Pharyngitis (Acute Sore Throat)

CHI Formulary Indication Review

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM-October 2023

To the CHI Original (Acute Sore throat) Clinical Guidance- Issued November 2019

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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

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Abbreviations

AAFP	American Academy of Family Physicians
ACP-ASIM	American College of Physicians–American Society of Internal Medicine
CADTH	Canadian Agency for Drugs and Technologies in Health
CDC	Centers for Disease Control and Prevention
CHI	Council of Health Insurance
COVID-19	Coronavirus Disease 2019
CPG	Clinical Practice Guideline
DP	Delayed Prescribing
EMA	European Medicines Agency
FDA	Food and Drug Administration
GABHS	Group A β-Hemolytic Streptococcus
GAS	Group A Streptococci
GCP	Good Clinical Practice
HAS	Haute Autorite de Sante
HTA	Health Technology Assessment
IDF	CHI Drug Formulary
IDSA	Infectious Disease Society of America
IQWIG	Institute for Quality and Efficiency in Health Care
MSF	Medecins Sans Frontieres (Doctors Without Borders)
NICE	National Institute for Health and Care Excellence
NSAID	Non-Steroidal Anti-Inflammatory Drug
PBAC	Pharmaceutical Benefits Advisory Committee
SFDA	Saudi Food and Drug Authority

Executive Summary

Pharyngitis is described as an infection or inflammation affecting the pharynx and/or tonsils. It is typically caused by infectious agents, with most cases stemming from viruses. In most instances, viral pharyngitis is mild and resolves on its own. Bacterial sources of pharyngitis are also self-resolving, but they raise concerns due to potential suppurative (pus-related) and nonsuppurative complications[1].

The most significant bacterial agent causing pharyngitis in both adults and children is Group A Streptococcus (GAS) infection (*Streptococcus pyogenes*). Mycoplasma pneumoniae, Chlamydia pneumoniae, and *Arcanobacterium haemolyticus* are other bacterial causes of pharyngitis, but these pathogens are rare[1].

Pharyngitis is more commonly reported on a global scale, and in certain countries, there may be a greater prevalence of antibiotic resistance due to excessive antibiotic prescriptions. Nevertheless, it is important to highlight that there has never been a documented instance of Group A Streptococcus (GAS) showing resistance to penicillin anywhere in the world[1]. A study was conducted in Makah city, Saudi Arabia to evaluate the prevalence of *Streptococcus pyogenes* among pre-school children aged between 4 and 6. The study involved 2,370 children, including both Saudi and non-Saudi children from 19 kindergarten schools in Makah, gathered between February and May 2014. Out of these asymptomatic children, 1.5% were found to carry GAS, with the highest prevalence in 5-year-olds. GAS was slightly more prevalent in boys (1.6%) than in girls (1.5%). Notably, all GAS isolates were susceptible to penicillin, but resistance to trimethoprim was observed in 33% of cases[2].

The origins of pharyngitis, whether viral or bacterial, share similarities, and distinguishing between them solely through medical history and physical examination is challenging. The main symptom of pharyngitis is sore throat, but patients may also experience other signs of infection such as fever, headache, joint and muscle aches. The preferred diagnostic approaches for diagnosing GAS infection include Group A β-hemolytic streptococcus (GABHS) rapid antigen detection test and throat culture[1].

Group A Streptococcus (GAS) pharyngitis typically follows a self-limiting course, with most symptoms naturally improving within 3-4 days. While antibiotics, when administered promptly, can reduce the illness duration by approximately one day, their primary purpose is the prevention of acute rheumatic fever[1].

Furthermore, pain-relieving medications like NSAIDs or acetaminophen, as well as steroids, can help alleviate the symptoms linked to GAS pharyngitis. Antibiotics do not provide protection against acute glomerulonephritis. Steroids may be employed in situations involving airway obstruction and for symptomatic relief. In specific rare

instances, antifungal and antiviral medications are employed with guidance from specialists[1].

Complications from pharyngitis can be purulent or non-purulent. Purulent complications occur due to the spread of the infection from the mucous membrane of the throat through the bloodstream, lymphatic system, or direct extension (more frequent with GAS). These complications may manifest as peritonsillar abscess, retropharyngeal abscess, or purulent cervical lymphadenitis[3].

Non-purulent complications (3% incidence) that are particular to GAS infection consist of acute rheumatic fever (typically appearing 3 to 5 weeks after the infection), poststreptococcal glomerulonephritis, and toxic shock syndrome[3].

CHI issued new guidelines related to the management of Pharyngitis. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations. Below is a description of sections that need updates. Below is a description of sections that need updates.

CHI issued Pharyngitis (Acute Sore throat) guidance after thorough review of renowned international and national clinical guidelines in November 2019. 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 Pharyngitis (Acute Sore throat) **clinical guidance** and seeks to offer guidance for the effective management of **Pharyngitis (Acute Sore throat).** It provides an **update** on the Pharyngitis (Acute Sore throat) 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 addition of new guidelines and review articles to the report** such as **German clinical practice guideline** on sore throat **(2021)**, **CDC guidelines** on Pharyngitis (Acute Sore Throat) **(last updated 2022), Medecins Sans Frontieres (MSF) guidelines** on acute pharyngitis **(2020) and** Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: **A Narrative Review (2020).**

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is recommended to include the SFDA registered drug Naproxen (NAPROX®), (ALEVE®), (PROXEN®) in the CHI formulary while removing Clavulanic acid as a single entity from the CHI formulary since it is no longer registered in the SFDA Drug List of September 2023. There have been no changes or updates made to any of the previously listed drugs in terms of drug information and prescribing edits since November 2019.

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 Pharyngitis (Acute Sore throat) management.

Below is a table summarizing the major changes based on the pharyngitis (Acute Sore throat) guidelines used to issue this report:

Table 1. General Recommendations for the Management of Pharyngitis (Acute Sore Throat)

Management of Pharyngitis (Acute Sore throat)		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
The guideline recommends using throat remedies like lozenges, gargle solutions, and sprays containing local anesthetics and/or NSAIDs.	Weak level of recommendation	German Clinical Practice Guideline (2020)[4]
The use of throat preparations with local antiseptics and/or antibiotics is strongly discouraged, especially since most acute sore throats are caused by viral infections.	Strong level of recommendation	German Clinical Practice Guideline (2020)[4]
Corticosteroids should not be used for pain relief in sore throat.	A, 1a	German Clinical Practice Guideline (2020)[4]
Ibuprofen or naproxen should be considered for short-term relief from sore throat symptoms.	O, Ib	German Clinical Practice Guideline (2020)[4]
A 2013 Cochrane review found insufficient evidence to support the effectiveness of paracetamol in alleviating common cold symptoms.	Not graded	German Clinical Practice Guideline (2020)[4]
The use of antibiotics for pharyngitis remains a contentious issue.	Not graded	Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A

		Narrative Review (2020)[5]
IDSA guidelines recommend a ten-day course of either penicillin or amoxicillin as the first-line therapy.	Not graded	Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review (2020)[5]
In cases of penicillin allergy, IDSA suggests considering azithromycin for five days or a ten-day course of a first-generation cephalosporin, clindamycin, or clarithromycin.	Not graded	Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review (2020)[5]
CDC/AAFP/ACP-ASIM guidelines advise erythromycin for individuals with penicillin allergies.	Not graded	Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review (2020)[5]
As for the prevention, practicing good hand hygiene and following proper respiratory etiquette are vital for reducing the spread of any types of Group A strep infections.	Not graded	CDC Guidelines on Pharyngitis (2022)[6]

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 pharyngitis report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

There are no guidelines that have been updated since November 2019.

