BACTERIAL CONJUNCTIVITIS

CHI Formulary Indication Review

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- September 2023

To the CHI Original Bacterial Conjunctivitis Clinical Guidance- Issued June 2020

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- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
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Abbreviations

CDC	Centers for Disease Control and Prevention
CHI	Council of Health Insurance
COO	The College of Optometrists
CPG	Clinical Practice Guideline
EMA	European Medicines Agency
FDA	Food and Drug Administration
GC	Gonococcal Conjunctivitis
IDF	CHI Drug Formulary
IM	Intramuscular
IV	Intravenous
MRSA	Methicillin-Resistant *Staphylococcus aureus*
ON	Ophthalmia Neonatorum
SFDA	Saudi Food and Drug Authority
USPSTF	US Preventive Services Task Force
WHO	World Health Organization

Executive Summary

Conjunctivitis, commonly referred to as "pink eye," is the predominant ophthalmologic condition observed in primary care clinics. Patients typically come in with complaints of redness in the eyes, sometimes accompanied by discomfort, itching, and discharge[1]. Bacterial Conjunctivitis is characterized by mucopurulent discharge and mattering of eyelids upon waking[2].

Conjunctivitis can be categorized into three primary types: allergic conjunctivitis, infectious conjunctivitis (which includes viral or bacterial conjunctivitis and ophthalmia neonatorum), and chemical conjunctivitis caused by exposure to harmful chemicals[3]. Although viral and allergic conjunctivitis are more common, bacterial conjunctivitis poses a greater health risk and presents a more complex clinical situation for physicians[1]. Complications from bacterial conjunctivitis are uncommon; however, severe infections can result in keratitis, corneal ulceration and perforation, and blindness[1].

About 1% of all primary care office visits in the United States are related to conjunctivitis, affecting about 6 million people annually[4]. Among general practitioner visits in developed countries, one to four percent are related to red eyes, with acute bacterial conjunctivitis being the most frequently diagnosed condition. Bacterial conjunctivitis tends to have a peak occurrence from December to April. Among infectious causes, bacterial conjunctivitis is the second most prevalent, and it affects children more frequently than other age groups[1].

The estimated annual direct cost of conjunctivitis in the United States is approximately $800 million[5].

The mainstay of treatment of bacterial conjunctivitis is topical antibiotic therapy. Systemic antibiotics are indicated for N gonorrhoeae and chlamydial infections[4].

CHI issued Bacterial Conjunctivitis clinical guidance after thorough review of renowned international and national clinical guidelines in June 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 Conjunctivitis clinical guidance and seeks to offer guidance for the effective management of Bacterial Conjunctivitis. It provides an **update on the Bacterial Conjunctivitis 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 updated versions of previously reviewed guidelines** namely Sexually Transmitted Infections

Summary of CDC Treatment Guidelines—**2021**, **the missing recommendations from** Conjunctivitis Preferred Practice Pattern [**2018** by the American Academy of Ophthalmology] adult and pediatric. Moreover, **new guidelines are added to the report** such as Primary Care Approach to Eye Conditions **2019**, A Systematic Review of Clinical Practice Guidelines for Infectious and Non-infectious Conjunctivitis **2021**, Conjunctivitis: A Systematic Review **2020**, Red Eye Diagnosis and Management in Primary Health Care **2019**, Report of the WHO Expert Committee on Selection and Use of Essential Medicines, **2021** (including the 22nd WHO Model List of Essential Medicines and the 8th WHO Model List of Essential Medicines for Children), Conjunctivitis (bacterial) Clinical Management Guidelines of the College of Optometrists **2023**, and Saudi Ministry of Health Conjunctivitis **2021.**

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is important to note that there have been **no newly approved drugs** for the treatment of Bacterial Conjunctivitis. It is recommended to **delist** Polymyxin b + Bacitracin + Neomycin sulfate combination from CHI formulary, as it is no longer registered on the SFDA Drug List of July 2023. Additionally, there have been **updates** regarding certain previously mentioned drugs in terms of drug information and prescribing edits since June 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 Bacterial Conjunctivitis therapeutic management.

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

Table 1. General Recommendations for the Management of Bacterial Conjunctivitis

Management of Bacterial Conjunctivitis		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
Patients with a suspected diagnosis of Neisseria conjunctivitis should be referred to an ophthalmologist for aggressive management as it can quickly lead to vision loss secondary to corneal ulceration and perforation	Not graded	Primary Care Approach to Eye Conditions 2019[6]
Chlamydial conjunctivitis: Treatment includes erythromycin ophthalmic ointment and oral therapy with	Not graded	Primary Care Approach to Eye Conditions 2019[6]

