CHRONIC OBSTRUCTIVE PULMONARY DISEASE: Antimicrobial Prescribing

CHI Formulary Indication Review

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- November 2023

To the CHI Original Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing Clinical Guidance- Issued February 2020

Table of Contents

Related Documents

Related SOPs

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

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

List of Tables

List of Figures

Abbreviations

AMC	Amoxicillin Clavulanic acid
CADTH	Canadian Agency for Drugs and Technologies in Health
CBI	Chronic Bronchial Infection
CDC	Centers for Disease Control and Prevention
CES	COPD Exacerbation Syndrome
CHI	Council of Health Insurance
COPD	Chronic Obstructive Pulmonary Disease
EMA	European Medicines Agency
FDA	Food and Drug Administration
HAS	Haute Autorité de Santé
HTA	Health Technology Assessment
IA	Inhaled Antibiotics
IDF	Insurance Drug Formulary
IQWIG	Institute for Quality and Efficiency in Health Care
NICE	National Institute for Health and Care Excellence
PBAC	Pharmaceutical Benefits Advisory Committee
PPM	Potentially Pathogenic Microorganism
SFDA	Saudi Food and Drug Authority
Tdap/dTap	Tetanus, Diphtheria, and Acellular Pertussis

Executive Summary

Chronic Obstructive Pulmonary Disease (COPD) is a diverse lung condition marked by persistent respiratory symptoms (such as dyspnea, cough, sputum production, and exacerbations). These symptoms are attributed to abnormalities in the airways (resulting in bronchitis or bronchiolitis) and/or the alveoli (leading to emphysema). COPD is characterized by chronic, frequently progressive, airflow obstruction[1].

Chronic Obstructive Pulmonary Disease (COPD) has become one of the leading causes of death globally, with 90% of these fatalities happening in low- and middle-income countries (LMICs). In 2012, over 3 million individuals lost their lives due to COPD, accounting for 6% of all global deaths[1]. COPD presents a significant public health issue that can be prevented and managed[1]. In 2019, the prevalence of COPD in Saudi Arabia was 2,053.04 cases per 100,000 population, which marked a 49% rise compared to 1990. This rate is lower than the global prevalence of 2,639.2 cases per 100,000 population[2].

An exacerbation in COPD is defined as an incident characterized by worsening dyspnea and/or cough along with sputum over a period of less than 14 days. These exacerbations are frequently linked to elevated inflammation, both locally and systemically, triggered by factors like airway infections, pollution, or other lung-related insults. Since the symptoms are not exclusive to COPD, it's essential to consider other possible diagnoses, particularly pneumonia, congestive heart failure, and pulmonary embolism. The objectives in treating COPD exacerbations are twofold: to minimize the negative impact of the current exacerbation and to prevent future occurrences[1].

COVID-19 vaccines are strongly recommended for individuals with COPD in accordance with national guidelines. Influenza vaccination reduces the occurrence of lower respiratory tract infections, and pneumococcal vaccination lowers the frequency of lower respiratory tract infections. The CDC suggests Tdap vaccination (pertussis, tetanus, and diphtheria) for COPD patients who were not previously vaccinated during adolescence, as well as routine administration of the shingles vaccine for all individuals with COPD[1]. Furthermore, the CDC recommends the new respiratory syncytial virus (RSV) vaccine for individuals over 60 years and or with chronic lung disease[3].

To manage an exacerbation, it is advised to start with short-acting inhaled beta2-agonists, either alone or in combination with short-acting anticholinergics, as the initial bronchodilators. Additionally, it's recommended to commence maintenance therapy with long-acting bronchodilators as early as possible. For patients experiencing frequent exacerbations and having elevated blood eosinophil levels, the possibility of adding inhaled corticosteroids to the dual bronchodilator regimen should be contemplated[1].

For individuals experiencing severe exacerbations, systemic corticosteroids can enhance lung function (measured by FEV1), improve oxygenation, and expedite recovery, which includes reducing the length of hospitalization. Generally, the course of corticosteroid therapy should not exceed 5 days. In cases where antibiotics are deemed necessary, they can hasten recovery, diminish the risk of early relapse, decrease the chances of treatment failure, and reduce the duration of hospitalization. The recommended duration for antibiotic therapy is 5 days[1].