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Version	**Updated Version**
NICE Guidelines for Acute Sore Throat (Anti-Microbial Prescribing) Guidelines (2018)	N/A*
American College of Physicians Clinical Guidelines (2016)	N/A*
European Society of Clinical Microbiology and Infectious Diseases Guidelines (2012)	N/A*
Saudi National Antimicrobial Therapy Guidelines (2018)	N/A*
IDSA Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis (2002)	N/A*

*: No updated version available: the existing version is the most recent one and no further updates or revisions have been made or released.

1.2 Additional Guidelines

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

Table 3. List of Additional Guidelines

Additional Guidelines
German clinical practice guideline on sore throat **(2021)**
CDC guidelines on Pharyngitis (Acute Sore Throat) **(last updated 2022)**
Medecins Sans Frontieres (MSF) guidelines on acute pharyngitis **(2020)**

Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review (**2020**)

1.2.1 German Clinical Practice Guideline on Sore Throat (2021)

The German clinical practice guideline on sore throat (2021)[4] introduced a set of recommendations accompanied by a grading scheme, outlined as follows:

Table 4. Grading Scheme for Recommendations

Strength of Recommendations	
A	High strength of recommendation
B	Medium strength of recommendation
O	Low strength of recommendation

Table 5. Level of Evidence and Definitions

Level of Evidence	
Ia	Highest level, evidence from meta-analyses or systematic reviews of randomized controlled trials
Ib	Evidence from individual randomized controlled studies
II	Evidence from cohort studies
III	Evidence from case-control studies
IV	Evidence from case series
V	Expert consensus with systematic literature search, no studies found
GCP	Expert consensus without a systematic literature search: Good Clinical Practice

Clinical Diagnosis

- From a clinical standpoint, it's challenging to definitively differentiate between viral, bacterial, and non-infectious forms of pharyngitis (Statement, Ia).
- Yet, by considering symptoms and observations, the chances of identifying a viral or bacterial origin for acute sore throat may be heightened. This could facilitate a collaborative decision regarding the initiation of antibiotic treatment.

Clinical Scores

- Clinical scores assess the likelihood of detecting beta-hemolytic streptococci through microbiological testing of a throat swab in cases of acute tonsillopharyngitis.
- One point each is assigned for defined findings in the medical history and clinical examination, such as elevated temperature, patient age, disease course, pharyngeal and tonsillar findings, as well as cervical lymph node swelling as detailed in table 6.

Table 6. Risk Assessment Scores. Adapted from the 2021 German Clinical Practice Guideline on Sore Throat

FeverPAIN score (1 point each)
Elevated temperature in the preceding 24 hours
Tonsillar exudates
Presentation to a physician within 3 days due to severity of symptoms
Pronounced redness and swelling of the tonsils
No cough or rhinitis
Center score (1 point each)
Tonsillar exudates
Cervical lymphadenopathy
History of temperature elevated above 38°C
No cough
McIsaac score (1 point each)
Tonsillar exudates
Cervical lymphadenopathy
History of temperature elevated above 38°C
No cough
Patient < 15 years: + 1 point
Patient > 45 years: - 1 point

- The guideline suggests that a clinical score should be calculated for patients (aged 3 years and older) experiencing acute sore throat without any concerning signs when contemplating the use of antibiotic treatment (B, Ib).

Determination of laboratory parameters

- Laboratory measurements like white blood cell count, C-reactive protein, erythrocyte sedimentation rate, and procalcitonin should not be routinely included in the diagnostic evaluation for patients with acute sore throat (lasting less than 14 days) unless there are concerning signs (Statement, Good Clinical Practice [GCP]).

Rapid tests for group A streptococci

- This guideline endorses the utilization of rapid tests when there is a moderate to high clinical suspicion of streptococcal tonsillopharyngitis (scoring 3 points or more) in children between 3 and 15 years of age. If the GAS rapid test yields a negative result, there is no need for unnecessary antibiotic treatment.
- Since 2020, COVID-19 needs to be considered in the differential diagnosis of all new-onset respiratory symptoms. If COVID-19 is suspected, additional diagnostic testing and treatment in line with the current guidelines need to be initiated.

Medical Consultation

Medical consultation is essential for collaborative decision-making. The following points should be addressed with all patients (age ≥ 3 years) presenting with acute sore throat (< 14 days duration) without red flags (GCP):

- Disease course is likely to be self-limiting (lasting approximately 1 week)
- Low risk of suppurative complications requiring treatment
- Self-management (for example, fluids, physical rest, other non-pharmacological measures)
- Estimated probability of the presence of bacterial tonsillopharyngitis based on medical history and assessment of findings
- Advantages and disadvantages of antibiotic treatment:
    - Shortening of symptoms by on average 16 hours
    - High number needed to treat (NNT) of approximately 200 patients to prevent suppurative complications
    - Rate of adverse drug reactions (diarrhea, anaphylaxis, mycoses) is approximately 10% with antibiotic treatment

Symptomatic treatment with throat preparations

- The guideline endorses with only a weak level of recommendation the use of throat preparations (lozenges, gargle solutions, sprays) containing local anesthetics and/or non-steroidal anti-inflammatory drugs (NSAIDs).

- The guideline explicitly advises against local anti-septic- and/or antibiotic-containing throat preparations with a strong level of recommendation since the vast majority of cases of acute sore throat are viral infections.

Symptomatic treatment with oral corticosteroids

- Corticosteroids should not be used for analgesic treatment of sore throat (A, 1a).

Symptomatic treatment with non-steroidal anti-inflammatory drugs and paracetamol

- Ibuprofen or naproxen can be considered for short-term relief from sore throat symptoms (O, Ib).
- A Cochrane review from 2013 reported insufficient evidence to support the effectiveness of paracetamol in alleviating common cold symptoms.

Benefits of antibiotic treatment

- A sore throat, even if caused by bacteria, is not a broad recommendation for the use of antibiotics (Statement, Ia).
- The main objective of administering antibiotics to individuals aged 3 years and older with acute sore throat is to reduce the duration of the illness rather than to prevent complications.
- If the doctor is considering, or the patient is anticipating, antibiotic therapy when no concerning signs are present, the guideline suggests that the treatment choice should rely on one of the three clinical scores (strength of recommendation B, II).
- When the point score is less than 3, antibiotic treatment is not advisable.
- It is recommended to consider the principle of delayed prescribing (DP) from a point score of 3.
- Immediate antibiotic therapy should only be considered at the earliest when the point score reaches 4.
- Delayed prescribing (DP) involves providing a prescription to the patient, which is only filled if their symptoms worsen or do not improve after 3-5 days.

Selection of the active substance and treatment duration

- When considering antibiotic treatment, whether through delayed prescription (DP) or immediate administration, the following active ingredients are recommended (A, Ia):
    - Adolescents (> 15 years) and adults:
        - Penicillin V 0.8–1.0 million IU orally three times daily for 5–7 days

        - In the case of penicillin intolerance: clarithromycin 250–500 mg orally twice daily for 5 days.
    - Children (3–15 years):
        - Penicillin V 0.05–0.1 million IU/kg body weight/day divided into three single oral doses for 5–7 days
        - In the case of penicillin intolerance: clarithromycin 15 mg/kg body weight/day divided into two single oral doses for 5 days.
- The risk of adverse drug reactions and the development of resistance increases with increasing duration of antibiotic use.
- Hence, the guideline suggests limiting the usage duration to a range of 5 to a maximum of 7 days. The use of a 10-day course of penicillin to eradicate pathogens should be reserved for specific cases with an elevated risk of experiencing a severe illness (GCP)
- Administering penicillin at noon might be challenging for patients aged 3 to 15 years, particularly if they attend community facilities. In such instances, it is acceptable to split the daily penicillin V dosage into two doses, one in the morning and one in the evening (Statement; Ia)

Recurrent acute tonsillitis

- From a frequency of six episodes or more in the preceding 12 months, tonsillectomy or tonsillotomy is a therapeutic option (GCP).
- If tonsillectomy is not a feasible or preferred option, a single attempt to pharmacologically eliminate the pathogens using amoxicillin/clavulanic acid or clindamycin can be considered during the episode of sore throat (0, Ia).