azithromycin (single one gram dose) or doxycycline (100 mg twice a day for 14 days) to clear the infection. The patient's sexual partner should also be treated to prevent further infections and reinfection.		
Observation without treatment was strongly recommended in bacterial conjunctivitis (except chlamydial and gonorrheal conjunctivitis or trachoma) due to the usually self-limiting nature of the conditions.	Not graded	A Systematic Review of Clinical Practice Guidelines for Infectious and Non-infectious Conjunctivitis 2021[7]
For neonates infected by chlamydia, systemic erythromycin or topical azithromycin 1.5% was recommended; those infected by gonorrhea were recommended systemic Penicillin G or cephalosporin; and neonates with other types of bacterial infection were recommended topical erythromycin, azithromycin 1.5% or chloramphenicol 0.5%.	Not graded	A Systematic Review of Clinical Practice Guidelines for Infectious and Non-infectious Conjunctivitis 2021[7]
Due to lengthening the course of the illness and potentiating the infection, topical steroids should be avoided.	Not graded	Conjunctivitis: A Systematic Review 2020[8]
All antibiotics eye drops are of similar efficacy. Factors that influence antibiotic choice are local availability, patient allergies, resistance patterns, and cost.	Not graded	Conjunctivitis: A Systematic Review 2020[8]
Suspected cases of MRSA-infected conjunctivitis need to be treated with fortified vancomycin eye drops or ointments (Not available on the Saudi market). Culture directed administration of antimicrobials, effective dosing, considering the local resistance patterns, and appropriate antiseptic strategies should be applied to restrict the spread of MRSA conjunctivitis	Not graded	Conjunctivitis: A Systematic Review 2020[8]

For trachoma, the treatment of choice is oral azithromycin as a single dose of 1 g (or 20 mg/kg body weight in children) because of the potentially better efficacy and adherence with the single-dose regimen.	Not graded	WHO Expert Committee 2021[9]
Contact lens wearers with a diagnosis of bacterial conjunctivitis should be treated with a topical antibiotic effective against Gram negative organisms, such as an aminoglycoside (e.g. gentamycin) or a quinolone (e.g. levofloxacin or moxifloxacin). Contact lenses should not be worn until the condition has resolved.	Level of evidence = low, Strength of recommendation = strong	COO Guidelines 2023[10]
Treatment is conservative in this case, and can help relieve symptoms by cold compresses, moisturizing drops, avoiding the use of contact lenses during the disease period. This is followed by the use of antibacterial drops prescribed by a doctor.	Not graded	Saudi Ministry of Health 2021[11]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Bacterial Conjunctivitis clinical and therapeutic management.**

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

This section is divided into two parts: one part includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Bacterial Conjunctivitis report, and another part 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 June 2020 CHI Bacterial Conjunctivitis Report and their corresponding recommendations.

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision		
Old Versions		**Updated versions**
1.1.1.	Evidence- for Disease Control and Prevention **[CDC]** Sexually Transmitted Diseases Treatment Guidelines **2015**	Sexually Transmitted Infections Summary of **CDC** Treatment Guidelines—**2021**
1.1.2.	Conjunctivitis Preferred Practice Pattern **[2018 by the American Academy of Ophthalmology]** adult and pediatric	N/A*
1.1.3.	Conjunctivitis A Systematic Review of Diagnosis and Treatment **[2013 American Medical Association]**	N/A*
1.1.4.	Optometric CLINICAL PRACTICE GUIDELINE CARE OF THE PATIENT WITH CONJUNCTIVITIS **[AMERICAN OPTOMETRIC ASSOCIATION 1995, 2002]** adults and pediatrics	N/A*
1.1.5.	Diagnosis and Management of Red Eye in Primary Care **[2010 American Family Physician]**	N/A*
1.1.6.	Ocular Prophylaxis for Gonococcal Ophthalmia Neonatorum US Preventive Services Task Force Reaffirmation Recommendation Statement **[2019 American Medical association]**	N/A*

*: *No updated versions available*

1.1.1 Evidence- for Disease Control and Prevention [CDC] Sexually Transmitted Diseases Treatment Guidelines (2015)

*Please refer to **Section 1.6** of CHI Bacterial Conjunctivitis original clinical guidance.*

The **2021 edition** of Sexually Transmitted Infections Summary of **CDC** Treatment Guidelines introduced a set of recommendations listed below[12]:

- Gonococcal conjunctivitis recommended regimen:
    - Ceftriaxone 1 gm IM in a single dose
- Ophthalmia in neonates and infants, recommended regimen:
    - Ceftriaxone 25–50 mg/kg body weight by IV or IM in a single dose, not to exceed 250 mg
- Ophthalmia in neonates and infants, ALTERNATIVES:
    - For neonates unable to receive ceftriaxone due to simultaneous administration of intravenous calcium: cefotaxime 100 mg/kg body, IV or IM as a single dose.

1.1.2 Conjunctivitis Preferred Practice Pattern [2018 by the American Academy of Ophthalmology] Adult and Pediatric

The recommendations provided below supplement the ones mentioned in the previous CHI Bacterial Conjunctivitis report[13]: *Please refer to **Section 1.2** of CHI Bacterial Conjunctivitis original clinical guidance.*

- Moderate to Severe Bacterial Conjunctivitis:
    - Methicillin-resistant Staphylococcus aureus has been isolated with increasing frequency from patients with bacterial conjunctivitis.
    - Increasing colonization of MRSA has been found in nursing home residents, and the incidence of community-acquired MRSA infections also has risen.
    - Methicillin-resistant S. aureus organisms are resistant to many commercially available topical antibiotics.
    - Microbiology laboratory testing may guide therapy, which may include compounded topical antibiotics such as vancomycin.