CHI issued new guidelines related to the management of Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing. 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 **CHI issued Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing guidance after thorough review of renowned international and national clinical guidelines in February 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 Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing **clinical guidance** and seeks to offer guidance for the effective management of **Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing**. It provides an **update on the** Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing **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 the **GOLD** Guidelines **[2023].** Moreover, **new guidelines are added to the report** such as ~~the COPD-X Plan:~~ **Australian and New Zealand Guidelines** for the management of Chronic Obstructive Pulmonary Disease **2023** and the **Spanish COPD Guidelines (GesEPOC) 2021 Update**: Diagnosis and Treatment of COPD Exacerbation Syndrome.

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is advisable to include the SFDA registered vaccines **Pneumococcal 15-valent Conjugate Vaccine (VAXNEUVANCE®)** and **Diphtheria and tetanus toxoids and acellular pertussis vaccines (ADACEL®), (TRIPACEL®), (BOOSTRIX ®)**, while removing **Clavulanic acid** and **Influenza vaccine surface antigen NYMC X-181, NYMC X-187, and NYMC BX-35** as they are no longer registered on 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 February 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 Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing therapeutic management.

Below is a table summarizing the major changes based on the chronic obstructive pulmonary disease: antimicrobial prescribing different guidelines used to issue this report:

Table 1. General Recommendations for Antimicrobial Prescribing in Chronic Obstructive Pulmonary Disease (COPD)

Antimicrobial Prescribing for Chronic Obstructive Pulmonary Disease		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
It is recommended that individuals diagnosed with COPD receive the influenza vaccine.	Evidence B	GOLD Guidelines 2023[1]
Both the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) endorse COVID-19 vaccination for individuals with a COPD diagnosis.	Evidence B	GOLD Guidelines 2023[1]
According to the CDC, individuals with COPD should receive either a single dose of the 20-valent pneumococcal conjugate vaccine (PCV20) or one dose of the 15-valent pneumococcal conjugate vaccine (PCV15) followed by the 23-valent pneumococcal polysaccharide vaccine (PPSV23).	Evidence B	GOLD Guidelines 2023[1]
The CDC suggests that individuals with COPD who did not receive the Tdap (dTAP/dTPa) vaccination during adolescence should consider it to protect against pertussis (whooping cough) (Supported by Evidence B). Additionally, individuals with COPD aged 50 and above are advised to	Evidence B	GOLD Guidelines 2023[1]

receive the Zoster vaccine to guard against shingles.		
The long-term use of macrolide antibiotics may have the potential to reduce the frequency of exacerbations in individuals with moderate to severe **who experience them frequently.**	I, weak	Australian and New Zealand Guidelines 2023[4]
Providing patients prone to exacerbations with azithromycin (250 mg/day or 500 mg three times per week) or erythromycin (250 mg twice a day) for a year led to a decreased risk of exacerbations in comparison to conventional care. Azithromycin use was associated with an increased incidence of bacterial resistance, prolongation of QTc interval, and impaired hearing tests	Not graded	GOLD Guidelines 2023[1]
The choice of antibiotic should be guided by the prevailing bacterial resistance patterns in the local region.	Not graded	GOLD Guidelines 2023[1]
Antibiotics should be prescribed for patients with acute COPD exacerbation, defined as an event characterized by dyspnea and /or cough and sputum that worsen over <14 days. COPD exacerbations are often associated with increase local and systemic inflammation caused by airway infection pollution or other insult to the lung.	Not graded	GOLD Guidelines 2023[1]
For all patients with COPD exacerbations requiring admission to the intensive care unit (ICU) or needing mechanical ventilation (invasive or noninvasive). antibiotics are recommended.	Strong, moderate	Spanish COPD Guidelines (GesEPOC) 2021 Update[5]

Antibiotics, when deemed necessary, have the potential to expedite recovery, diminish the risk of early recurrence, treatment inefficacy, and the length of hospitalization. Typically, the treatment course should span 5 days.	Evidence B	GOLD Guidelines 2023[1]
The choice of antibiotic should be guided by the prevailing bacterial resistance patterns in the local region.	Not Graded	GOLD Guidelines 2023[1]
As a general practice, the initial empirical treatment usually involves an aminopenicillin with clavulanic acid, a macrolide, tetracycline, or, in specific instances, a quinolone.	Not Graded	GOLD Guidelines 2023[1]
Oral corticosteroids are strongly recommended for individuals experiencing severe exacerbations.	Strong, moderate	Spanish COPD Guidelines (GesEPOC) 2021 Update[5]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **antimicrobial prescribing for COPD.**

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 Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing CHI report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This section contains the **updated versions** of the guidelines mentioned in the February 2020 CHI Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing Report and the corresponding recommendations:

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
1.1 **Global strategy** for the diagnosis, management, and prevention of Chronic obstructive pulmonary disease **[2019]**	1.1.1 **GOLD** Guidelines **[2023]**
1.2 **National institute for health and care excellence** guidelines for COPD in over 16s: Diagnosis and management **[2018]**	N/A*
1.3 **National institute for health and care excellence** guidelines for Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing **[2018]**	N/A*
1.4 **The Saudi Guidelines** for the Diagnosis and Management of COPD **2014**	N/A*

*: *No updated versions available*

1.1.1 GOLD Report: Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2023)

The aim of the GOLD Report is to provide a non-biased review of the current evidence for the assessment, diagnosis, and treatment of people with COPD. The GOLD report is revised annually and has been used worldwide by healthcare professionals as a tool to implement effective management programs based on local healthcare systems[1]. Levels of evidence have been assigned to evidence-based recommendations where appropriate (table 3).

Table 3. Description of Levels of Evidence

Evidence Category	Sources of Evidence	Definition
A	Randomized controlled trials (RCTs)	Evidence is from endpoints of well-designed RCTs that provide consistent findings in the population for which the recommendation is made without any important limitations.
	Rich body of high-quality evidence without any significant limitation or bias	Requires high quality evidence from ≥ 2 clinical trials involving a substantial number of subjects, or a single high quality RCT involving substantial numbers of patient without any bias.
B	Randomized controlled trials (RCTs) with important limitations	Evidence is from RCTs that include only a limited number of patients, post hoc or subgroup analyses of RCTs or meta-analyses of RCTs.
	Limited body of evidence	Also pertains when few RCTs exist, or important limitations are evident (methodologic flaws, small numbers, short duration, undertaken in a population that differs from the target population of the

		recommendation, or the results are somewhat inconsistent)
C	Non-randomized trials Observational studies	Evidence is from outcomes of uncontrolled or non-randomized trials or from observational studies
D	Panel consensus judgment	Provision of guidance is deemed valuable but clinical literature addressing the subject is insufficient. Panel consensus is based on clinical experience or knowledge that does not meet the above stated criteria.

Vaccination

- People diagnosed with COPD are advised to receive influenza vaccination (Evidence B).
- Both the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) endorse COVID-19 vaccination for individuals diagnosed with COPD (Evidence B).
- According to the CDC, individuals with COPD should receive either a single dose of the 20-valent pneumococcal conjugate vaccine (PCV20) or one dose of the 15-valent pneumococcal conjugate vaccine (PCV15) followed by the 23-valent pneumococcal polysaccharide vaccine (PPSV23) (Evidence B).
- Research has demonstrated that pneumococcal vaccination can decrease the occurrence of community-acquired pneumonia and exacerbations in individuals diagnosed with COPD (Evidence B).
- The CDC advises individuals with COPD who didn't receive Tdap (dTAP/dTPa) vaccination during adolescence to consider it for protection against pertussis (whooping cough) (Evidence B). Additionally, people with COPD aged 50 and above are recommended to receive the Zoster vaccine to safeguard against shingles (Evidence B).

Prophylactic antibiotics in stable COPD

- In earlier research, the consistent use of antibiotics as a preventive measure did not show any impact on the occurrence of exacerbations in individuals with COPD, as indicated by previous studies. Additionally, a study conducted over a 5-year period during winter months to assess the effectiveness of chemoprophylaxis reached the conclusion that it did not provide any advantages. However, more recent studies have indicated that the regular use of certain antibiotics might lower the rate of exacerbations.
- Azithromycin (250 mg/day or 500 mg three times per week) or erythromycin (250 mg two times per day) for one year in patients prone to exacerbations reduced the risk of exacerbations compared to usual care.
- Azithromycin use was associated with a higher occurrence of bacterial resistance, prolongation of QTc interval, and impaired hearing tests.
- Pulse therapy with moxifloxacin (400 mg/day for 5 days every 8 weeks) in patients with chronic bronchitis and frequent exacerbations had no beneficial effect on the exacerbation rate overall.

Management of acute exacerbations

- Although the infectious agents in COPD exacerbations can be viral or bacterial, the use of antibiotics in exacerbations remains controversial.
- There is evidence supporting the use of antibiotics in exacerbations when patients have clinical signs of a bacterial infection e.g., increased sputum purulence.
- Due to the inconsistent findings in different studies, we are currently unable to endorse the utilization of procalcitonin-based protocols for determining antibiotic use in patients experiencing COPD exacerbations. Nevertheless, we emphasize the need for further trials with robust methodology to provide conclusive evidence.
- In summary, antibiotics should be given to patients with exacerbations of COPD characterized by dyspnea and/or cough and sputum that worsen over <14 days, or patients with COPD exacerbations requiring admission to the intensive care unit (ICU) or needing mechanical ventilation (invasive or noninvasive). COPD exacerbations are often associated with increased local and systemic inflammation.
- The recommended length of antibiotic therapy is 5-7 days.
- We recommend a duration of ≤ 5 days of antibiotic treatment for outpatient treatment of COPD exacerbations.

- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should normally be 5 days (Evidence B).
- Our recommendation is to limit outpatient treatment of COPD exacerbations to a maximum duration of 5 days for antibiotic therapy.
- The choice of the antibiotic should be based on the local bacterial resistance pattern.
- Usually, initial empirical treatment is an aminopenicillin with clavulanic acid, macrolide, tetracycline or, in selected patients, quinolone.
- For individuals experiencing frequent exacerbations, severe airflow obstruction, or those who have required mechanical ventilation during exacerbations, it is advisable to conduct cultures from sputum or other lung materials. This is important because gram-negative bacteria, such as Pseudomonas species, or antibiotic-resistant pathogens that may not respond to the antibiotics mentioned earlier could be present.
- The choice between oral and intravenous administration of antibiotics should be determined based on the patient's ability to eat and the pharmacokinetics of the antibiotic, although oral administration is preferred when possible.
- Clinical improvement, as indicated by reduced dyspnea and sputum purulence, suggests a positive treatment outcome.

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing report, along with their recommendations.

Table 4. List of Additional Guidelines

Additional Guidelines
The COPD-X Plan: Australian and New Zealand Guidelines for the Management of Chronic Obstructive Pulmonary Disease (**2023**)
Spanish COPD Guidelines (**GesEPOC**) Diagnosis and Treatment of COPD Exacerbation Syndrome (**2021**)

1.2.1 The COPD-X Plan: Australian and New Zealand Guidelines for the Management of Chronic Obstructive Pulmonary Disease (2023)

COPD-X provides guidance for **C**ase finding and confirming diagnosis, **O**ptimizing function, **P**revention of deterioration, **D**evelopment of care plans and management of e**X**acerbations[4]. For this report, we will focus on the prevention through vaccination as well as the management of exacerbations.

Table 5. National Heart, Lung, and Blood Institute (NHLBI) Categories and Levels of Evidence

NHLBI category	Sources of evidence	Definition
A	Randomized controlled trials (RCTs) extensive body of data	Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	Randomized controlled trials (RCTs) limited body of data	Evidence is from endpoints of intervention studies that include only a limited number of patients, post-hoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Non-randomized trials, observational studies	Evidence is from outcomes of uncontrolled or non-randomized trials or from observational studies.
D	Panel consensus, judgement	The panel consensus is based on clinical experience or knowledge that does not meet the above criteria.

Table 6. National Health and Medical Research Council (NHMRC) Levels of Evidence and Corresponding National Heart, Lung, and Blood Institute (NHLBI) Categories

NHLBI category	NHMRC level	Basis of evidence
A	I	Evidence obtained from a systematic review of all relevant randomized controlled trials.
B	II	Evidence obtained from at least one properly designed randomized controlled trial.
C	III-1	Evidence obtained from well-designed pseudorandomized controlled trials (alternate allocation or some other method).
C	III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomized, cohort studies, case-control studies, or interrupted time series with a control group.
C	III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel group.
C	IV	Evidence obtained from case series, either post-test or pre-test/post-test.

Table 7. Grading Scheme for Recommendations

Grading Scheme for Recommendations	
Strong recommendation	We recommend
Weak recommendation	We suggest

Prevention and management of COPD exacerbations

- Vaccination lowers the likelihood of experiencing complications related to influenza and pneumococcal infections (I, Strong).
    i. For individuals aged 65 years and older, receiving an annual influenza vaccination can reduce the chances of contracting influenza and is likely to decrease the risk of influenza-like illness.
    ii. Pneumococcal immunization is recommended for all patients with COPD. For those with newly diagnosed COPD who have never received

pneumococcal immunization: a first dose of 13vPCV (conjugated vaccine) is recommended at diagnosis followed by up to two additional doses of 23vPPV regardless of age.