1.2.2 CDC Guidelines on Pharyngitis (Acute Sore Throat) (2022)

The following recommendations are retrieved from the CDC guidelines on Pharyngitis (Acute Sore Throat) (last updated 2022)[6]

Etiology

- Streptococcus pyogenes, often referred to as Group A strep, is responsible for causing a throat infection known as streptococcal pharyngitis. These bacteria are characterized by their gram-positive cocci shape and tendency to grow in chains.

Clinical features

- Streptococcal pharyngitis, or Group A strep pharyngitis, is an acute inflammation of the throat that typically manifests with the following symptoms:

a. Abrupt onset of a painful throat
b. Discomfort or pain while swallowing
c. Elevation of body temperature (fever)

- Additional symptoms may encompass a headache, abdominal discomfort, and, particularly in children, symptoms such as nausea and vomiting.
- Patients with Group A strep pharyngitis can also exhibit a rash with a scarlet-like appearance. This particular condition is referred to as scarlet fever or scarlatina.
- In children under 3 years old, respiratory illness resulting from a Group A strep infection seldom appears as acute pharyngitis. Instead, these children typically experience mucopurulent rhinitis, which is followed by symptoms like fever, irritability, and reduced appetite, often termed as "streptococcal fever" or "streptococcosis."
- Unlike the typical acute presentation of Group A strep pharyngitis, this subacute manifestation in young children rarely involves high fever.

Transmission

- The primary mode of transmission for Group A strep pharyngitis is direct person-to-person contact.
- It is typically spread through respiratory droplets but can also happen when coming into contact with an infected person's secretions, including saliva, discharge from wounds, or nasal secretions.
- Administering the right antibiotic treatment for a duration of 12 hours or more restricts an individual's capacity to transmit Group A strep.
- Individuals with Group A strep pharyngitis or scarlet fever should refrain from attending work, school, or daycare until two conditions are met:
    a. They no longer have a fever (afebrile).
    b. They have been on appropriate antibiotic therapy for a minimum of 12-24 hours.

Incubation period

- The incubation period of group A strep pharyngitis is approximately 2 to 5 days.

Risk factors

- The primary risk factor is close proximity to an individual with Group A strep pharyngitis. Adults at higher risk for Group A strep pharyngitis encompass parents of school-aged children and adults who frequently interact with children.

- Environments with increased crowding, such as schools, military training facilities, and daycare centers, elevate the risk of disease transmission.

Diagnosis and testing

- The range of potential diagnoses for acute pharyngitis encompasses various viral and bacterial agents. Viruses are the predominant culprits behind pharyngitis in individuals of all age groups.
- When evident viral symptoms such as cough, rhinorrhea, hoarseness, or conjunctivitis are apparent, the diagnosis of viral pharyngitis can be established through a patient's medical history and clinical evaluation.
- Clinicians need to use either a rapid antigen detection test (RADT) or throat culture (gold standard) to confirm group A strep pharyngitis.

Treatment

- Using the prescribed antibiotic regimen to address Group A strep pharyngitis yields several benefits:
    1. Reduces the duration of symptoms.
    2. Lowers the likelihood of transmitting the infection to family members, classmates, and close contacts.
    3. Prevents the development of complications, including acute rheumatic fever.
- When left untreated, the symptoms of Group A strep pharyngitis typically resolve on their own. However, the risk of acute rheumatic fever and purulent complications (e.g., peritonsillar abscess, mastoiditis) increases when the infection goes untreated.
- Patients, regardless of age, who test positive through RADT or throat culture require antibiotics.
- It is important not to prescribe antibiotics for viral pharyngitis.
- Penicillin or amoxicillin represents the antibiotic of choice for treating Group A strep pharyngitis.
- It is worth noting that there have been no reported cases of clinical isolates of Group A strep showing resistance to penicillin. However, resistance to azithromycin and clarithromycin is common in some communities.
- For patients with a penicillin allergy, recommended alternatives include narrow-spectrum cephalosporins (such as cephalexin and cefadroxil), clindamycin, azithromycin, and clarithromycin.

Table 7. Antibiotic Regimens Recommended for Group A Streptococcal Pharyngitis. Adapted from the CDC Guidelines on Pharyngitis (Acute Sore Throat) (Last Updated 2022)

Drug, Route	Dose or Dosage	Duration or Quantity
For individuals without penicillin allergy		
Penicillin v, oral	Children: 250 mg twice daily or 3 times daily; adolescents and adults: 250 mg 4 times daily or 500 mg twice daily	10 days
Amoxicillin, oral	50 mg/kg once daily (max = 1000 mg); alternate: 25 mg/kg (max = 500 mg) twice daily	10 days
Benzathine penicillin G, intramuscular	< 27 kg: 600 000 U; ≥ 27 kg: 1 200 000 U	1 dose
For individuals with penicillin allergy		
Cephalexin,[a] oral	20 mg/kg/dose twice daily (max = 500 mg/dose)	10 days
Cefadroxil,[a] oral	30 mg/kg once daily (max = 1 g)	10 days
Clindamycin, oral	7 mg/kg/dose 3 times daily (max = 300 mg/dose)	10 days
Azithromycin,[b] oral	12 mg/kg once (max = 500 mg), then 6 mg/kg (max=250 mg) once daily for the next 4 days	5 days
Clarithromycin[b], oral	7.5 mg/kg/dose twice daily (max = 250 mg/dose)	10 days

Abbreviation: Max, maximum.

[a] Avoid in individuals with immediate type hypersensitivity to penicillin.
[b] Resistance of group A strep to these agents is well-known and varies geographically and temporally.

Carriage

- Typically, individuals who carry Group A strep without displaying any symptoms do not necessitate treatment. These carriers may exhibit positive results in throat cultures or RADT, but they do not manifest clinical symptoms or an immunological reaction to Group A strep antigens during laboratory tests.
- In comparison to those with symptomatic pharyngitis, carriers have a significantly lower likelihood of transmitting Group A strep to others.

Furthermore, carriers are at very low risk of developing either purulent or non-purulent complications.

Prognosis and Complications

- In exceptional cases, both purulent and non-purulent complications may arise following Group A strep pharyngitis.
- Purulent complications stem from the extension of Group A strep infection beyond the pharynx and can encompass conditions such as: peritonsillar abscess, retropharyngeal abscess, cervical lymphadenitis, and mastoiditis.
- Other localized infections or septic conditions are even rarer occurrences.

Prevention

- Effective hand hygiene and adhering to proper respiratory manners are essential in mitigating the transmission of all forms of Group A strep infections. Emphasizing hand hygiene is particularly crucial following coughing or sneezing and before handling food or eating.
- Solid respiratory etiquette involves covering one's mouth when coughing or sneezing.
- Administering an antibiotic treatment for a minimum of 12 hours also diminishes an individual's potential to transmit the bacteria.

1.2.3 Medecins Sans Frontieres (MSF) Guidelines on Acute Pharyngitis (2020)

The following recommendations are retrieved from Medecins sans frontieres guidelines on acute pharyngitis (2020)[7]

Clinical features

- Shared characteristics among all varieties of pharyngitis include throat discomfort, difficulty swallowing (dysphagia), tonsil and pharynx inflammation, as well as tender cervical lymph nodes in the front of the neck. Fever may or may not be present.
- Specific traits can vary based on the underlying cause.
- The most common forms include:
    1. **Erythematous pharyngitis (a red throat) or exudative pharyngitis (a red throat with whitish exudate)** can be found in both viral and Group A Streptococcus (GAS) pharyngitis cases.

- ✓ The Centor criteria are used to assess these appearances and reduce the indiscriminate use of antibiotics, particularly in situations where rapid GAS testing is unavailable.
- ✓ A Centor score below 2 effectively excludes Group A Streptococcus (GAS) infection. However, it is important to note that in individuals with risk factors such as immunosuppression, a personal or family history of acute rheumatic fever (ARF), or those at risk of local or systemic complications, the Centor score should not be relied upon, and instead, empirical antibiotic treatment should be prescribed.