1.2 Additional References

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

Table 3. List of Additional References

Additional References
Primary Care Approach to Eye Conditions 2019
A Systematic Review of Clinical Practice Guidelines for Infectious and Non-infectious Conjunctivitis 2021
Conjunctivitis: A Systematic Review 2020
Red Eye Diagnosis and Management in Primary Health Care 2019
Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2021 (including the 22nd WHO Model List of Essential Medicines and the 8th WHO Model List of Essential Medicines for Children)
Conjunctivitis (bacterial) Clinical Management Guidelines of the College of Optometrists 2023

1.2.1 Primary Care Approach to Eye Conditions (ACOFP 2019)

This review article was published in the American College of Osteopathic Family Physicians. Its recommendations are summarized below[6]:

- Bacterial conjunctivitis is usually unilateral and can be classified as **hyperacute**, **acute,** or **chronic**. It usually consists of a greater amount of discharge and lid swelling than viral conjunctivitis.
- **Hyperacute** bacterial conjunctivitis:
    - Neisseria gonorrhoeae is an important cause of hyperacute conjunctivitis. Those at risk include newborns who acquire the infection during delivery and young adults who acquire the infection during sexual activity.
    - Patients with a suspected diagnosis of Neisseria conjunctivitis should be referred to an ophthalmologist for aggressive management as it can quickly lead to vision loss secondary to corneal ulceration and perforation.

- **Acute** bacterial conjunctivitis:
    - It has the classic symptoms of discomfort, blurry vision, and mucopurulent secretions with “sticky” eyelids upon awakening. Symptoms usually last for less than seven days.
    - *Staphylococcus aureus* and *Staphylococcus epidermidis* are common etiologies of conjunctivitis in adults, while *Streptococcus pneumonia* and *Haemophilus influenza* tend to affect children.
    - There are various antibiotic eye drops available for treatment, and they are generally well tolerated. Table 4 lists the common ophthalmic antibiotics for acute bacterial conjunctivitis.

Table 4. Common Ophthalmic Antibiotics for Acute Bacterial Conjunctivitis

Ophthalmic Antibiotics
Trimethoprim/polymyxin B
Ofloxacin 0.3%
Azithromycin 1%
Besifloxacin 0.6%
Ciprofloxacin 0.3%
Erythromycin 0.5%
Levofloxacin 1.5%
Gentamicin 0.3%
Sulfacetamide 10%

- **Chronic** bacterial conjunctivitis:
    - It occurs when symptoms last longer than four weeks with frequent relapses. The patient complains of sore eyelids and ocular discomfort with little discharge. Upon examination, the eyelids appear thickened, slightly inflamed and crusty. The conjunctiva may appear normal or slightly erythematous.
    - Bacterial culture is usually needed to identify the organism responsible for patients with chronic bacterial conjunctivitis.
    - Patients with this diagnosis typically require referral to an ophthalmologist for further management.

- **Chlamydial** conjunctivitis:
    - It is often seen in young sexually active adults. It is very similar to acute bacterial conjunctivitis, though it may be seen as smoldering chronic conjunctivitis in some cases.
    - The common symptoms include ocular irritation, scant mucopurulent discharge, glued eyelids upon awakening and blurred vision.
    - Patients do not respond well or fully to typical antibiotics that are prescribed for acute bacterial conjunctivitis. Bacterial culture (Giemsa stain) and ELISA testing can reveal the diagnosis of Chlamydial conjunctivitis.
    - Treatment includes erythromycin ophthalmic ointment and oral therapy with azithromycin (single one gram dose) or doxycycline (100 mg twice a day for 14 days) to clear the infection. The patient's sexual partner should also be treated to prevent further infections and reinfection.

1.2.2 A Systematic Review of Clinical Practice Guidelines for Infectious and Non-infectious Conjunctivitis (2021)

This systematic review was published by Chan et al. in the Journal of Ophthalmic Epidemiology (Taylor and Francis Online), and its recommendations are summarized below[7]:

- Observation without treatment was strongly recommended in bacterial conjunctivitis (except chlamydial and gonorrheal conjunctivitis) due to the usually self-limiting nature of the conditions.
- Cold compress, artificial tears and lubricating ointments were suggested for symptomatic relief of bacterial conjunctivitis.
- Lid hygiene was strongly recommended where mucopurulent discharge with crusting on the lids is present.
- Pharmacological interventions:
    - Antibacterial medications:
        - Ocular antibiotic prophylaxis was recommended for neonates with ophthalmia neonatorum (ON) (recommended with high certainty in USPSTF guideline).

- For neonates infected by chlamydia, systemic erythromycin or topical azithromycin 1.5% was recommended; those infected by gonorrhea were recommended systemic Penicillin G or cephalosporin; and neonates with other types of bacterial infection were recommended topical erythromycin, azithromycin 1.5% or chloramphenicol 0.5%.
- For chlamydial conjunctivitis in adults, systemic azithromycin and doxycycline were recommended, while in gonorrheal conjunctivitis, systemic ceftriaxone or spectinomycin was recommended in addition to the interventions used to manage chlamydial infection.
- In bacterial conjunctivitis, which did not resolve within three days, topical chloramphenicol 0.5% drops or 1% ointment, fusidic acid 1% drops or azithromycin 1.5% were strongly recommended.
- Topical gentamycin or moxifloxacin was included as interventions for infection related to contact lens wear (strongly recommended by COO guideline).
- In settings where medical supply is limited, povidone-iodine 1.25% may be used in mild bacterial or chlamydia infection.

