics** ▪ Amoxicillin/clavulanate 1 g every 8 h Or ○ **In patients with beta-lactam allergy** ▪ Ciprofloxacin 500 mg every 8 h + Metronidazole 500 mg every 8 h ○ **In patients at risk for CA-MRSA or who do not respond to first-line therapy add one of following oral antibiotics** ▪ Minocycline 100 mg every 12 h ▪ Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h ▪ Doxycycline 100 mg every 12 h Or ○ **Inpatient therapy -** One of following intravenous antibiotics ▪ Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h ▪ Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h ▪ Piperacillin/tazobactam 4,5 g every 6 h Or ○ **In patients with beta-lactam allergy** ▪ Ciprofloxacin 400 mg every 8 h + Metronidazole 500 mg every 8 h

	○ **In patients at risk for CA-MRSA or who do not respond to first-line therapy add one of following intravenous antibiotics** ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h ▪ Linezolid 600 mg every 12 h • Treatment of bite wounds (animal and human bites) ○ Irrigation of the wound and debridement of necrotic tissue ○ Antibiotic prophylaxis as principle is not recommended. It is recommended in selected patients. ○ Antibiotic therapy in selected patients for 5 days. The duration may be extended up to 7–10 days if lack of symptom resolution at 5 days. ○ Tetanus prophylaxis in bite wounds • Treatment of pressure ulcers: ○ Prevention by pressure redistribution devices such as high-specification foam mattresses or cushions, or both and by frequent patient repositioning ○ Debridement of devitalized tissue and biofilm and abscess drainage ○ Appropriate selection of dressings and topical agents ○ Routine use of systemic antibiotics is not currently recommended for the treatment of uninfected pressure ulcers. Systemic antibiotics should be administered only when there are systemic signs of inflammation (serious infection), spreading cellulitis (deep skin infection) or underlying osteomyelitis. ○ Medical and nutritional patient optimization • Treatment of burn wounds: ○ Early initiation of dressings and effective topical antimicrobial therapy ○ Daily inspection of the wounds by a qualified surgeon or wound care expert ○ Early excision of all full thickness and deep partial thickness burns ○ Systemic antibiotic for infected wounds ○ Graft and coverage options ○ **Empiric antibiotic regimens. Normal renal function - Target Pathogen:**

	Gram-positive and Gram-negative - Outpatient therapy or step-down, one of the following antibiotics ▪ Amoxicillin/clavulanate 1 g every 8 h Or ○ **In patients with beta-lactam allergy** ▪ Ciprofloxacin 500 mg every 12 h + Metronidazole 500 mg every 8 h ○ *First-generation cephalosporins, such as cephalexin, penicillinase-resistant penicillins, macrolides such as erythromycin, and clindamycin, all have poor in vitro activity against Pasteurella multocida and should be avoided in animal bites.* ○ **In patients at risk for CA-MRSA or who do not respond to first-line therapy add - One of following oral antibiotics** ▪ Minocycline 100 mg every 12 h ▪ Trimethoprim and sulfamethoxazole 160/800–320/1600 mg every 12 h ▪ Doxycycline 100 mg every 12 h Or ○ **Inpatient therapy, one of following intravenous antibiotics** ▪ Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h ▪ Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h ▪ Piperacillin/tazobactam 4,5 g every 6 h Or ○ **In patients with beta-lactam allergy** ▪ Ciprofloxacin 200 mg every 8 h + Metronidazole 500 mg every 8 h ○ **In patients at risk for CA-MRSA or who do not respond to first-line therapy add** ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 12 h ▪ Linezolid 600 mg every 12 h • Treatment of necrotizing fasciitis:

	○ Surgical source control as soon as possible within 6 h after admission. Delay in early surgical increases mortality. ○ Appropriate and effective debridement techniques. Skin-sparing debridement techniques focusing on tissue directly involved in necrosis. ○ Re-explorations should be repeated until the time when very little or no debridement is required. ○ Empiric antibiotic therapy optimizing Pharmacokinetics (PK) and Pharmacodynamics (PD) targets. ○ Deep samples collected at the interface between healthy and necrotized tissues during initial debridement and blood cultures allow the identification of causative pathogens in most cases. ○ De-escalation of antibiotic therapy be based on clinical improvement, cultured pathogens, and results of rapid diagnostic tests where available ○ (Organ) supportive measures ○ Hyperbaric oxygen therapy where it is available ○ Intravenous immunoglobulin (IVIG) in patients with streptococcal NSTIs • Wound management after source control: ○ Empiric antibiotic regimens. Normal renal function - The initial empirical antibiotic regimen should comprise broad-spectrum drugs, including anti-MRSA and anti-Gram-negative coverage. Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs. ○ **In stable patients,** one of the following antibiotics ▪ Amoxicillin/clavulanate 1.2/2.2 g every 8 h ▪ Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h ▪ Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h + ▪ Clindamycin 600–900 mg every 8 h ○ **In unstable patients,** one of the following antibiotics