Table 8. Centor Criteria. Adapted from the MSF Pharyngitis Guidelines.

Criteria	Score
Temperature > 38°C	1
Absence of cough	1
Tender anterior cervical lymph node(s)	1
Tonsillar swelling or exudate	1

2. **Pseudomembranous pharyngitis:** (red tonsils/pharynx covered with an adherent greyish white false membrane).
3. **Vesicular pharyngitis (clusters of tiny blisters or ulcers on the tonsils):** always viral (coxsackie virus or primary herpetic infection).
4. **Ulcero-necrotic pharyngitis:** hard and painless syphilitic chancre of the tonsil; tonsillar ulcer soft on palpation in a patient with poor oral hygiene and malodorous breath (Vincent tonsillitis).

- Other forms of pharyngitis include:

  Spots on oral mucosa (Koplik's spots) accompanied by conjunctivitis and skin rash as in measles;

  Strawberry" (red and bumpy) tongue accompanied by a skin rash as in scarlet fever caused by GAS.

Complications

- **Local complications** include peritonsillar, retropharyngeal, or lateral pharyngeal abscess (fever, intense pain, dysphagia, hoarse voice, trismus (limitation of mouth opening), unilateral deviation of the uvula).
- **General complications:** diphtheria, acute rheumatic fever, acute glomerulonephritis, severe dehydration, severe difficulty swallowing, upper airway compromise and deterioration of general condition.

Treatment

- Paracetamol or ibuprofen PO are indicated for the symptomatic treatment (fever and pain).
- If the Centor score is equal to or less than 1, this suggests the presence of viral pharyngitis, which usually resolves naturally in a few days (or weeks in the case of infectious mononucleosis). In such instances, antibiotic treatment is not necessary.
- If the Centor score is equal to or greater than 2 or scarlet fever is present: antibiotic treatment for GAS infections is recommended:
    1. If single-use injection equipment is available, **benzathine benzylpenicillin** is the drug of choice as streptococcus A resistance to penicillin remains rare; it is the only antibiotic proven effective in reducing the incidence of rheumatic fever; and the treatment is administered as a single dose.
        - Children under 30 kg (or under 10 years): 600 000 IU single dose
        - Children 30 kg and over (or 10 years and over) and adults: 1.2 MIU single dose
    2. **Phenoxymethylpenicillin** (Penicillin V) is the oral reference treatment, but poor adherence is predictable due to the length of treatment (PO for 10 days).
        - Children 1 to < 6 years: 250 mg 2 times daily
        - Children 6 to < 12 years: 500 mg 2 times daily
        - Children 12 years and over and adults: 1 g 2 times daily
        - Children under 1 year: 125 mg 2 times daily
    3. **Amoxicillin** (PO for 6 days) is an alternative and the treatment has the advantage of being relatively short. However, it can cause adverse skin reactions in patients with undiagnosed Infectious mononucleosis (IM) and thus should be avoided when IM has not been excluded.
        - Children: 25 mg/kg 2 times daily
        - Adults: 1 g 2 times daily
    4. **Macrolides** should be reserved for penicillin allergic patients as resistance to macrolides is frequent and their efficacy in the prevention of rheumatic fever has not been studied.
        i. **Azithromycin** PO for 3 days
            - Children: 20 mg/kg once daily (max. 500 mg daily)
            - Adults: 500 mg once daily

1.2.4 Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review (2020)

This review published in 2020 covers methods for diagnosing the infection, clinical guidelines for strep throat, and the question of treatment. The main recommendations are detailed below[5]:

Diagnostic methods for Group A β-hemolytic streptococcus (GABHS)

- The initial step in diagnosing GABHS involves a thorough physical examination and gathering the patient's medical history.
- Following the completion of a physical examination and patient history, there are five different approaches for confirming the existence of a GABHS infection. These methods include clinical scoring systems, rapid antigen detection tests, throat culture, nucleic acid amplification tests, and machine learning and artificial intelligence.

Treatment for GABHS

- The treatment for GABHS aims to achieve five objectives. Firstly, it aims to alleviate symptoms. Secondly, it seeks to reduce the duration of the illness. Thirdly, it intends to prevent both nonsuppurative and suppurative complications. Fourthly, it aims to lower the risk of transmission. Lastly, it aims to minimize unnecessary antibiotic use, thereby contributing to the prevention of antibiotic resistance development.
- Symptom relief for GABHS is straightforward and can be achieved through the use of analgesic and antipyretic agents like acetaminophen.
- Appropriate antibiotics reduce the duration of illness by approximately one day, with the greatest reduction in symptoms seen on the third day of treatment.
- The extent of symptom improvement could be influenced by how quickly antibiotics are given. Numerous studies have observed that initiating treatment within 48 hours of the symptom onset offers the highest likelihood of symptom relief.
- To achieve these goals, it is essential to consider the advantages of antibiotic therapy in comparison to the associated costs. There is substantial evidence indicating that antibiotics are frequently prescribed excessively for GABHS treatment, and this trend is observed across various medical specialties.
- There is broad agreement that antibiotics with narrow spectrums of activity are appropriate for treating GABHS.
- Penicillin V is the preferred antibiotic for numerous doctors and is supported by the guidelines of CDC/AAFP/ACP-ASIM. There is no documented resistance

of GABHS to penicillin, and the incidence of allergic reactions is below 4%. The IDSA guidelines propose a ten-day regimen of either penicillin or amoxicillin. These antibiotics are cost-effective, have a limited spectrum of activity, and exhibit low rates of side effects.

- In cases where individuals have allergies to these medications, the IDSA recommends considering azithromycin for a five-day course, first-generation cephalosporin for ten days, or clindamycin or clarithromycin for ten days. As per the CDC/AAFP/ACP-ASIM guidelines, erythromycin is suggested for patients who are allergic to penicillin.
- Whether and when patients should be treated with antibiotics for pharyngitis remains a controversial question.
- The absence of a superior treatment standard suggests that greater emphasis should be placed on how physicians and pharmacists dispense antibiotics in practice, and how patients view the care they receive.
- Physicians should possess the ability to effectively communicate the advantages and potential drawbacks of antibiotic use to their patients. Overall, the quality of the doctor-patient relationship and the effectiveness of their communication can be equally significant as the specific diagnostic and treatment approaches employed for pharyngitis.

Section 2.0 Drug Therapy in Pharyngitis

This section comprises four subsections: the first one contains the newly recommended drugs, the second one covers drug modifications, the third one outlines the drugs that have been withdrawn from the market and the fourth one details other drugs that are not currently SFDA registered.

2.1 Additions

After November 2019, there have been no pharyngitis drugs that have received FDA or EMA approval. However, Naproxen is registered in the SFDA list and is recommended by guidelines for the management of sore throat symptoms. Hence, relevant information pertaining to this drug can be found below.

2.1.1 Naproxen

This section includes pertinent information regarding the use of Naproxen (NAPROX®), (ALEVE®), (PROXEN®)[8] in the management of sore throat symptoms.