- Long term macrolide antibiotics may reduce exacerbations in people with moderate to severe COPD and frequent exacerbations (I, weak)
- No significant benefits were associated with use of long-term quinolones or tetracyclines, compared to placebo.
- Considering the possible substantial negative effects of such treatment plans, which may encompass cardiac issues, hearing problems, gastrointestinal disturbances, and the emergence of antibiotic resistance impacting both individuals and the wider community, it is advisable to seek guidance from experts prior to initiating long-term antibiotic therapy.
- Antibiotics are prescribed when dealing with purulent sputum to address both common and uncommon microorganisms.
- Exacerbations with signs of infection (such as increased sputum volume, change in color, and/or fever) benefit from antibiotic therapy (I, Strong).
- If pneumonia, Pseudomonas or staphylococci or resistant organisms are suspected, appropriate antibiotics should be used.
- Typically, a course of antibiotics should be five days.
- Gram-negative organisms, Legionella spp. and even anaerobic organisms may be responsible.

1.2.2 Spanish COPD Guidelines (GesEPOC) Diagnosis and Treatment of COPD Exacerbation Syndrome (2021)

This section details the GesEPOC 2021 recommendations on the diagnosis and treatment of COPD exacerbation syndrome (CES). The guidelines propose a definition-based syndromic approach, a new classification of severity, and the recognition of different treatable traits (TT), representing a new step toward personalized medicine. The evidence is evaluated using GRADE[5].

Table 8. Assessment of the Quality of Evidence and Modifying Factors

Study Design	Quality of evidence	Decrease if	Increase if
Randomized controlled trial	High	Design limitations: 1 Important 2 Very important	Strong association: 1 Strong 2 Very strong
	Moderate	Inconsistent results: 1 Inconsistent 2 Very inconsistent	Presence of a dose response gradient: 1 Evidence for a gradient
Observational study	Low	Absence of direct evidence: 1 Indirect 2 Very indirect	Potential confounders: 1 Would reduce a demonstrated effect or 1 Would suggest a spurious effect when results show no effect
	Very low	Inaccurate results: 1 Imprecise 2 Very imprecise Publication bias 1 Probable 2 Very likely	

Table 9. Implications of the Strengths of Recommendations

	Strong recommendation	Weak recommendation
For patients	Most people would agree with the recommended intervention and only a small one part would not.	Most people would agree with the recommended action but a significant number of them would not.
For healthcare professionals	Most patients should receive the recommended intervention.	It is recognized that different options are appropriate for different patients, and the doctor has to assist each patient in reaching the decision most consistent with their values and preferences.

For managers	The recommendation can be adopted as a health policy in most situations.	There is a need for a significant debate involving stakeholders' participation.

- To accurately diagnose and classify the COPD Exacerbation Syndrome (CES), it's essential to first confirm that it is indeed an exacerbation syndrome in a COPD patient. This involves making an appropriate preliminary differential diagnosis. Afterward, the severity of the condition should be determined, trigger factors assessed, and potential treatment targets (TTs) identified. The diagnostic approach may vary based on whether the CES happens in an outpatient or inpatient setting.
- Antibiotics are recommended for individuals experiencing an outpatient COPD exacerbation (Weak, low).
- Antibiotics are suggested for patients with COPD exacerbation who require hospital admission (Weak, low).
- Antibiotics are recommended for all patients who have COPD exacerbation and require ICU admission (Strong, moderate).
- Antibiotics are recommended when there is a shift in sputum color (from clear to dark) in individuals experiencing a COPD exacerbation (Weak, very low).
- It is recommended to consider antibiotic therapy based on CRP (C-reactive protein) levels in patients with COPD exacerbation when evaluating the change in sputum color is inconclusive. Antibiotic treatment should be indicated in patients with elevated CRP (≥20 mg/L). This biomarker can be used in both hospital and outpatient settings (capillary CRP) (Weak, low).
- Using oral corticosteroids is advisable for patients experiencing severe exacerbations (Strong, moderate).
- The suggested dosage of oral corticosteroids is 0.5 mg per kilogram of body weight per day, using prednisone or an equivalent, for a duration of up to 5 days in cases of moderate exacerbations and up to 14 days in cases of severe exacerbations. In instances of very severe exacerbations, the preferred administration route is parenteral.
- Oral corticosteroids are advised for patients experiencing moderate exacerbations (Weak, moderate).
- Oral corticosteroid treatment is recommended for patients with eosinophil counts equal to or exceeding 300 cells/mm^3. The efficacy of oral corticosteroids in COPD exacerbations is higher in patients with eosinophil counts ≥ 300 cells/mm3 (Weak, low).

Table 10. Recommendations on the Use of Antibiotics in COPD Exacerbation Syndrome (CES). Adapted from the GesEPOC 2021 Guidelines.