	▪ Piperacillin/tazobactam 4.5 g every 6 h ▪ Meropenem 1 g every 8 h ▪ Imipenem/Cilastatin 500 mg every 6 h + o One of the following antibiotics ▪ Linezolid 600 mg every 12 h ▪ Tedizolid 200 mg every 24 h Or o Another anti-MRSA-antibiotic as ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 8 h ▪ Daptomycin 6–8 mg/kg every 24 h * ▪ Telavancin 10 mg/kg every 24 h + ▪ Clindamycin 600–900 mg every 8 h *Approved at the dosage of 4–6 mg/kg/24 h, it is currently used at higher dosages. • Fournier's gangrene: o Surgical source control as soon as possible. Re-explorations should be repeated until the time when very little or no debridement is required. o Diverting colostomy or rectal diversion devices o Antibiotic therapy o (Organ) supportive measures o The initial empirical antibiotic regimen should comprise broad-spectrum drugs, including anti-MRSA and anti-Gram-negative coverage. Antitoxin active antibiotics such as clindamycin or linezolid should be included in the empirical antibiotic regimen to treat NSTIs. o **In stable patients, one of the following antibiotics** ▪ Amoxicillin/clavulanate 1.2/2.2 g every 8 h ▪ Ceftriaxone 2 g every 24 h + Metronidazole 500 mg every 8 h

	▪ Cefotaxime 2 g every 8 h + Metronidazole 500 mg every 8 h + ▪ Clindamycin 600–900 mg every 8 h o **In unstable patients, one of the following antibiotics** ▪ Piperacillin/tazobactam 4.5 g every 6 h ▪ Meropenem 1 g every 8 h ▪ Imipenem/Cilastatin 500 mg every 6 h + o One of the following antibiotics ▪ Linezolid 600 mg every 12 h ▪ Tedizolid 200 mg every 24 h Or o Another anti-MRSA-antibiotic as ▪ Vancomycin 25–30 mg/kg loading dose then 15–20 mg/kg/dose every 8 h ▪ Teicoplanin LD 12 mg/kg 12-hourly for 3 doses, then 6 mg/kg every 12 h ▪ Daptomycin 6–8 mg/kg every 24 h * ▪ Telavancin 10 mg/kg every 24 h + ▪ Clindamycin 600–900 mg every 8 h *Approved at the dosage of 4 mg/kg/24 h, it is currently used at higher dosages. • Water and soil-borne nectrotizing fasciitis: o Most cases of A. hydrophila wound infection occur in healthy people. In particular, A. hydrophila wound infection is reported following natural disasters, such as the tsunami and hurricane. The wound infections due to A. hydrophila can progress rapidly to NSTIs. o Patients with a presumptive diagnosis of V. vulnificus should be treated immediately by antibiotics and managed aggressively by a prompt debridement and resuscitation in an intensive care unit to minimize the

	possible consequences of hypotension, septic shock, and the risk of multiorgan system failure. • Treatment of gas gangrene: o Because the infection is rapidly progressive, it is important to treat patients aggressively, by early surgical debridement, antibiotics and intravenous fluid resuscitation. • New agents to treat NSTIs: o Reltecimod (previously known as AB103 or p2TA), a peptide derived from the T-cell receptor CD28, modulates the host immune response by targeting the costimulatory pathway, which is essential for the induction of multiple pro-inflammatory cytokines. o Consequently, reltecimod has demonstrated beneficial effects against different bacterial infections such as NSTIs. o A randomized, double-blind, placebo-controlled trial of single dose reltecimod (0.5 mg/kg) administered within 6 h of NSTI diagnosis was recently published. o Reltecimod was associated with improved resolution of organ dysfunction and hospital discharge status. o Further studies are warranted to establish the real efficacy in clinical practice. • Mesh infection: o The usual causative micro-organisms associated mesh infection are S. aureus including MRSA, S. epidermidis and streptococci and Gram-negative bacteria including Enterobacteriaceae. o The aim of the infection prevention and control strategies including surgical antibiotic prophylaxis is to minimize bacterial count in the wound and decrease adherence to the mesh preventing biofilm production; thereby blocking the key step for mesh infection. o The management of mesh infections is challenging and always requires an individualized approach combining medical and surgical approaches. o Although, several studies have demonstrated that in certain instances, non-

	operative strategies with conservative (non-surgical) management have been successful for salvaging a mesh in many cases complete surgical removal of the mesh is suggested to reduce the risk of infection recurrence or severe complications, such as visceral adhesions and fistulae. o After removing the infected mesh, the intra-operative options are (a) no implant of a new mesh, (b) re-implantation of a new synthetic light-weight, microporous mesh, and (c) replacement of the infected synthetic by a biological mesh.
Section 1.1.8 **NHS Foundation Trust Guideline for skin and soft tissue infection including diabetic foot ulcer 2022**	Management of cellulitis: • Mark area of redness on skin (this will help with review of clinical progress) • Start empirical antibiotic as stated in table below. • Consider switch to oral antibiotic with good clinical response. • Review antibiotics at day 5, can extend if not fully resolved. • The choice of antimicrobial therapy may be guided by: o History of presenting complaint ▪ Acute or chronic ▪ Circumstances surrounding the development of the skin & soft tissue infection (SSTI) o Significant past medical history: ▪ Diabetes ▪ Immunocompromised state ▪ Similar presentation with SSTI previously, etc. o Recent antimicrobial history within the last one month o Previous or recent positive microbiology results Management of Necrotizing fasciitis: • Necrotising fasciitis can be categorized into 2 groups o **Type 1** is a mixed infection including anaerobes, gram negative organisms and gram-positive organisms. Mostly occurs in immunocompromised individuals.