Table 9. Naproxen Drug Information

SCIENTIFIC NAME Naproxen	
SFDA Classification	OTC
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	J00, J02
Drug Class	Analgesic
Drug Sub-class	Nonsteroidal Anti-inflammatory Drug (NSAID)
ATC Code	M01AE02
Pharmacological Class (ASHP)	28:08.04.92 Other Nonsteroidal Anti-inflammatory Agents
DRUG INFORMATION	
Dosage Form	Tablet
Route of Administration	Oral use

Dose (Adult) [DDD]*	**Pain (monotherapy or as adjunctive agent): Oral:** *Immediate release:* Initial: 500 mg once, followed by 250 to 500 mg every 12 hours as needed **or** 250 mg every 6 to 8 hours as needed; maximum dose: 1.25 g on day 1, then 1 g/day thereafter. For postoperative pain, doses may be scheduled initially (Schwenk 2020, manufacturer's labeling). *Extended release:* 1 g once daily; may increase to 1.5 g once daily for acute pain, then reduce to a usual maximum dose of 1 g/day. *OTC labeling (patient-guided therapy): Immediate release:* Initial: 200 to 400 mg once, followed by 200 mg every 8 to 12 hours as needed; maximum dose: 400 mg in any 8- to 12-hour period or 600 mg in a 24-hour period. **Fever (alternative agent):** **Oral:** *OTC labeling (patient-guided therapy): Immediate release:* Initial: 200 to 400 mg once, followed by 200 mg every 8 to 12 hours as needed; maximum dose: 400 mg in any 8- to 12-hour period or 600 mg in a 24-hour period.
Maximum Daily Dose Adults*	400 mg in any 8- to 12-hour
Dose (pediatrics)	**Analgesia/pain, mild to moderate:** - Children and Adolescents <60 kg: Limited data available: Oral: 5 to 7 mg/kg/dose every 8 to 12 hours; maximum daily dose: 1,000 mg/day.

	- Children and Adolescents ≥60 kg: Limited data available: Oral: 5 to 7 mg/kg/dose every 8 to 12 hours; maximum daily dose: 1,000 mg/day (Berde 2002; Zeltzer 2020). Note: Usual adult dose is 500 mg once, followed by 250 to 500 mg every 12 hours as needed or 250 mg every 6 to 8 hours as needed (manufacturer's labeling). - OTC labeling: Children ≥12 years and Adolescents: Immediate release (eg, Aleve): Oral: 200 mg every 8 to 12 hours; if needed may use 400 mg for the initial dose; maximum daily dose: 600 mg/day. **Fever: OTC labeling:** Children ≥12 years and Adolescents: Immediate release (eg, Aleve): Oral: 200 mg every 8 to 12 hours; if needed may use 400 mg for the initial dose; maximum daily dose: 600 mg/day.
Maximum Daily Dose Pediatrics*	Pain: 1000 mg/day, Fever: 600 mg/day
Adjustment	**Altered kidney function:** - CrCl ≥60 mL/minute: No dosage adjustment necessary (<1% of unchanged drug excreted in the urine). - CrCl >30 to <60 mL/minute: No dosage adjustment necessary (<1% of unchanged drug excreted in the urine) However, use the lowest effective dose for the shortest duration possible. Use of analgesics other than nonsteroidal anti-inflammatory drugs (NSAIDs) or topical NSAIDs may be preferred. Avoid use in patients at high risk for acute kidney injury (ie, volume depleted,

	hypotensive, elderly, or taking concurrent nephrotoxic medications) - CrCl ≤30 mL/minute: Avoid use due to increased risk of acute kidney injury (KDIGO 2013); use of analgesics other than NSAIDs or topical NSAIDs are preferred. However, in select patients where alternatives are not effective, after careful assessment of risks versus benefits, use of naproxen may be considered; use the lowest effective dose for the shortest duration possible with close monitoring of kidney function (expert opinion). **Hemodialysis, intermittent (thrice weekly): Not significantly dialyzable:** Avoid use, as patients with end-stage kidney disease may be at increased risk for bleeding (eg, GI), cardiovascular adverse effects, and loss of residual kidney function (Kurella 2003; expert opinion). However, in select patients after careful assessment of risks versus benefits, use of naproxen may be considered; use the lowest effective dose for the shortest duration possible (Koncicki 2017; expert opinion). **Peritoneal dialysis:** Unlikely to be significantly dialyzable (high protein binding): Avoid use, as patients with end-stage kidney disease may be at increased risk for bleeding (eg, GI), cardiovascular adverse effects, and loss of residual kidney function (Kurella 2003; expert opinion). However, in select patients after careful assessment of risks versus benefits, use of naproxen may be considered; use the lowest effective dose

	for the shortest duration possible (Koncicki 2017; expert opinion). **CRRT:** Avoid use (expert opinion). **PIRRT:** (eg, sustained, low-efficiency diafiltration): Avoid use (expert opinion). **Acute kidney injury while on naproxen therapy:** Discontinue use (expert opinion).
Prescribing edits*	N/A
AGE (Age Edit): N/A	
CU (Concurrent Use Edit): N/A	
G (Gender Edit): N/A	
MD (Physician Specialty Edit): N/A	
PA (Prior Authorization): N/A	
QL (Quantity Limit): N/A	
ST (Step Therapy): N/A	
EU (Emergency Use Only): N/A	
PE (Protocol Edit): N/A	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Dyspepsia, headache **Most serious:** Acute Myocardial infarction (MI), cerebrovascular accident, new-onset hypertension or exacerbation of hypertension, new-onset or exacerbation of heart failure, gastrointestinal inflammation, gastrointestinal hemorrhage, gastrointestinal ulcer, and gastrointestinal perforation, hemorrhage, hemolytic anemia, agranulocytosis, neutropenia, thrombocytopenia, mild transaminase elevations, angioedema, hemodynamically-mediated acute kidney injury, interstitial nephritis (with or without nephrotic syndrome), and renal papillary necrosis.
	Category X:

	• Abrocitinib • Acemetacin • Aminolevulinic Acid (Systemic) • Diflunisal • Ketorolac (Nasal) • Ketorolac (Systemic) • Macimorelin • Mifamurtide • Nonsteroidal Anti-Inflammatory Agents • Phenylbutazone • Tenoxicam • Urokinase
Special Population	**Pediatric:** Not for self-medication (OTC use) in children < 12 years.
Pregnancy	Naproxen crosses the placenta. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) close to conception may be associated with an increased risk of miscarriage due to cyclooxygenase-2 inhibition interfering with implantation. Birth defects have been observed following in utero NSAID exposure in some studies; however, data are conflicting. Nonteratogenic effects, including prenatal constriction of the ductus arteriosus, persistent pulmonary hypertension of the newborn, oligohydramnios, necrotizing enterocolitis, renal dysfunction or failure, and intracranial hemorrhage, have been observed in the fetus/neonate following in utero NSAID exposure. Maternal NSAID use may cause fetal renal dysfunction leading to oligohydramnios. Although rare, this may occur as early as 20 weeks' gestation and is more likely to occur with prolonged maternal use. Oligohydramnios may be reversible

	following discontinuation of the NSAID. In addition, nonclosure of the ductus arteriosus postnatally may occur and be resistant to medical management. Avoid maternal use of NSAIDs beginning at 20 weeks' gestation. If NSAID use is necessary between 20 and 30 weeks' gestation, limit use to the lowest effective dose and shortest duration possible; consider ultrasound monitoring of amniotic fluid if treatment extends beyond 48 hours and discontinue the NSAID if oligohydramnios is found (FDA 2020). Because NSAIDs may cause premature closure of the ductus arteriosus, product labeling for naproxen specifically states to avoid use starting at 30 weeks' gestation. Based on available information, NSAIDs can be continued during the first 2 trimesters of pregnancy in patients with rheumatic and musculoskeletal diseases; use in the third trimester is not recommended.
Lactation	Naproxen is present in breast milk. Data related to the presence of naproxen in breast milk are available following maternal administration of oral naproxen 375 mg twice daily for 3 weeks to 1 woman ~6 months postpartum. Naproxen breast milk concentrations were 1.76 to 2.37 mcg/mL with the highest concentration occurring 4 hours after the dose. Naproxen was detected in the urine of the breastfeeding infant. The cumulative amount of naproxen found in the urine of the infant was 0.26% of the cumulative maternal urinary excretion. - Using a milk concentration of 2.37 mcg/mL, the estimated exposure