Severity of exacerbation	Microorganisms	Antibiotic of choice
Mild CES	*H. influenzae* *S. pneumoniae* *M. catarrhalis*	Amoxicillin-clavulanic acid Cefditorene Levofloxacin[a] Moxifloxacin[a]
Moderate CES	Same as group A + *S. pneumoniae* with reduced sensitivity to penicillin. Enterobacteria	Amoxicillin-clavulanic acid Cefditorene Levofloxacin[a] Moxifloxacin[a]
Severe-very severe CES <u>with no risk</u> of Pseudomonas infection	Same as group A + *S. pneumoniae* with reduced sensitivity to penicillin. Enterobacteria	Amoxicillin-clavulanic acid Ceftriaxone Cefotaxime Levofloxacin[a] Moxifloxacin[a]
Severe-very severe CES <u>with risk</u> of Pseudomonas infection	Same as group B + *P. aeruginosa*	β-lactam with antipseudomonal activity[b] Alternatives: quinolones[a] with antipseudomonal activity[c]

[a] The FDA and EMA recommend avoiding fluoroquinolones if there is an alternative treatment, due to their adverse effects.

[b] Piperacillin-tazobactam, ceftazidime, cefepime, meropenem, ceftolozan-tazobactam, ceftazidime-avibactam.

[c] Ciprofloxacin 500-750 mg every 12 hours or levofloxacin 500 mg every 12 hours.

Section 2.0 Drug Therapy for Antimicrobial Prescribing in Chronic Obstructive Pulmonary Disease (COPD)

This section comprises four subsections: the first contains the newly recommended drugs, the second covers drug modifications, the third outlines the drugs that have been withdrawn from the market, and the fourth details drugs that are approved in the antimicrobial prescribing of COPD but are not yet registered by the SFDA.

2.1 Additions

After February 2020, there have been no antimicrobials drugs prescribed for chronic obstructive pulmonary disease that have received SFDA approval. However, new vaccines recommended by the CDC in people with COPD according to GOLD guidelines 2023[1] were recently added to the list:

- In July 2021, FDA approved VAXNEUVANCE® (Pneumococcal 15-valent Conjugate Vaccine)[6].
- Tdap/Dtap vaccine has been registered on the list for a while and should be added to the CHI formulary.

2.1.1 Pneumococcal 15-valent Conjugate Vaccine (PCV15)

This section includes pertinent information regarding the use of Pneumococcal 15-valent Conjugate Vaccine (VAXNEUVANCE®) in Chronic Obstructive Pulmonary Disease[7].

Table 11. Pneumococcal 15-Valent Conjugate Vaccine Drug Information

SCIENTIFIC NAME **Pneumococcal 15-valent Conjugate Vaccine**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	No
Indication (ICD-10)	J44
Drug Class	Inactivated Vaccine (Bacterial)
Drug Sub-class	N/A
ATC Code	J07AL02

Pharmacological Class (ASHP)	80:12 Vaccines
DRUG INFORMATION	
Dosage Form	Suspension for injection in pre-filled syringe
Route of Administration	Intramuscular use
Dose (Adult) [DDD]*	**Pneumococcal disease prevention:** CDC recommendations (CDC 2023; CDC/ACIP [Kobayashi 2022]): Adults 19 to 64 years of age: PCV15: IM: 0.5 mL as a single dose; see the following recommendations based on age, prior pneumococcal vaccination, and comorbid conditions/risk factors.
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	N/A
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Renal Impairment:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:** There are no dosage adjustments provided in the manufacturer's labeling.
Prescribing edits*	PE
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): Followed by PPSV23 ≥ 1 year later	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Decreased appetite, erythema at injection site, pain at injection site, swelling at injection site, headache, fatigue, arthralgia, myalgia, fever.

	Most serious: Apnea, febrile seizure, anaphylactoid reactions, syncope.
Drug Interactions	**Category X**: • Elivaldogene Autotemcel
Special Population	• **Older Adult:** CDC recommendations: Adults ≥65 years of age: PCV15: IM: 0.5 mL as a single dose; see the following recommendations based prior pneumococcal vaccination and comorbid conditions/risk factors. • **Altered immunocompetence:** Postpone vaccination during periods of severe immunosuppression (eg, patients receiving chemo-/radiation therapy or other immunosuppressive therapy [including high-dose corticosteroids]) if appropriate; may have a reduced response to vaccination. In general, household and close contacts of persons with altered immunocompetence may receive all age-appropriate vaccines. Non live vaccines should be administered ≥2 weeks prior to planned immunosuppression when feasible; non live vaccines administered during chemotherapy should be readministered after immune competence is regained. • **Premature infants:** Apnea following IM vaccination has been observed in some preterm infants; consider clinical status implications.