1.2.3 Red Eye Diagnosis and Management in Primary Health Care (2019)

The recommendations from this original article published by Alattas et al. in the Archives of Pharmacy Practice are summarized below[14]:

- Many patients may recover well after one to two weeks from the bacterial conjunctivitis presentation with no drugs given.
- Topical antibiotics reduce the duration of the disease, decrease transmission, and hasten the return to normal lifestyle.
- Moreover, contact lens wearers should always receive topical antibiotics and removal of the lens is recommended to be done by the family physician.
- The choice of topical antibiotic is not very difficult. All broad-spectrum antibiotics lead almost to the same results. Therefore, choosing the topical antibiotic should depend on the availability, cost, patient's allergies, and resistance patterns.
- Clinicians should avoid topical steroids due to the risk of potentiating the infection and prolonging the course of the disease.

- The wait and see policy, and/or antibiotic treatment are strategies that both can be done in cases of uncomplicated conjunctivitis. However, antibiotic therapy is recommended in cases of purulent or mucopurulent conjunctivitis, severe discomfort, immunocompromised patients, and when chlamydia or gonococcal infection is suspected.
- An important indication for referral is when a methicillin resistant *S. aureus* (MRSA) conjunctivitis is suspected.
- The other causes of bacterial conjunctivitis that may need special care is chlamydia (needing oral antibiotic to both sexual partners), gonococci (topical and oral antibiotics needed), and trachoma (single dose of azithromycin or topical antibiotics or other oral antibiotics).

1.2.4 Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2021 (including the 22nd WHO Model List of Essential Medicines and the 8th WHO Model List of Essential Medicines for Children)

The WHO Expert Committee's recommendations are summarized below[9]:

- If bacterial conjunctivitis is suspected, treatment with topical antibiotics is indicated for moderate to severe infection and can also be considered in mild cases.
- No specific topical antibiotic can be recommended because of the lack of direct comparisons; therefore, the choice for empiric antibiotics should be based on local availability. Topical antibiotics containing fluoroquinolone are proposed (e.g. ofloxacin).
- For trachoma, the treatment of choice is oral azithromycin as a single dose of 1 g (or 20 mg/kg body weight in children) because of the potentially better efficacy and adherence with the single-dose regimen.

1.2.5 Conjunctivitis (Bacterial) Clinical Management Guidelines of the College of Optometrists (2023)

The recommendations for principles of treatment were developed using the GRADE approach[15]. The recommendations issued by the clinical guideline are summarized below[10]:

- Nonpharmacological:
    - Bathe/clean the eyelids with proprietary sterile wipes, lint or cotton wool dipped in sterile saline or boiled (cooled) water to remove crusting (Level of evidence: low; Strength of recommendation: strong)
    - Advise patients that the condition is contagious (do not share towels, etc.)
    - Public health guidance in all UK Nations states that school or nursery exclusion is not required for children with this condition.
- Pharmacological:
    - Often resolves in 5-7 days without treatment

        > The use of topical antibiotics may modestly improve short-term clinical remission and reduce a patient's contagiousness to others. Nevertheless, it's important to weigh the potential benefit of antibiotics against the risk of antibiotic resistance. (Level of evidence: high; Strength of recommendation: strong)

    - Topical antibiotics (with no evidence of superiority of particular antibiotics) may include chloramphenicol 0.5% eye drops, chloramphenicol 1% ointment, azithromycin 1.5% eye drops, or fusidic acid 1% viscous eye drops which has a higher cost and narrower spectrum of activity than chloramphenicol)
    - Based on the supportive evidence for antibiotic efficacy, findings from a comprehensive Cochrane Review (Sheikh and Hurwitz 2012), which examined trials in both primary and secondary healthcare settings, indicate the advantages of antibiotics. Nevertheless, an individual meta-analysis that specifically concentrated on primary care studies (Jefferis et al 2011) discovered a relatively minor advantage of antibiotics over a placebo. Predictors of a positive bacterial culture upon presentation encompass the existence of purulent discharge and an age below 5 years. The NICE Clinical Knowledge Summary (CKS) proposes a potential delayed treatment approach, suggesting that individuals be advised to initiate topical antibiotics only if their symptoms persist beyond 3 days from the onset.
    - Contact lens wearers with a diagnosis of bacterial conjunctivitis should be treated with a topical antibiotic effective against Gram –ve organisms, such as an aminoglycoside (e.g. gentamycin) or a quinolone (e.g. levofloxacin or moxifloxacin). Contact lenses should not be worn until the condition has resolved. (Level of evidence: low; Strength of recommendation = strong).