	to the breastfeeding infant would be 0.36 mg/kg/day (relative infant dose: 3.3% based on the weight adjusted maternal dose of 750 mg/day). - In general, breastfeeding is considered acceptable when the relative infant dose (RID) is <10%. A prospective cohort study evaluated the outcomes of breastfed infants whose mothers were taking various medications. Within the study, 20 mother-infant pairs reported naproxen exposure (dose, duration, relationship to breastfeeding not provided). There were two cases of drowsiness and one case of vomiting in the breastfed infants. Nonopioid analgesics, including nonsteroidal anti-inflammatory drugs (NSAIDs), are preferred for breastfeeding patients who require pain control peripartum or for surgery outside of the postpartum period. Short-term use of naproxen is acceptable but avoid long-term use (>1 week) in breastfeeding patients. NSAIDs are considered compatible for the treatment of rheumatic and musculoskeletal diseases. NSAIDs may be used to treat acute migraine in lactating patients. According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and benefits of treatment to the mother. Avoid maternal use of NSAIDs if the breastfeeding infant has platelet dysfunction, thrombocytopenia, or a ductal-dependent cardiac lesion.
Contraindications	Hypersensitivity to naproxen (eg, anaphylactic reactions, serious skin

	reactions) or any component of the formulation; history of asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs; use in the setting of coronary artery bypass graft (CABG) surgery. *Canadian labeling:* Additional contraindications (not in US labeling): Active gastric, duodenal, or peptic ulcers; active GI bleeding; cerebrovascular bleeding or other bleeding disorders; active GI inflammatory disease; severe liver impairment or active liver disease; severe renal impairment (CrCl <30 mL/minute) or deteriorating renal disease; severe uncontrolled heart failure; known hyperkalemia; third trimester of pregnancy; breast-feeding; inflammatory lesions or recent bleeding of the rectum or anus (suppository only); use in patients <16 years of age (suppository only); use in patients <18 years of age (naproxen enteric coated and sustained release tablets and naproxen sodium tablets); use in children <2 years (naproxen tablets and suspension).
Monitoring Requirements	Monitor CBC (if hemoglobin ≤10 g at initiation, continue to monitor hemoglobin periodically during long-term therapy), chemistry profile (periodically during long-term therapy), LFTs, renal function tests (urine output, serum BUN and creatinine), BP (at initiation and during therapy), signs/symptoms of fluid retention, periodic ophthalmic exam (with any vision changes occurring during long-term therapy), signs of bleeding (occult

	or gross blood loss, especially in patients with coagulation disorders or who are receiving anticoagulants); monitor for anemia with long-term therapy; monitor for signs/symptoms of immediate or delayed hypersensitivity reactions.
Precautions	- CNS effects: May cause drowsiness, dizziness, blurred vision, and other neurologic effects that may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (eg, operating machinery or driving). Discontinue use with blurred or diminished vision and perform ophthalmologic exam. Periodically evaluate vision in all patients receiving long-term therapy. - Hyperkalemia: NSAID use may increase the risk of hyperkalemia, particularly in patients ≥65 years of age, in patients with diabetes or renal disease, and with concomitant use of other agents capable of inducing hyperkalemia (eg, ACE-inhibitors). Monitor potassium closely. - Aseptic meningitis: May increase the risk of aseptic meningitis, especially in patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders. - Asthma: Contraindicated in patients with aspirin-sensitive asthma; severe and potentially fatal bronchospasm may occur. Use caution in patients with other forms of asthma. - Bariatric surgery: Gastric ulceration: Avoid chronic use of oral nonselective NSAIDs after bariatric surgery; development of anastomotic ulcerations/perforations may occur.

	Short-term use of celecoxib or IV ketorolac are recommended as part of a multimodal pain management strategy for postoperative pain. - Hepatic impairment: Use with caution in patients with hepatic impairment. - Renal impairment: Use with caution in patients with renal impairment. - Self-medication (OTC use): Prior to self-medication, patients should contact healthcare provider if they have had recurring stomach pain or upset, ulcers, bleeding problems, asthma, high BP, heart or kidney disease, other serious medical problems, are currently taking a diuretic, anticoagulant, other NSAIDs, or are ≥60 years of age. Do not exceed recommended dosages and duration, due to an increased risk of GI bleeding, MI, and stroke. Patients should stop use and consult a healthcare provider if symptoms get worse, newly appear, or continue; if an allergic reaction occurs; if feeling faint, vomit blood or have bloody/black stools; if having difficulty swallowing or heartburn, or if fever lasts for >3 days or pain >10 days. Consuming ≥3 alcoholic beverages/day or taking longer than recommended may increase the risk of GI bleeding. - Surgical/dental procedures: Withhold for at least 4 to 6 half-lives prior to surgical or dental procedures.
Black Box Warning	Serious cardiovascular thrombotic events, Serious gastrointestinal bleeding, ulceration, and perforation
REMS	N/A

Health Technology Assessment (HTA)

After conducting a comprehensive analysis of several HTA bodies, such as NICE, CADTH, HAS, IQWIG, and PBAC, it was found that **none of them have provided specific recommendations regarding the use of *naproxen* for the management of sore throat symptoms**. However, ***naproxen*** has been marketed for many years, with multiple generics available, leading to a relatively low cost of treatment.

Conclusion Statement – Naproxen

As mentioned in the guidelines, naproxen can be used as an option to relieve the symptoms associated with pharyngitis (Acute Sore throat) such as pain and fever. Therefore, it is recommended to be included in the CHI formulary.

2.2 Modifications

No modifications have been made since November 2019.

2.3 Delisting

The medication below is no longer SFDA registered, therefore, it is advisable to delist it from CHI formulary. *Please refer to **Drug therapy in pharyngitis - section 2** of CHI Pharyngitis original clinical guidance.*

- Clavulanic acid

Section 3.0 Key Recommendations Synthesis

- The rapid antigen detection test (RADT) is advised for identifying the requirement for antimicrobial treatment because of its notably high specificity.[9]
- If the rapid antigen detection test (RADT) yields a negative result, it should be followed up with a throat culture.
- The modified Centor criteria are the most employed clinical scoring guidelines. This is because the Centor criteria have a limited positive predictive value when it comes to identifying the existence of a group A streptococcal infection.[10]
- The guideline supports the utilization of throat remedies like lozenges, gargle solutions, and sprays containing local anesthetics and/or non-steroidal anti-inflammatory drugs (NSAIDs), but with a relatively weak level of recommendation[4].
- The guideline strongly advises against the use of throat preparations that contain local antiseptics and/or antibiotics because the majority of acute sore throat cases are caused by viral infections[4].
- Corticosteroids should not be used for analgesic treatment of sore throat (A, 1a)[4].
- Ibuprofen or naproxen can be considered for short-term relief from sore throat symptoms (O, Ib)[4].
- The role of acetaminophen and its efficacy compared to NSAIDs is still debated. A meta-analysis (2004) showed that in children, single doses of ibuprofen (4-10 mg/kg) and acetaminophen (7-15 mg/kg) proved to have similar efficacy for relieving moderate to severe pain, and similar safety as analgesics or antipyretics[11]. A Cochrane review from 2013 reported insufficient evidence to support the effectiveness of paracetamol in alleviating common cold symptoms[4]. Finally, another meta-analysis (2021) found that ibuprofen is more effective in reducing temperature and pain at various follow-up periods compared with acetaminophen[12].
- A sore throat, even when of bacterial origin, is not a general indication for the administration of antibiotics (Statement, Ia)[4].
- The question of whether and when patients should receive antibiotics for pharyngitis is a topic of ongoing debate and controversy[5].
- Many doctors favor the use of penicillin V as the top choice antibiotic, a preference that aligns with the guidelines provided by CDC/AAFP/ACP-ASIM[5].