Typically occurs in the perineum and trunk, and
    - **Type 2** is mainly due to Group A streptococcus with or without Staphylococcus aureus. This is less common than the type 1. Typically occur in the limbs and affects healthy individuals, with often associated history of trauma (usually minor).
- If necrotizing fasciitis is suspected the patient must be referred for IMMEDIATE review by a senior clinician, as this is a rapidly progressing, life threatening infection.
- Surgical exploration is essential to definitively establish the diagnosis from other entities, also in obtaining samples for culture to identify the pathogen involved and as part of treatment, which consist of wide debridement of skin, subcutaneous tissue, fascia and any necrotic muscle, and may require multiple debridements. The use of antibiotics without debridement is associated with mortality rate approaching 100%.
- Discuss with microbiologist if the region involved includes the perineum, scrotum (as in Fournier's gangrene) or if there is risk of polymicrobial involvement.
- Blood cultures are positive in about 60% and 20% of type 2 and type 1 necrotizing fasciitis respectively.
- The table below showcases the empirical antibiotic guide for skin and soft tissue infection by the NHS foundation trust 2022:

CLINICAL CONDITION	FIRST LINE	PENICILLIN ALLERGY	MRSA	Duration
Mild to moderate cellulitis	Oral Flucloxacillin 500mg -1g, 6 hourly	Oral Clarithromycin 500mg 12 hourly	**Use options in Penicillin allergy.** **If resistant** to Clarithromycin and Clindamycin, use: IV Vancomycin (refer to Trust	5-7 days **OR** until full resolution, whichever is later.
Moderate to severe cellulitis	IV Flucloxacillin 1-2g, 6 hourly	IV Clindamycin 600mg -1.2g, 6 hourly		
Erysipelas and impetigo	Oral Flucloxacillin 500mg -1g, 6 hourly (consider IV if severe)	Oral Clarithromycin 500mg 12		

			hourly	policy for dosing) **OR** Oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring)	
	Necrotising fasciitis: Type 1	IV Piperacillin/tazobactam 4.5g 8 hourly **AND** IV Clindamycin 1.2g 6 hourly	IV Meropenem 1g 8 hourly **AND** IV Clindamycin 1.2g 6 hourly	**If resistant** to Clindamycin use: IV Meropenem 1g 8 hourly **AND** IV Linezolid 600mg 12 hourly	5-7 days **OR** until full resolution, whichever is later.
	Necrotising fasciitis: Type 2	IV Benzylpenicillin 1.2 - 2.4gm 6 hourly **AND** IV Clindamycin 1.2g 6 hourly	**Non-severe allergy:** IV Ceftriaxone 1 - 2g 12 hourly **AND** IV Clindamycin 1.2g 6 hourly **Penicillin anaphylaxis:**	**If resistant** to Clindamycin use: IV Ceftriaxone 1 – 2g 12 hourly **AND** IV Linezolid 600mg 12 hourly (Ensure no drug	

			IV Ciprofloxacin 400mg 8 - 12 hourly **AND** IV Clindamycin 1.2g 6 hourly	interactions. Requires weekly FBC monitoring)	
		Consider administering IVIG for patients with Type 2 infections who are critically unwell			
	Cellulitis associated with bite (e.g. Human, dog, cat)	IV Co-amoxiclav 1.2g, 8 hourly **OR** Oral Co-amoxiclav 625mg, 8 hourly if mild to moderate	Oral Ciprofloxacin 500mg, 12 hourly **AND** Oral Clindamycin 300mg-450mg, 6 hourly	**If resistant** to Clindamycin and Ciprofloxacin: Add oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring)	10 days
	Cutaneous abscess (including Intravenous Drug Abuser)	IV Flucloxacillin 1-2g, 6 hourly **AND** Oral Metronidazole 400mg 8 hourly **OR** Oral Flucloxacillin 500mg-1g, 6 hourly **AND** Oral Metronidazole 400mg 8 hourly	**Non-severe allergy**: IV Cefuroxime 750mg -1.5g 8hrly **AND** Oral Metronidazole 400mg 8hrly	Oral Clindamycin 450mg 6 hourly **If resistant to Clindamycin use:** Oral	5-7 days **OR** until full resolution, whichever is later.