- It is advisable for the patient to return/seek further help if symptoms persist beyond 7 days
- Possible management by ophthalmologist:
  - If resistant to treatment, or recurrent:
    - Conjunctival swabs taken for microscopy and culture and/or PCR analysis
    - Treatment with other antibiotics, based on culture results

Section 2.0 Drug Therapy in Bacterial Conjunctivitis

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

2.1 Additions

No new drugs have been approved by the FDA or EMA for the treatment Bacterial Conjunctivitis since June 2020.

2.2 Modifications

Below are the modifications made to the list of Bacterial Conjunctivitis drugs since the CHI report in June 2020, reflecting the changes and updates.

Table 5. Prescribing Edits Modifications of Certain Bacterial Conjunctivitis Drugs

Drugs	PE modifications
Antibiotics with previous PA	**PA** was removed from all antibiotics listed.
Doxycycline	**AGE**: Doxycycline was traditionally avoided in ages < 8 years, but use has more recently been accepted for short courses (< 21 days) for all ages when necessary, with a maximum dose for children and adolescents of 100 mg/day.
Erythromycin	**QL**: Erythromycin is used both in adult and pediatric for 7 days

Normal saline	**CU** was added: concomitant saline irrigation of the ocular surface along with single dose of ceftriaxone (25 to 50 mg/kg), or cefotaxime (100 mg/kg IV or IM) for neonates with gonococcal conjunctivitis (Irrigation of the ocular surface with saline solution is not necessary in adults). also, used to bathe/clean the eyelids with proprietary sterile wipes, lint or cotton wool dipped in sterile saline or boiled (cooled) water to remove crusting
Tetracycline	**CU:** mainly used for trachoma treatment with oral azithromycin (20 mg/kg) single dose for three weeks. Can also be used for 6 weeks as topical antibiotic ointment for the management of trachoma.

2.3 Delisting

The medications below are no longer SFDA registered[16], therefore, it is advisable to delist the following drugs from CHI formulary. *Please refer to **Drugs in the disease - section 2** of CHI Bacterial Conjunctivitis original clinical guidance*

- Polymyxin B + Bacitracin + Neomycin sulfate

Section 3.0 Key Recommendations Synthesis

- Patients with a suspected diagnosis of Neisseria conjunctivitis should be referred to an ophthalmologist for aggressive management as it can quickly lead to vision loss secondary to corneal ulceration and perforation[6].
- Chlamydial conjunctivitis: Treatment includes erythromycin ophthalmic ointment and oral therapy with azithromycin (single one gram dose) or doxycycline (100 mg twice a day for 14 days) to clear the infection. The patient's sexual partner should also be treated to prevent further infections and reinfection[6].
- Observation without treatment was strongly recommended in bacterial conjunctivitis (except chlamydial and gonorrheal conjunctivitis or trachoma) due to the usually self-limiting nature of the conditions[7].
- For neonates infected by chlamydia, systemic erythromycin or topical azithromycin 1.5% was recommended; those infected by gonorrhea were recommended systemic Penicillin G or cephalosporin; and neonates with other types of bacterial infection were recommended topical erythromycin, azithromycin 1.5% or chloramphenicol 0.5%[7].

- In bacterial conjunctivitis, which did not resolve within three days, topical chloramphenicol 0.5% drops or 1% ointment, fusidic acid 1% drops or azithromycin 1.5% were strongly recommended[7].
- In settings where medical supply is limited, povidone-iodine 1.25% may be used in mild bacterial or chlamydia infection[7].
- Gonococcal conjunctivitis (GC)[8]:
    - The suggested treatment for neonates includes single dose of ceftriaxone (25 to 50 mg/kg), or cefotaxime (100 mg/kg IV or IM), in addition to hourly saline irrigation of the ocular surface.
    - Non-neonates can be treated with the combination of 1 gm of IM ceftriaxone given in a single dose and 1 gm of oral azithromycin (which is used to treat the frequently encountered chlamydial coinfection).
- For trachoma, the treatment of choice is oral azithromycin as a single dose of 1 g (or 20 mg/kg body weight in children) because of the potentially better efficacy and adherence with the single-dose regimen[9].
- The NICE Clinical Knowledge Summary (only available to people residing in UK) proposes a potential delayed treatment approach, suggesting that individuals be advised to initiate topical antibiotics only if their symptoms persist beyond 3 days from the onset[10].
- Treatment is conservative in this case, and can help relieve symptoms by cold compresses, moisturizing drops, avoiding the use of contact lenses during the disease period. This is followed by the use of antibacterial drops prescribed by a doctor[11].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Bacterial Conjunctivitis report** and aims to provide recommendations to aid in the management of Bacterial Conjunctivitis. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Bacterial Conjunctivitis. 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 Conjunctivitis Scope