- The IDSA guidelines propose a ten-day regimen of either penicillin or amoxicillin[5].
- When patients are allergic to penicillins, the IDSA suggests contemplating a five-day course of azithromycin or a ten-day course of a first-generation cephalosporin, clindamycin, or clarithromycin[5].
- According to the guidelines of CDC/AAFP/ACP-ASIM, erythromycin is recommended for individuals who have a penicillin allergy[5].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI pharyngitis (acute sore throat) report** and aims to provide recommendations to aid in the management of Pharyngitis (Acute Sore throat). 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 Pharyngitis (Acute Sore throat). 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. Pharyngitis Scope

2020	Changes	2023	Rationale
Section 1.0 Pharyngitis Clinical Guidelines			
NICE Guidelines for acute sore throat (Anti-microbial prescribing) Guidelines, Published date: 26 January 2018	N/A		
Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American College of Physicians and the Centers for Disease Control and Prevention (2016)	N/A		
Guideline for the management of acute sore throat: The European Society for Clinical Microbiology and Infectious Diseases (2012)	N/A		
Saudi National Antimicrobial Therapy Guidelines for Community and Hospital Acquired Infections in Adults (2018)	N/A		
	Missing	German clinical practice guideline on sore throat (2021)[4]	• **Clinical diagnosis** • **Clinical scores:** The guideline suggests that a clinical score should be calculated for patients (aged 3 years and older) experiencing acute sore throat without any concerning signs when contemplating the use of antibiotic treatment (B, Ib).

			• **Determination of laboratory parameters:** Laboratory measurements like white blood cell count, C-reactive protein, erythrocyte sedimentation rate, and procalcitonin should not be routinely included in the diagnostic evaluation for patients with acute sore throat (lasting less than 14 days) unless there are concerning signs (Statement, Good Clinical Practice [GCP]). • **Symptomatic treatment with throat preparations:** The guideline endorses with only a weak level of recommendation the use of throat preparations (lozenges, gargle solutions, sprays) containing local anesthetics and/or non-steroidal anti-inflammatory drugs (NSAIDs). • **Symptomatic treatment with oral corticosteroids:** Corticosteroids should not be used for analgesic treatment of sore throat (A, 1a). • **Symptomatic treatment with non-steroidal anti-inflammatory drugs and paracetamol:** • Ibuprofen or naproxen can be considered for short-term relief from sore throat symptoms (O, Ib). • A Cochrane review from 2013 reported insufficient evidence to support the effectiveness of paracetamol in alleviating common cold symptoms. • **Benefits of antibiotic treatment:** • A sore throat, even if caused by bacteria, is not a broad recommendation for the use of antibiotics (Statement, Ia).

			• If the doctor is considering, or the patient is anticipating, antibiotic therapy when no concerning signs are present, the guideline suggests that the treatment choice should rely on one of the three clinical scoring systems (strength of recommendation B, II). **Selection of the active substance and treatment duration** • When considering antibiotic treatment, whether through delayed prescription (DP) or immediate administration, the following active ingredients are recommended (strength of recommendation A, Ia): • Adolescents (> 15 years) and adults: • Penicillin V 0.8–1.0 million IU orally three times daily for 5–7 days • In the case of penicillin intolerance: clarithromycin 250–500 mg orally twice daily for 5 days. • Children (3–15 years): • Penicillin V 0.05–0.1 million IU/kg body weight/day divided into three single oral doses for 5–7 days • In the case of penicillin intolerance: clarithromycin 15 mg/kg body weight/day divided into two single oral doses for 5 days. • Hence, the guideline suggests limiting the usage duration to a range of 5 to a maximum of 7 days. The use of a 10-day course of penicillin to eradicate pathogens should be reserved for specific cases with an elevated risk of experiencing a severe illness (GCP). **Recurrent acute tonsillitis**

			• From a frequency of six episodes or more in the preceding 12 months, tonsillectomy or tonsillotomy is a therapeutic option (GCP). • If tonsillectomy is not a feasible or preferred option, a single attempt to pharmacologically eliminate the pathogens using amoxicillin/clavulanic acid or clindamycin can be considered during the episode of sore throat (0, Ia).
	Missing	CDC Guidelines on pharyngitis (sore throat) (last updated 2022)[6]	**Etiology** • Streptococcus pyogenes, often referred to as Group A strep, is responsible for causing a throat infection known as streptococcal pharyngitis. These bacteria are characterized by their gram-positive cocci shape and tendency to grow in chains. **Clinical features** **Transmission** • The primary mode of transmission for Group A strep pharyngitis is direct person-to-person contact. • The incubation period of group A strep pharyngitis is approximately 2 to 5 days. **Risk factors** • The primary risk factor is close proximity to an individual with Group A strep pharyngitis. Adults at higher risk for Group A strep pharyngitis encompass: parents of school-aged children and adults who frequently interact with children. **Diagnosis and testing**

			• Clinicians need to use either a rapid antigen detection test (RADT) or throat culture (gold standard) to confirm group A strep pharyngitis. **Treatment** • Penicillin or amoxicillin represents the antibiotic of choice for treating Group A strep pharyngitis. • It is worth noting that there have been no reported cases of clinical isolates of Group A strep showing resistance to penicillin. However, resistance to azithromycin and clarithromycin is common in some communities. • For patients with a penicillin allergy, recommended alternatives include narrow-spectrum cephalosporins (such as cephalexin and cefadroxil), clindamycin, azithromycin, and clarithromycin. **Carriage** • Typically, individuals who carry Group A strep without displaying any symptoms do not necessitate treatment. **Prognosis and Complications** • In exceptional cases, both purulent and non-purulent complications may arise following Group A strep pharyngitis. **Prevention** • Effective hand hygiene and adhering to proper respiratory manners are essential in mitigating the transmission of all forms of Group A strep infections. • Solid respiratory etiquette involves covering one's mouth when coughing or sneezing.

			• Administering an antibiotic treatment for a minimum of 12 hours also diminishes an individual's potential to transmit the bacteria.
	Missing	Medecins sans frontieres guidelines on acute pharyngitis (2020)[7]	**Clinical features** • Shared characteristics among all varieties of pharyngitis include throat discomfort, difficulty swallowing (dysphagia), tonsil and pharynx inflammation, as well as tender cervical lymph nodes in the front of the neck. Fever may or may not be present. • Specific traits can vary based on the underlying cause. • The Centor criteria are used to assess these appearances and reduce the indiscriminate use of antibiotics, particularly in situations where rapid GAS testing is unavailable. **Complications** • Local vs general recommendations **Treatment** • Paracetamol or ibuprofen PO are indicated for the symptomatic treatment (fever and pain). • If the Centor score is equal to or less than 1, this suggests the presence of viral pharyngitis, which usually resolves naturally in a few days (or weeks in the case of infectious mononucleosis). In such instances, antibiotic treatment is not necessary. • If the Centor score is equal to or greater than 2 or scarlet fever is present : antibiotic treatment for GAS infections is recommended. • Options include: benzathine benzylpenicillin, Penicillin V,

			amoxicillin and macrolides (azithromycin).
	Missing	Diagnostic Methods, Clinical Guidelines, and Antibiotic Treatment for Group A Streptococcal Pharyngitis: A Narrative Review (2020)[5]	**Diagnostic methods for Group A β-hemolytic streptococcus (GABHS)** • The initial step in diagnosing GABHS involves a thorough physical examination and gathering the patient's medical history. • Following the completion of a physical examination and patient history, there are five different approaches for confirming the existence of a GABHS infection. These methods include clinical scoring systems, rapid antigen detection tests, throat culture, nucleic acid amplification tests, and machine learning and artificial intelligence. **Treatment for GABHS** • Symptom relief for GABHS is straightforward and can be achieved through the use of analgesic and antipyretic agents like acetaminophen. • Appropriate antibiotics reduce the duration of illness by approximately one day, with the greatest reduction in symptoms seen on the third day of treatment. • There is broad agreement that antibiotics with narrow spectrums of activity are appropriate for treating GABHS. • Penicillin V is the preferred antibiotic for numerous doctors and is supported by the guidelines of CDC/AAFP/ACP-ASIM. • In cases where individuals have allergies to these medications, the IDSA recommends considering

			azithromycin for a five-day course, first-generation cephalosporin for ten days, or clindamycin or clarithromycin for ten days. As per the CDC/AAFP/ACP-ASIM guidelines, erythromycin is suggested for patients who are allergic to penicillin.