			Penicillin anaphylaxis: Oral Clindamycin 450mg 6hrly	Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring) **AND** Oral Metronidazole 400mg 8 hourly	
	Cellulitis associated with sea or fresh water contact	Oral Doxycycline 100mg 12 hourly **AND** IV Ceftazidime 2g 8 hourly	Oral Doxycycline 100mg 12 hourly **AND** Oral Ciprofloxacin 500mg, 12 hourly	**If resistant** to Doxycycline then use: Oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring) **AND** Oral Ciprofloxacin 500mg 12 hourly	5-7 days **OR** until full resolution, whichever is later.
	Cellulitis associated	Contact Microbiologist			

	with fish tank water exposure				
	Orbital cellulitis	IV Ceftriaxone 1-2g, 12 hourly **AND** Oral Metronidazole 400mg 8 hourly	Contact Microbiologist	Add Linezolid 600mg 12 hourly IV/PO (Ensure no drug interactions. Requires weekly FBC monitoring)	10 days
	Mild to moderate infected foot ulcer	IV Flucloxacillin 1-2g 6 hourly **AND** oral Metronidazole 400mg 8 hourly	IV Clindamycin 600mg 6 hourly (monotherapy) **OR** Oral Clarithromycin 500mg 12 hourly **AND** oral Metronidazole 400mg 8 hourly		5-7 days OR until full resolution, whichever is later Review antimicrobial choice with culture results. Surgical debridement is essential
	Severe infected foot ulcer	IV Co-amoxiclav 1.2g 8 hourly **OR** Oral Co-amoxiclav 625mg 8 hourly **OR** treat according to culture	IV Clindamycin 600mg -1.2gm 6 hourly **OR** Oral Clindamycin		

		and sensitivity	450mg 6 hourly **OR** Treat according to culture and sensitivity		
	Clinical evidence of osteomyelitis at site of foot ulcer (in mild to severe foot ulcer)	IV Flucloxacillin 1-2g 6 hourly **AND** oral Fusidic acid 500mg 8 hourly **OR** treat according to culture and sensitivity	IV Clindamycin 600mg – 1.2g 6 hourly **AND** oral Fusidic acid 500mg 8 hourly **OR** Treat according to culture and sensitivity		4-6 weeks
	History of positive MRSA from foot ulcer swab/tissue sample (in mild to severe cases)	Oral Linezolid 600mg 12 hourly (Ensure no drug interactions. Requires weekly FBC monitoring) **AND** Oral Metronidazole 400mg 8 hourly	Discuss with Microbiologist if patient cannot have any of first line treatment.		5-7 days **OR** until full resolution, whichever is later
	➔ NOTE: Never use Fusidic acid on its own				
HTA Pharmacoeconomics Analysis	Recommendations from HTA bodies should be added under each drug therapy section as they are missing from the previous/initial document.				

Appendix C. MeSH Terms PubMed

C.1 PubMed Search for Bacterial Skin Infections:

Query	Filters	Search Details	Results
(((((((Fasciitis, Necrotizing[MeSH Terms]) OR (Fasciitides, Necrotizing[Title/Abstract])) OR (Necrotizing Fasciitides[Title/Abstract])) OR (Necrotizing Fasciitis[Title/Abstract])) OR (Fascitis, Necrotizing[Title/Abstract])) OR (Fascitides, Necrotizing[Title/Abstract])) OR (Necrotizing Fascitides[Title/Abstract])) OR (Necrotizing Fascitis[Title/Abstract])	Guideline, in the last 10 years	("fasciitis, necrotizing"[MeSH Terms] OR (("Fasciitis"[MeSH Terms] OR "Fasciitis"[All Fields] OR "Fasciitides"[All Fields]) AND "Necrotizing"[Title/Abstract]) OR (("necrosis"[MeSH Terms] OR "necrosis"[All Fields] OR "necrotic"[All Fields] OR "necrotizing"[All Fields] OR "necrotization"[All Fields] OR "necrotize"[All Fields] OR "necrotized"[All Fields] OR "Necrotizing"[All Fields]) AND "Fasciitides"[Title/Abstract]) OR "necrotizing fasciitis"[Title/Abstract] OR (("Fasciitis"[MeSH Terms] OR "Fasciitis"[All Fields] OR "Fascitis"[All Fields]) AND "Necrotizing"[Title/Abstract]) OR (("Fasciitis"[MeSH Terms] OR "Fasciitis"[All Fields]) AND "Necrotizing"[Title/Abstract]) OR "necrotizing fascitis"[Title/Abstract]) AND ((y_10[Filter]) AND (guideline[Filter]))	5
(((((((Fasciitis, Necrotizing[MeSH Terms]) OR (Fasciitides, Necrotizing[Title/Abstract])) OR (Necrotizing Fasciitides[Title/Abstract])) OR (Necrotizing Fasciitis[Title/Abstract])) OR (Fascitis,	Meta-Analysis, Randomized Controlled Trial, in the last 5 years	("fasciitis, necrotizing"[MeSH Terms] OR (("Fasciitis"[MeSH Terms] OR "Fasciitis"[All Fields] OR "Fasciitides"[All Fields]) AND "Necrotizing"[Title/Abstract]) OR (("necrosis"[MeSH Terms] OR "necrosis"[All Fields] OR "necrotic"[All Fields] OR	13