Pregnancy	Adverse fetal effects were not observed in animal developmental toxicity studies. Non live bacterial vaccines have not been shown to cause increased risks to the fetus. Although specific recommendations for vaccination of pregnant patients is not available, pneumococcal vaccines may be administered during pregnancy in persons at increased risk of severe disease due to underlying medical conditions.
Lactation	It is not known if the components of this vaccine are present in breast milk. According to the manufacturer, the decision to breastfeed following immunization should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of vaccination to the mother. Nonlive vaccines have not been shown to affect the safety of the breastfed infant or mother. Breastfeeding infants should be vaccinated according to the recommended schedules.
Contraindications	Severe hypersensitivity (eg, anaphylaxis) to pneumococcal conjugate vaccine, any component of the formulation, or to diphtheria toxoid.
Monitoring Requirements	Monitor for hypersensitivity and syncope for 15 minutes following administration. If seizure-like activity associated with syncope occurs, maintain patient in supine or Trendelenburg position to reestablish adequate cerebral perfusion.
Precautions	**Concerns related to adverse effects:** • Anaphylactoid/hypersensitivity reactions: Immediate treatment (including epinephrine 1 mg/mL)

	for anaphylactoid and/or hypersensitivity reactions should be available during vaccine use. • Shoulder injury related to vaccine administration: Vaccine administration that is too high on the upper arm may cause shoulder injury (eg, shoulder bursitis, tendinopathy) resulting in shoulder pain and reduced range of motion following injection. Use proper injection technique for vaccines administered in the deltoid muscle (eg, injecting in the central, thickest part of the muscle) to reduce the risk of shoulder injury related to vaccine administration. • Syncope: Syncope has been reported with use of injectable vaccines and may result in serious secondary injury (eg, skull fracture, cerebral hemorrhage); typically reported in adolescents and young adults and within 15 minutes after vaccination. Procedures should be in place to avoid injuries from falling and to restore cerebral perfusion if syncope occurs. **Disease-related concerns:** • Acute illness: The decision to administer or delay vaccination because of current or recent febrile illness depends on the severity of symptoms and the etiology of the disease. Postpone administration in patients with moderate or severe acute illness (with or without fever);

	vaccination should not be delayed for patients with mild acute illness (with or without fever). • Bleeding disorders: Use with caution in patients with bleeding disorders (including thrombocytopenia); bleeding/hematoma may occur from IM administration; if the patient receives antihemophilia or other similar therapy, IM injection can be scheduled shortly after such therapy is administered. **Concurrent drug therapy issues:** • Anticoagulant therapy: Use with caution in patients receiving anticoagulant therapy; bleeding/hematoma may occur from IM administration. • Vaccines: To maximize vaccination rates, the Advisory Committee on Immunization Practices (ACIP) recommends simultaneous administration (ie, >1 vaccine on the same day at different anatomic sites) of all age-appropriate vaccines (live or nonlive) for which a person is eligible at a single visit, unless contraindications exist.
Black Box Warning	N/A
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 Pneumococcal 15-valent Conjugate Vaccine for the prevention of pneumonia in COPD.**

Conclusion Statement – Pneumococcal 15-valent Conjugate Vaccine

The CDC vaccination recommends either a single PCV-20, or if PCV 15 is used, it should be followed by PPSV-23 in 1 year in people with COPD. It is important to note that there is currently no available data or recommendations from HTA bodies specifically addressing the use of PCV15 in pneumonia prevention, however, PCV15 is recommended to be added to CHI formulary.

2.1.2 Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccines (Tdap/dTap)

This section includes pertinent information regarding the use of Diphtheria and tetanus toxoids and acellular pertussis vaccines (ADACEL®), (TRIPACEL®), (BOOSTRIX®) in Chronic Obstructive Pulmonary Disease[7].