Appendix C. MeSH Terms PubMed

C.1 Pubmed Search for Pharyngitis

The following is the result of the PubMed search conducted for pharyngitis guideline search:

Query	Filters	Search Details	Results
((((Pharyngitis[MeSH Terms]) OR (Pharyngitides[Title/Abstract])) OR (Sore Throat[Title/Abstract])) OR (Sore Throats[Title/Abstract])) OR (Throat, Sore[Title/Abstract])	Guideline, in the last 5 years	("pharyngitis"[MeSH Terms] OR "Pharyngitides"[Title/Abstract] OR "sore throat"[Title/Abstract] OR "sore throats"[Title/Abstract] OR "throat sore"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	3

Appendix D. Treatment Algorithms

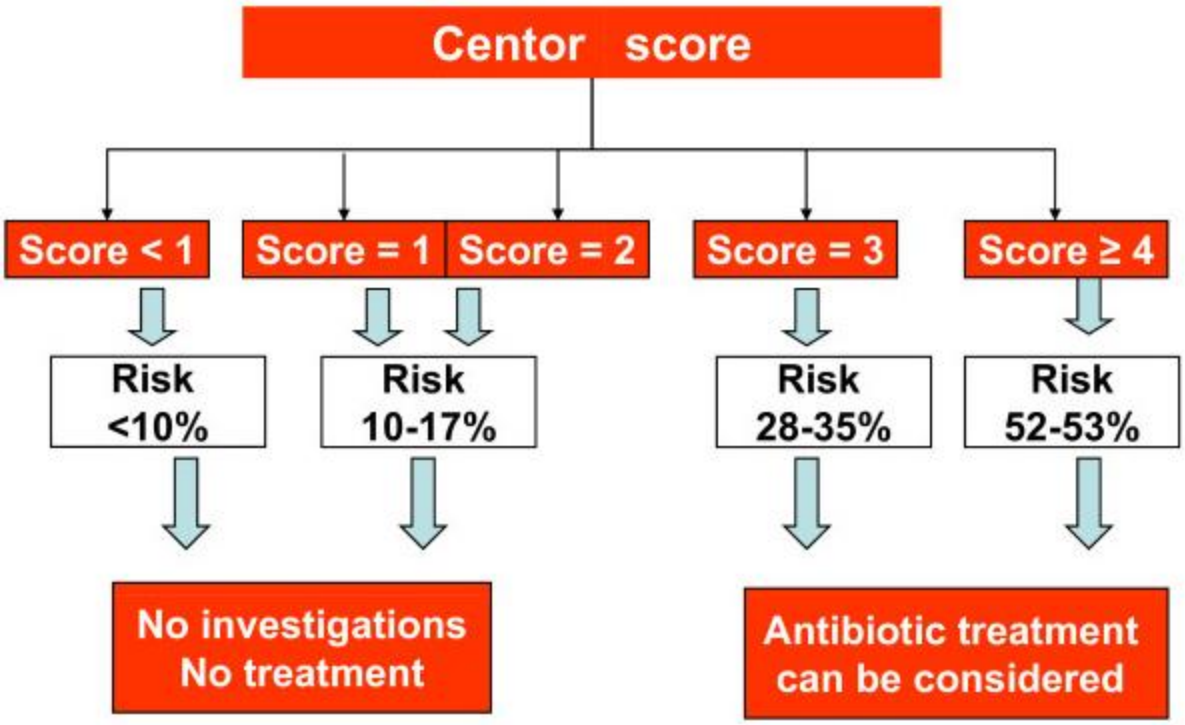

Figure 1. *Approach to Diagnosis and Treatment of Pharyngitis*[3]

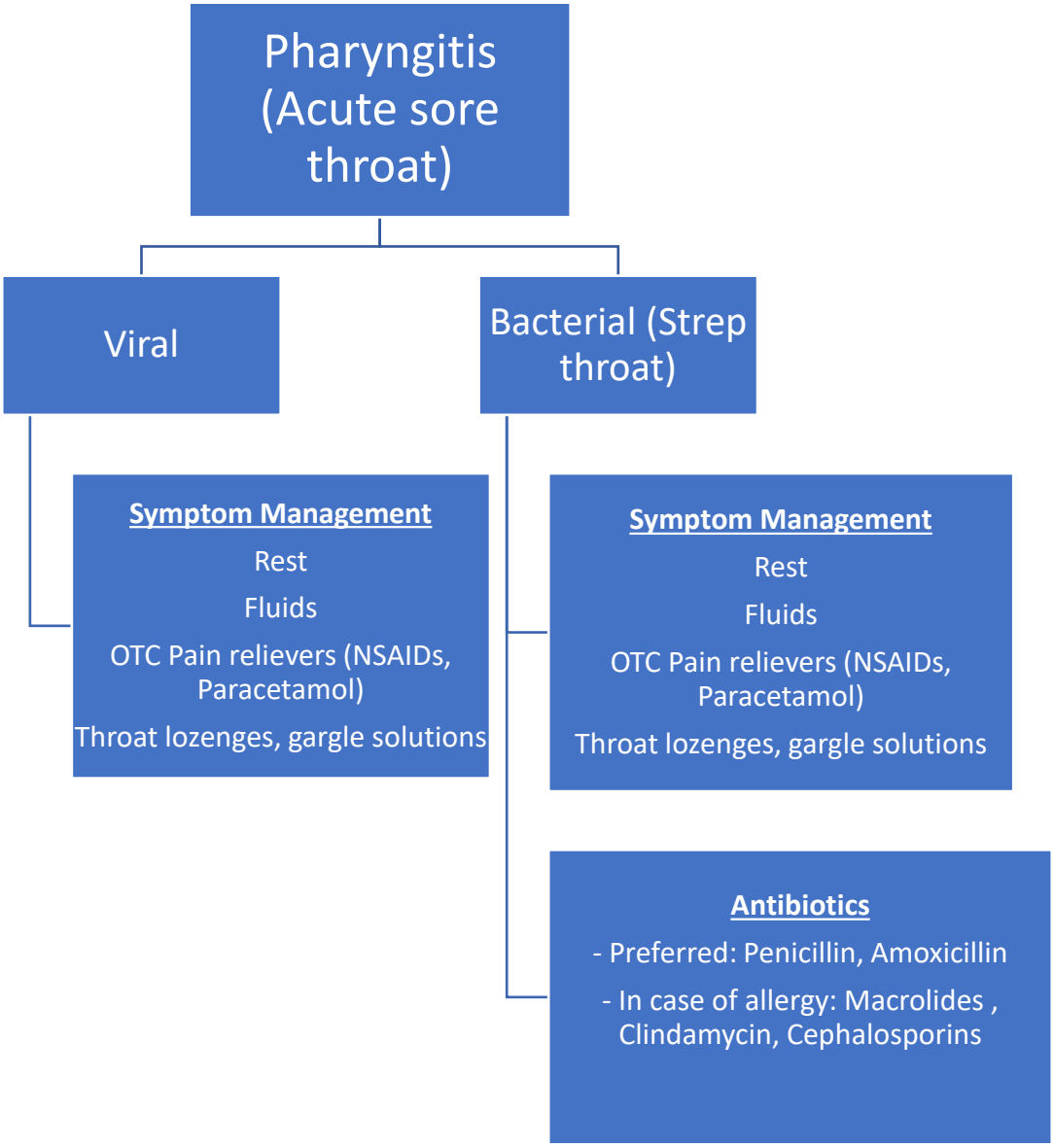

Figure 2. *Treatment Algorithm for the Management of Pharyngitis*[4,5,9,10]