Necrotizing[Title/Abstract])) OR (Fascitides, Necrotizing[Title/Abstract])) OR (Necrotizing Fascitides[Title/Abstract])) OR (Necrotizing Fascitis[Title/Abstract])		"necrotizing"[All Fields] OR "necrotization"[All Fields] OR "necrotize"[All Fields] OR "necrotized"[All Fields] OR "Necrotizing"[All Fields]) AND "Fasciitides"[Title/Abstract]) OR "necrotizing fasciitis"[Title/Abstract] OR (("Fasciitis"[MeSH Terms] OR "Fasciitis"[All Fields] OR "Fascitis"[All Fields]) AND "Necrotizing"[Title/Abstract]) OR (("Fasciitis"[MeSH Terms] OR "Fasciitis"[All Fields]) AND "Necrotizing"[Title/Abstract]) OR "necrotizing fascitis"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomized controlled trial[Filter]))	
(((Wound Infection[MeSH Terms]) OR (Infection, Wound[Title/Abstract])) OR (Infections, Wound[Title/Abstract])) OR (Wound Infections[Title/Abstract])	Meta-Analysis, Randomized Controlled Trial, in the last 5 years	("wound infection"[MeSH Terms] OR "infection wound"[Title/Abstract] OR "infections wound"[Title/Abstract] OR "wound infections"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomized controlled trial[Filter]))	1,091
(((Wound Infection[MeSH Terms]) OR (Infection, Wound[Title/Abstract])) OR (Infections, Wound[Title/Abstract])) OR (Wound Infections[Title/Abstract])	Guideline, in the last 5 years	("wound infection"[MeSH Terms] OR "infection wound"[Title/Abstract] OR "infections wound"[Title/Abstract] OR "wound infections"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	14

(Lymphangitis[MeSH Terms]) OR (Lymphangitides[Title/Abstract])	Meta-Analysis, Randomized Controlled Trial, in the last 5 years	("lymphangitis"[MeSH Terms] OR "Lymphangitides"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomized controlled trial[Filter]))	1
(Lymphangitis[MeSH Terms]) OR (Lymphangitides[Title/Abstract])	Guideline, in the last 10 years	("lymphangitis"[MeSH Terms] OR "Lymphangitides"[Title/Abstract]) AND ((y_10[Filter]) AND (guideline[Filter]))	0
(Cellulitis[MeSH Terms]) OR (Phlegmon[Title/Abstract])	Guideline, in the last 10 years	("cellulitis"[MeSH Terms] OR "Phlegmon"[Title/Abstract]) AND ((y_10[Filter]) AND (guideline[Filter]))	3
(Cellulitis[MeSH Terms]) OR (Phlegmon[Title/Abstract])	Meta-Analysis, Randomized Controlled Trial, in the last 5 years	("cellulitis"[MeSH Terms] OR "Phlegmon"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomized controlled trial[Filter]))	31
(((Lymphadenitis[MeSH Terms]) OR (Lymphadenitides[Title/Abstract])) OR (Adenitis[Title/Abstract])) OR (Adenitides[Title/Abstract])	Meta-Analysis, Randomized Controlled Trial, in the last 5 years	("lymphadenitis"[MeSH Terms] OR "Lymphadenitides"[Title/Abstract] OR "Adenitis"[Title/Abstract] OR "Adenitides"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomized controlled trial[Filter]))	9
(((Lymphadenitis[MeSH Terms]) OR (Lymphadenitides[Title/Abstract])) OR (Adenitis[Title/Abstract])) OR (Adenitides[Title/Abstract])	Guideline, in the last 10 years	("lymphadenitis"[MeSH Terms] OR "Lymphadenitides"[Title/Abstract] OR "Adenitis"[Title/Abstract] OR "Adenitides"[Title/Abstract]) AND ((y_10[Filter]) AND	3

		(guideline[Filter]))	
((((((Impetigo[MeSH Terms])) OR (Impetigo Contagiosa[Title/Abstract])) OR (Impetigos[Title/Abstract])) OR (Contagiosa, Impetigo[Title/Abstract])) OR (Contagiosas, Impetigo[Title/Abstract])) OR (Impetigo Contagiosas[Title/Abstract])	Guideline, in the last 10 years	("Impetigo"[MeSH Terms] OR "impetigo contagiosa"[Title/Abstract] OR "Impetigos"[Title/Abstract] OR ("Contagiosa"[All Fields] AND "Impetigo"[Title/Abstract]) OR ("Contagiosas"[All Fields] AND "Impetigo"[Title/Abstract])) AND ((y_10[Filter]) AND (guideline[Filter]))	0
((((((Impetigo[MeSH Terms])) OR (Impetigo Contagiosa[Title/Abstract])) OR (Impetigos[Title/Abstract])) OR (Contagiosa, Impetigo[Title/Abstract])) OR (Contagiosas, Impetigo[Title/Abstract])) OR (Impetigo Contagiosas[Title/Abstract])	Meta-Analysis, Randomized Controlled Trial, in the last 5 years	("Impetigo"[MeSH Terms] OR "impetigo contagiosa"[Title/Abstract] OR "Impetigos"[Title/Abstract] OR ("Contagiosa"[All Fields] AND "Impetigo"[Title/Abstract]) OR ("Contagiosas"[All Fields] AND "Impetigo"[Title/Abstract])) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomized controlled trial[Filter]))	6
((Furunculosis[MeSH Terms]) OR (Boils[Title/Abstract])) OR (Furuncles[Title/Abstract])	Meta-Analysis, Randomized Controlled Trial, in the last 5 years	("furunculosis"[MeSH Terms] OR "Boils"[Title/Abstract] OR "Furuncles"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomized controlled trial[Filter]))	2
((Furunculosis[MeSH Terms]) OR (Boils[Title/Abstract])) OR (Furuncles[Title/Abstract])	Guideline, in the last 5 years	("furunculosis"[MeSH Terms] OR "Boils"[Title/Abstract] OR "Furuncles"[Title/Abstract]) AND ((y_5[Filter]) AND	0