Bacterial Conjunctivitis Scope

Section	Rationale/Updates
Section 1.1.1 **Conjunctivitis Preferred Practice Pattern [2018 by the American Academy of Ophthalmology] adult and pediatric** [13]	Additional Recommendations: • Moderate to Severe Bacterial Conjunctivitis: o Methicillin-resistant Staphylococcus aureus has been isolated with increasing frequency from patients with bacterial conjunctivitis. o Increasing colonization of MRSA has been found in nursing home residents, and the incidence of community-acquired MRSA infections also has risen. o Methicillin-resistant S. aureus organisms are resistant to many commercially available topical antibiotics. o Microbiology laboratory testing may guide therapy, which may include compounded topical antibiotics such as vancomycin
Section 1.1.2 **Centers for Disease Control and Prevention [CDC]Sexually Transmitted Diseases Treatment Guidelines, 2015**	**Sexually Transmitted Infections Summary of CDC Treatment Guidelines—2021**[12]**:** • Gonococcal infections conjunctivitis, recommended regimen: o Ceftriaxone 1 gm IM in a single dose • Ophthalmia in neonates and infants, recommended regimen: o Ceftriaxone 25–50 mg/kg body weight by IV or IM in a single dose, not to exceed 250 mg • Ophthalmia in neonates and infants, ALTERNATIVES: o For neonates unable to receive ceftriaxone due to simultaneous administration of intravenous calcium: cefotaxime 100 mg/kg body, IM or IV, single dose
Section 1.1.3 **Primary Care Approach to Eye Conditions 2019**[6]	• Bacterial conjunctivitis is usually unilateral and can be classified as hyperacute, acute or chronic. It usually consists of a greater amount of discharge and lid swelling than viral conjunctivitis. • Neisseria gonorrhoeae: o It is an important cause of hyperacute conjunctivitis. Those at risk include newborns who acquire the infection during delivery and young adults who acquire the infection during sexual activity. o Patients with a suspected diagnosis of Neisseria conjunctivitis should be referred to an ophthalmologist for aggressive management as it can quickly lead to vision loss secondary to corneal ulceration and perforation. • Acute bacterial conjunctivitis: o It has the classic symptoms of discomfort, blurry vision, and mucopurulent secretions with “sticky” eyelids upon awakening. Symptoms usually last for less than seven days.

	○ Staphylococcus aureus and Staphylococcus epidermidis are common etiologies of conjunctivitis in adults, while Streptococcus pneumonia and Haemophilus influenza tend to affect children. ○ There are various antibiotic eye drops available for treatment, and they are generally well tolerated (Table 4). • Chronic bacterial conjunctivitis: ○ It occurs when symptoms last longer than four weeks with frequent relapses. The patient complains of sore eyelids and ocular discomfort with little discharge. Upon examination, the eyelids appear thickened, slightly inflamed and crusty. The conjunctiva may appear normal or slightly erythematous. ○ Bacterial culture is usually needed to identify the organism responsible for patients with chronic bacterial conjunctivitis. ○ Patients with this diagnosis typically require referral to an ophthalmologist for further management. • Chlamydial conjunctivitis: ○ It is often seen in young sexually active adults. It presents very similarly to acute bacterial conjunctivitis, though it may be seen as smoldering chronic conjunctivitis in some cases. ○ The common symptoms include ocular irritation, scant mucopurulent discharge, glued eyelids upon awakening and blurred vision. ○ Patients do not respond well or fully to typical antibiotics that are prescribed for acute bacterial conjunctivitis. Bacterial culture (Giemsa stain) and ELISA testing can reveal the diagnosis of Chlamydial conjunctivitis. ○ Treatment includes erythromycin ophthalmic ointment and oral therapy with azithromycin (single one gram dose) or doxycycline (100 mg twice a day for 14 days) to clear the infection. The patient's sexual partner should also be treated to prevent further infections and reinfection.
Section 1.1.4 **A Systematic Review of Clinical Practice Guidelines for Infectious and Non-infectious Conjunctivitis 2021** [7]	• Observation without treatment was strongly recommended in bacterial conjunctivitis (except chlamydial and gonorrheal conjunctivitis) due to the usually self-limiting nature of the conditions. • Cold compress, artificial tears and lubricating ointments were suggested for symptomatic relief of bacterial conjunctivitis. • Lid hygiene was strongly recommended where mucopurulent discharge with crusting on the lids is present. • Pharmacological interventions: ○ Antibacterial - Ocular antibiotic prophylaxis was recommended for neonates with

	ophthalmia neonatorum (ON) (recommended with high certainty in USPSTF guideline). - For neonates infected by chlamydia, systemic erythromycin or topical azithromycin 1.5% was recommended; those infected by gonorrhea were recommended systemic Penicillin G or cephalosporin; and neonates with other types of bacterial infection were recommended topical erythromycin, azithromycin 1.5% or chloramphenicol 0.5%. - For chlamydial conjunctivitis in adults, systemic azithromycin and doxycycline were recommended, while in gonorrheal conjunctivitis, systemic ceftriaxone or spectinomycin was recommended in addition to the interventions used to manage chlamydial infection. - In bacterial conjunctivitis, which did not resolve within three days, topical chloramphenicol 0.5% drops or 1% ointment, fusidic acid 1% drops or azithromycin 1.5% were strongly recommended. - Topical gentamycin or moxifloxacin was included as interventions for infection related to contact lens wear (strongly recommended by COO guideline). - In settings where medical supply is limited, povidone-iodine 1.25% may be used in mild bacterial or chlamydia infection.
Section 1.1.5 **Conjunctivitis: A Systematic Review 2020** [8]	• Acute bacterial conjunctivitis is most often caused by Staphylococcus species, Haemophilus influenza, Streptococcus species, Moraxella catarrhalis, and gram-negative intestinal bacteria. • In younger children, minor epidemics may occur secondary to H. influenza or S. pneumonia. • In more than 60% of cases, spontaneous cure occurs within one–two weeks, and serious complications are extremely rare. However, presence of a large population of bacteria on the conjunctiva exposes the patient to a higher risk of keratitis, particularly in conditions associated with corneal epithelial defects, such as dry eye. • Although topical antibiotics reduce the duration of the disease, no difference in the outcome is seen. • All broad-spectrum antibiotic eye drops seem to be effective in treating bacterial conjunctivitis and it is unlikely that there is a significant difference among various antibiotics in achieving clinical cure. • Factors that influence antibiotic choice are local availability, patient allergies, resistance patterns, and cost. • From a large systematic review, it was concluded that topical antibiotics were more effective in achieving clinical and microbial cure when patients had positive bacterial cultures. However, no significant difference has been reported in clinical cure rate when different frequencies of the antibiotics were administered.