		(guideline[Filter]))	
(((folliculitis[MeSH Terms]) OR (Folliculitides[Title/Abstract])) OR (Sycosis[Title/Abstract])) OR (Sycoses[Title/Abstract])	Guideline, in the last 5 years	("folliculitis"[MeSH Terms] OR "Folliculitides"[Title/Abstract] OR "Sycosis"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	0
(((folliculitis[MeSH Terms]) OR (Folliculitides[Title/Abstract])) OR (Sycosis[Title/Abstract])) OR (Sycoses[Title/Abstract])	Meta-Analysis, Systematic Review, in the last 5 years	("folliculitis"[MeSH Terms] OR "Folliculitides"[Title/Abstract] OR "Sycosis"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR systematic review[Filter]))	6
erythrasma[MeSH Terms]	Meta-Analysis, Systematic Review, in the last 5 years	("erythrasma"[MeSH Terms]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR systematic review[Filter]))	0
erythrasma[MeSH Terms]	Guideline, in the last 10 years	("erythrasma"[MeSH Terms]) AND ((y_10[Filter]) AND (guideline[Filter]))	0
(Carbuncle[MeSH Terms]) OR (Carbuncles[Title/Abstract])	Guideline, in the last 10 years	("carbuncle"[MeSH Terms] OR "Carbuncles"[Title/Abstract]) AND ((y_10[Filter]) AND (guideline[Filter]))	0
(Carbuncle[MeSH Terms]) OR (Carbuncles[Title/Abstract])	Meta-Analysis, Systematic Review, in the last 5 years	("carbuncle"[MeSH Terms] OR "Carbuncles"[Title/Abstract]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR systematic review[Filter]))	3
ecthyma[MeSH Terms]	Guideline, in the last 10 years	("ecthyma"[MeSH Terms]) AND ((y_10[Filter]) AND (guideline[Filter]))	0
Erysipelas[MeSH Terms]	Guideline, in the last 10 years	("erysipelas"[MeSH Terms]) AND ((y_10[Filter]) AND (guideline[Filter]))	0
Erysipelas[MeSH Terms]	Meta-	("erysipelas"[MeSH Terms])	3

	Analysis, Systematic Review, in the last 5 years	AND ((y_5[Filter]) AND (meta-analysis[Filter] OR systematic review[Filter]))	
((((((Staphylococcal Skin Infections[MeSH Terms]) OR (Staphylococcal Skin Diseases[Title/Abstract])) OR (Staphylococcal Infections, Skin[Title/Abstract])) OR (Infections, Staphylococcal Skin[Title/Abstract])) OR (Skin Infections, Staphylococcal[Title/Abstract])) OR (Staphylococcal Diseases, Skin[Title/Abstract])) OR (Skin Diseases, Staphylococcal[Title/Abstract])	Guideline, in the last 10 years	("staphylococcal skin infections"[MeSH Terms] OR "staphylococcal skin diseases"[Title/Abstract] OR (("staphylococcic"[All Fields] OR "staphylococcus"[MeSH Terms] OR "staphylococcus"[All Fields] OR "Staphylococcal"[All Fields]) AND "infections skin"[Title/Abstract]) OR "infections staphylococcal skin"[Title/Abstract] OR "skin infections staphylococcal"[Title/Abstract] OR (("staphylococcic"[All Fields] OR "staphylococcus"[MeSH Terms] OR "staphylococcus"[All Fields] OR "Staphylococcal"[All Fields]) AND "diseases skin"[Title/Abstract]) OR (("Skin"[MeSH Terms] OR "Skin"[All Fields]) AND "diseases staphylococcal"[Title/Abstract])) AND ((y_10[Filter]) AND (guideline[Filter]))	0
((((((Staphylococcal Skin Infections[MeSH Terms]) OR (Staphylococcal Skin Diseases[Title/Abstract])) OR (Staphylococcal Infections, Skin[Title/Abstract])) OR (Infections, Staphylococcal	Meta-Analysis, Systematic Review, in the last 5 years	("staphylococcal skin infections"[MeSH Terms] OR "staphylococcal skin diseases"[Title/Abstract] OR (("staphylococcic"[All Fields] OR "staphylococcus"[MeSH Terms] OR	12

Skin[Title/Abstract])) OR (Skin Infections, Staphylococcal[Title/Abstract])) OR (Staphylococcal Diseases, Skin[Title/Abstract])) OR (Skin Diseases, Staphylococcal[Title/Abstract])		"staphylococcus"[All Fields] OR "Staphylococcal"[All Fields]) AND "infections skin"[Title/Abstract]) OR "infections staphylococcal skin"[Title/Abstract] OR "skin infections staphylococcal"[Title/Abstract] OR (("staphylococcic"[All Fields] OR "staphylococcus"[MeSH Terms] OR "staphylococcus"[All Fields] OR "Staphylococcal"[All Fields]) AND "diseases skin"[Title/Abstract]) OR (("Skin"[MeSH Terms] OR "Skin"[All Fields]) AND "diseases staphylococcal"[Title/Abstract])) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR systematic review[Filter]))	
Ecthyma[MeSH Terms]	Meta-Analysis, Systematic Review, in the last 5 years	("ecthyma"[MeSH Terms]) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR systematic review[Filter]))	0

Appendix D. Treatment Algorithm of Bacterial Skin Infections

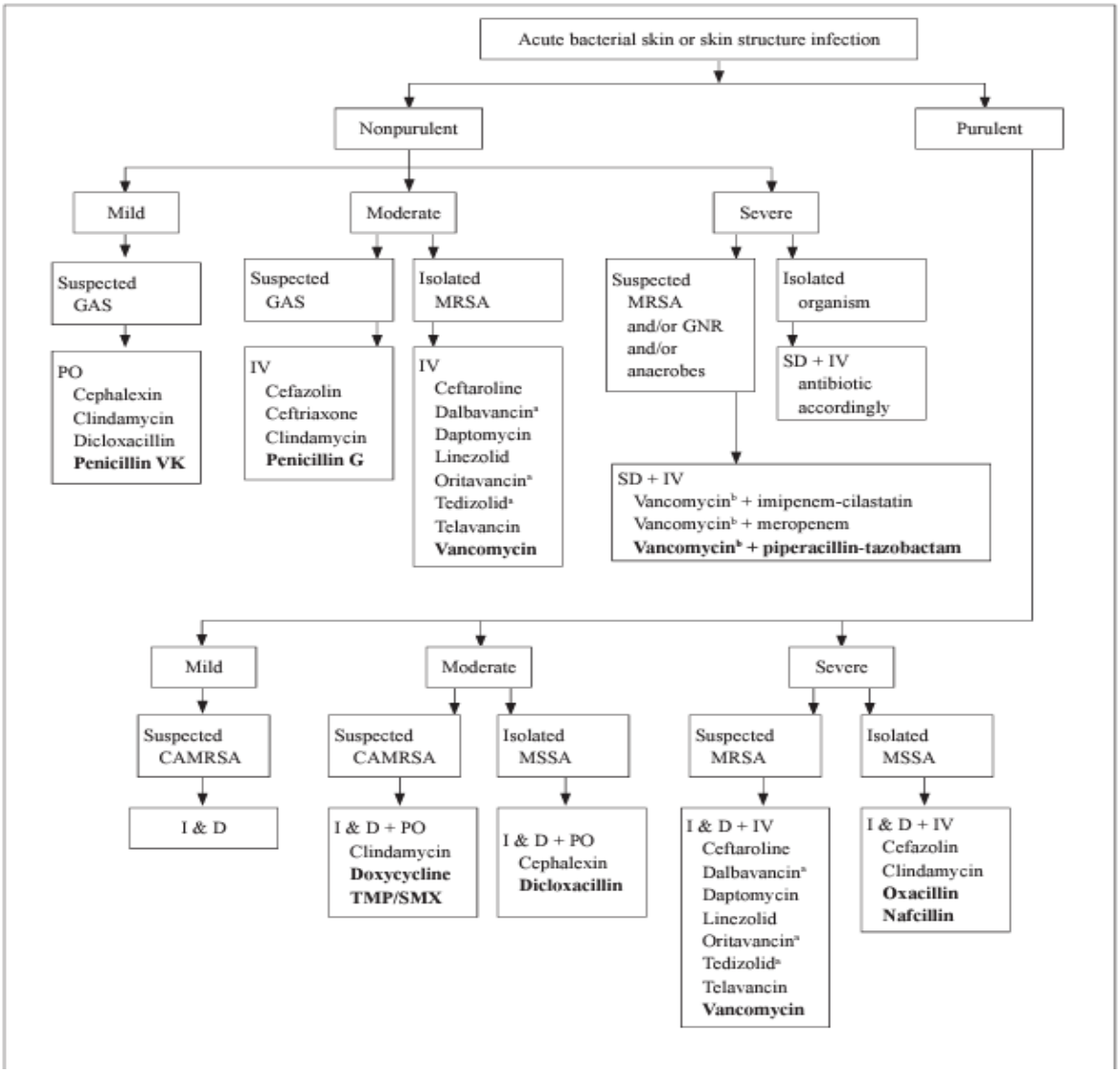

Figure 1. *General Approach to the Management of Acute Bacterial Skin and Skin Structure Infections. Bolding Indicates Antibiotic of Choice.*

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[1] [a]Not included in the 2014 IDSA guidelines for the management of skin and soft tissue infections.
[b]An alternative new anti-MRSA antibiotic can also be used.
CAMRSA = community-associated methicillin-resistant Staphylococcus aureus; GAS = Group A β-hemolytic Streptococcus; GNR = gram-negative rods; I & D = incision and drainage; IV = intravenous; MRSA = methicillin-resistant Staphylococcus aureus; MSSA = methicillin-sensitive Staphylococcus aureus; PO = oral; SD = surgical debridement. Information from: Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis 2014;59:e10-52.