	• Due to lengthening the course of the illness and potentiating the infection, topical steroids should be avoided.
	• The term methicillin-resistant S. aureus (MRSA) refers to Staphylococcus aureus species that are resistant to methicillin antibiotic; however, nowadays the term is used to describe resistance to all β-lactam antimicrobials. Growing in prevalence, 3–64% of all ocular Staphylococcus conjunctival infections are MRSA conjunctivitis.
	• Suspected cases need to be treated with fortified vancomycin eye drops or ointments. Culture directed administration of antimicrobials, effective dosing, considering the local resistance patterns, and appropriate antiseptic strategies should be applied to restrict the spread of MRSA conjunctivitis.
	• Chlamydial conjunctivitis:
	  o Treatment with systemic antibiotics such as oral azithromycin and doxycycline is efficacious, while addition of topical antibiotics is not beneficial.
	  o Treatment of sexual partners and looking for the evidence of coinfection with gonorrhea must be instituted.
	• Trachoma:
	  o As the leading cause of infectious blindness in the world, trachoma affects 40 million individuals worldwide; this infection is prevalent in areas with poor hygiene. Although mucopurulent discharge is the initial presenting sign, in the later stages, scarring of the eyelids, conjunctiva, and cornea may lead to loss of vision.
	  o A single dose of oral azithromycin (20 mg/kg) in addition to oral tetracycline or erythromycin for three weeks is very effective.
	  o Patients may also be treated with topical antibiotic ointments, such as tetracycline and erythromycin, for six weeks.
	• Gonococcal conjunctivitis (GC):
	  o The suggested treatment for neonates include single dose of ceftriaxone (25 to 50 mg/kg), or cefotaxime (100 mg/kg IV or IM), in addition to hourly saline irrigation of the ocular surface.
	  o Non-neonates can be treated with combination of 1 gm of IM ceftriaxone given in a single dose and 1 gm of oral azithromycin (which is used to treat the frequently encountered chlamydial coinfection).
	  o Irrigation of the ocular surface with saline solution is not necessary in adults.

Section 1.1.6 **Red Eye Diagnosis and Management in**	• New studies have shown that bacterial conjunctivitis can be self-limiting in some cases. • Many patients may recover well after one to two weeks from presentation

Primary Health Care 2019 [14]	with no drugs given. • Topical antibiotics reduce the duration of the disease, decrease transmission, and hasten the return to normal lifestyle. • Moreover, contact lens wearers should always receive topical antibiotics and removal of the lens is recommended to be done by the family physician. • The choice of topical antibiotic is not very difficult. All broad-spectrum antibiotics lead almost to the same results. Therefore, choosing the topical antibiotic should depend on the availability, cost, patient's allergies, and resistance patterns. • Clinicians should avoid topical steroids due to the risk of potentiating the infection and prolonging the course of the disease. • The wait and see policy, and/or antibiotic treatment are strategies that both can be done in cases of uncomplicated conjunctivitis. However, the antibiotic therapy is recommended in cases of purulent or mucopurulent conjunctivitis, severe discomfort, immunocompromised patients, and when chlamydia or gonococcal infection is suspected. • An important indication for referral is when a methicillin resistant S.aureus conjunctivitis is suspected. • The other causes of bacterial conjunctivitis that may need special care is chlamydia (needing oral antibiotic to both sexual partners), gonococci (topical and oral antibiotics needed), and trachoma (single dose of azithromycin or topical antibiotics or other oral antibiotics).
Section 1.1.7 **Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2021 (including the 22nd WHO Model List of Essential Medicines and the 8th WHO Model List of Essential Medicines for Children)**[9]	• If bacterial conjunctivitis is suspected, treatment with topical antibiotics is indicated for moderate to severe infection and can also be considered in mild cases. • No specific topical antibiotic can be recommended because of the lack of direct comparisons; therefore, the choice for empiric antibiotics should be based on local availability. Topical antibiotics containing fluoroquinolone are proposed (e.g. ofloxacin). • For trachoma, the treatment of choice is oral azithromycin as a single dose of 1 g (or 20 mg/kg body-weight in children) because of the potentially better efficacy and adherence with the single-dose regimen.
Section 1.1.8 **Conjunctivitis (bacterial) Clinical Management Guidelines of the**	• Nonpharmacological: o Bathe/clean the eyelids with proprietary sterile wipes, lint or cotton wool dipped in sterile saline or boiled (cooled) water to remove crusting (**GRADE**: Level of evidence = low, Strength of recommendation = strong)