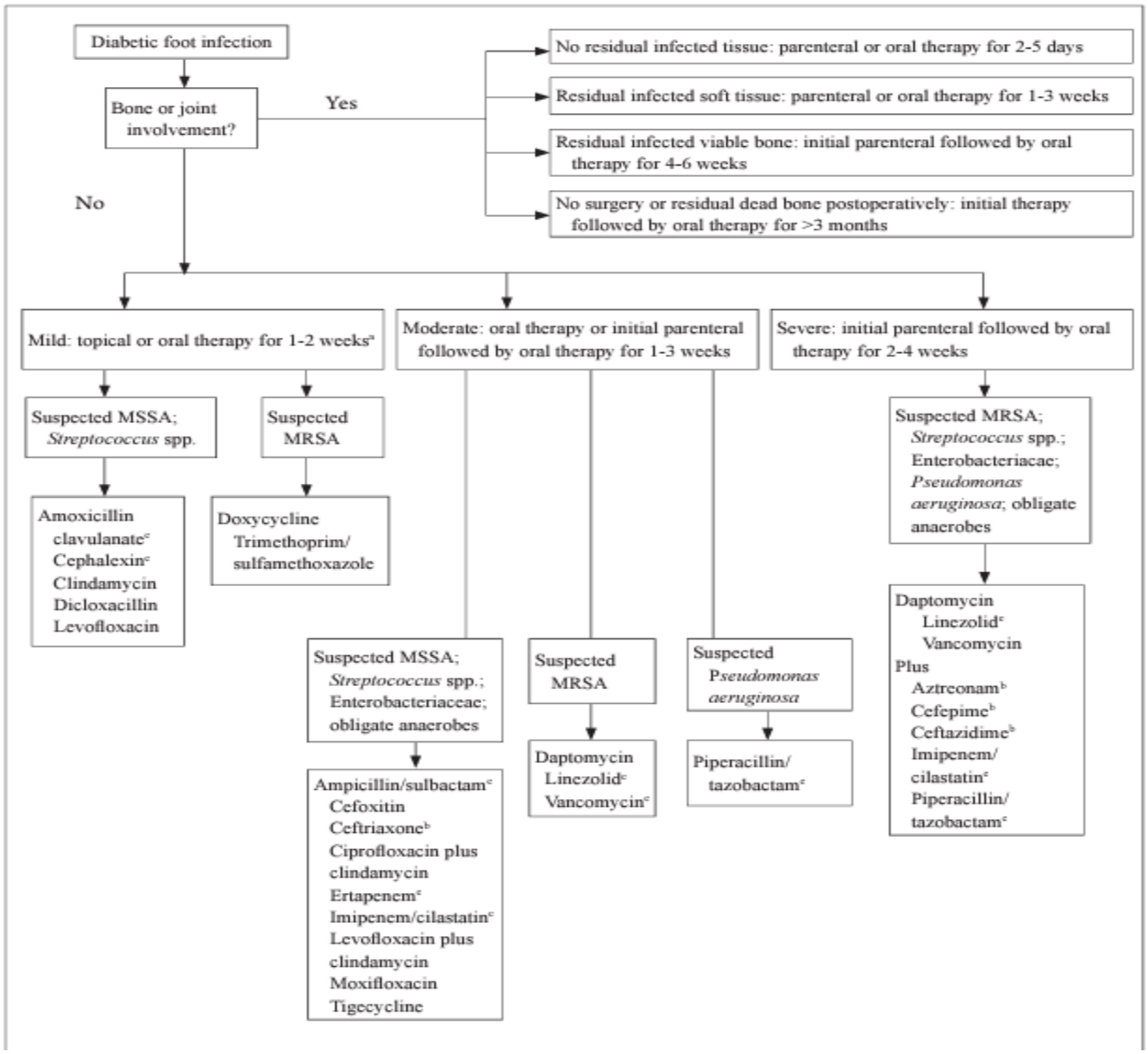

Figure 2. *General approach to the Management of Diabetic Foot Infection. Note: Agents Similar to those Listed in this Algorithm Can Be Substituted Based on Clinical, Epidemiologic, and Financial Considerations.*

[2]

[2]

[a]May extend up to 4 weeks if slow to resolve. [b]Consider adding an antibiotic with activity against obligate anaerobes cAgents commonly used as comparators in clinical trials for the treatment of diabetic foot infections. MRSA = methicillin-resistant Staphylococcus aureus; MSSA = methicillin-sensitive Staphylococcus aureus. Information from: Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54:e132-73.