College of Optometrists 2023[10]	○ Advise patient that condition is contagious (do not share towels, etc.) ○ Public health guidance in all UK Nations states that school or nursery exclusion is not required for children with this condition. • Pharmacological: ○ Often resolves in 5-7 days without treatment ○ Treatment with topical antibiotics may modestly improve short-term clinical remission and render patient less infectious to others; however the potential benefit of antibiotics needs to be balanced against the risk of antibiotic resistance (**GRADE**: Level of evidence = high, Strength of recommendation = strong) ○ Topical antibiotics (with no evidence of superiority of particular antibiotics) may include: chloramphenicol 0.5% eye drops, chloramphenicol 1% ointment, azithromycin 1.5% eye drops or fusidic acid 1% viscous eye drops which has a higher cost and narrower spectrum of activity than chloramphenicol) ○ According to evidence supporting the efficacy of antibiotics, the conclusions drawn from a Cochrane Review (Sheikh and Hurwitz 2012), which encompassed trials conducted in both primary and secondary care settings, indicate their benefits. However, an individual patient meta-analysis focusing solely on primary care studies (Jefferis et al 2011) found a relatively minor advantage of antibiotics over a placebo. Predictors for positive bacterial culture at presentation include the presence of purulent discharge and age below 5 years. ○ The NICE Clinical Knowledge Summary (CKS) proposes a potential delayed treatment approach, suggesting that individuals be advised to initiate topical antibiotics only if their symptoms persist beyond 3 days from the onset. ○ Contact lens wearers with a diagnosis of bacterial conjunctivitis should be treated with a topical antibiotic effective against Gram – ve organisms, such as an aminoglycoside (e.g. gentamycin) or a quinolone (e.g. levofloxacin or moxifloxacin). Contact lenses should not be worn until the condition has resolved. (**GRADE**: Level of evidence = low, Strength of recommendation = strong). ○ Advise patient to return/seek further help if symptoms persist beyond 7 days • Possible management by ophthalmologist: ○ If resistant to treatment, or recurrent: ▪ Conjunctival swabs taken for microscopy and culture and/or PCR analysis

	▪ Treatment with other antibiotics, based on culture results
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 Conjunctivitis:

Query	Filters	Search Details	Results
((((((((((Conjunctivitis, Bacterial[MeSH Terms]) OR (Conjunctivitis, Purulent[Title/Abstract])) OR (Conjunctivitides, Purulent[Title/Abstract])) OR (Purulent Conjunctivitides[Title/Abstract])) OR (Purulent Conjunctivitis[Title/Abstract])) OR (Bacterial Conjunctivitis[Title/Abstract])) OR (Conjunctivitis, Mucopurulent[Title/Abstract])) OR (Conjunctivitides, Mucopurulent[Title/Abstract])) OR (Mucopurulent Conjunctivitides[Title/Abstract])) OR (Mucopurulent Conjunctivitis[Title/Abstract])) OR (Bacterial Conjunctivitides[Title/Abstract])) OR (Conjunctivitides, Bacterial[Title/Abstract])	Guideline, in the last 5 years	("conjunctivitis, bacterial"[MeSH Terms] OR "conjunctivitis purulent"[Title/Abstract] OR (("conjunctivities"[All Fields] OR "Conjunctivitis"[MeSH Terms] OR "Conjunctivitis"[All Fields] OR "Conjunctivitides"[All Fields]) AND "Purulent"[Title/Abstract]) OR (("purulence"[All Fields] OR "Purulent"[All Fields]) AND "Conjunctivitides"[Title/Abstract]) OR "purulent conjunctivitis"[Title/Abstract] OR "bacterial conjunctivitis"[Title/Abstract] OR "conjunctivitis mucopurulent"[Title/Abstract] OR (("conjunctivities"[All Fields] OR "Conjunctivitis"[MeSH Terms] OR "Conjunctivitis"[All Fields] OR "Conjunctivitides"[All Fields]) AND "Mucopurulent"[Title/Abstract]) OR (("mucopurulence"[All Fields] OR "Mucopurulent"[All Fields]) AND "Conjunctivitides"[Title/Abstract]) OR "mucopurulent conjunctivitis"[Title/Abstract] OR (("Bacterial"[All Fields] OR "bacterially"[All Fields] OR "bacterials"[All Fields]) AND "Conjunctivitides"[Title/Abstract]) OR (("conjunctivities"[All Fields] OR "Conjunctivitis"[MeSH Terms] OR "Conjunctivitis"[All Fields] OR "Conjunctivitides"[All Fields]) AND "Bacterial"[Title/Abstract])) AND ((y_5[Filter]) AND (guideline[Filter]))	2

Appendix D. Bacterial Conjunctivitis Treatment Algorithm