Table 12. Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccines (Tdap/dTap) Drug Information

SCIENTIFIC NAME **Diphtheria and tetanus toxoids and acellular pertussis vaccines**	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	J44
Drug Class	Inactivated Vaccine (Bacterial)
Drug Sub-class	N/A
ATC Code	J07CA, J07AJ52
Pharmacological Class (ASHP)	80:12 Vaccines
DRUG INFORMATION	
Dosage Form	Suspension for injection
Route of Administration	Intramuscular use
Dose (Adult) [DDD]*	**IM:** 0.5 mL per dose. Any patient who has not previously received a dose of Tdap should receive a dose of Tdap, regardless of interval since last tetanus- or diphtheria-containing vaccine. A booster dose of either Td or Tdap should

	be administered every 10 years throughout life.
Maximum Daily Dose Adults*	N/A
Dose (pediatrics)	N/A
Maximum Daily Dose Pediatrics*	N/A
Adjustment	**Renal Impairment:** There are no dosage adjustments provided in the manufacturer's labeling. **Hepatic Impairment:** There are no dosage adjustments provided in the manufacturer's labeling.
Prescribing edits*	PE
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): Tdap administered as a 3-dose series at 0, ≥ 4 weeks, and 6-12 months for catch-up immunization (at least 1 dose should be Tdap; preferably dose 1, with either Td or Tdap appropriate for doses 2 and 3). A booster dose of either Td or Tdap should be administered every 10 years throughout life.	
SAFETY	
Main Adverse Drug Reactions (Most common and most serious)	**Most common:** Nausea, erythema at injection site, pain at injection site, swelling at injection site, body pain, chills, fatigue, headache, malaise, myasthenia, arthralgia, joint swelling, myalgia, fever. **Most serious:** Syncope, myocarditis, lymphadenopathy, thrombocytopenia, hypersensitivity reaction (including anaphylaxis, angioedema, nonimmune anaphylaxis), seizures, myositis, hypotonic/hyporesponsive episode.
Drug Interactions	**Category X**:

	• Elivaldogene Autotemcel
Special Population	• **Older Adult:** Booster immunization: IM: Adults ≥65 years of age: The Advisory Committee on Immunization Practices (ACIP) recommendations: Refer to adult dosing. In adults ≥65 years of age Boostrix should be used if feasible; however, ACIP has concluded that either Tdap vaccine (Boostrix or Adacel) may be used. • **Altered immunocompetence:** Postpone vaccination during periods of severe immunosuppression (eg, patients receiving chemo/radiation therapy or other immunosuppressive therapy [including high dose corticosteroids]); if appropriate, may have a reduced response to vaccination. May be used in patients with HIV infection. In general, household and close contacts of persons with altered immunocompetence may receive all age-appropriate vaccines. Nonlive vaccines should be administered ≥2 weeks prior to planned immunosuppression when feasible; nonlive vaccines administered during chemotherapy should be readministered after immune competence is regained. • **Pediatric:** Apnea has been reported following IM vaccine administration in premature infants; consider clinical status

	implications. In general, preterm infants should be vaccinated at the same chronological age as full-term infants.
Pregnancy	Nonlive bacterial vaccines have not been shown to cause increased risks to the fetus. Specifically, an increased risk of miscarriage, stillbirth, preterm birth, SGA, or major birth defects has not been observed following maternal use of the Tdap vaccine. Following Tdap vaccination, maternal antibodies reach the fetus and provide protection against pertussis in infants too young to be immunized. Concentrations of pertussis toxin antibodies are significantly increased in cord blood when maternal vaccination is administered per current CDC guidelines. Maternal Tdap vaccination during pregnancy decreases the risk of infant pertussis disease, hospitalization, and death. Neonatal and obstetrical tetanus is also decreased following maternal Tdap vaccination. All patients should receive a single dose of Tdap during each pregnancy regardless of previous vaccination status. Although the vaccine may be given any time during pregnancy, it should be administered between 27 and 36 weeks gestation, preferably during the early part of this time period, to maximize passive antibody transfer to the infant. Alternately, administration of Tdap can be given immediately postpartum to all patients who have not previously been vaccinated with Tdap in order to protect the mother and infant from pertussis.

	In case of an ongoing local pertussis epidemic, pregnant patients should be vaccinated with Tdap for their own protection as is recommended for nonpregnant patients, regardless of gestational age. If a tetanus toxoid-containing vaccine is needed as standard care for wound management, Tdap is preferred over Td, regardless of gestational age if otherwise indicated; however, if Tdap is used prior to 27 to 36 weeks' gestation in these instances, patients should not receive >1 dose during the same pregnancy.
Lactation	It is not known if components of this vaccine are present in breast milk. However, pertussis-specific antibodies are present in breast milk following vaccination. Information is available from a study that compared breast milk from lactating women vaccinated with Tdap vaccine between 24 and 32 weeks' gestation (n=213) to women not vaccinated during pregnancy (n=27). Breast milk and maternal serum samples were collected at 72 hours, 4, 8, and 12 weeks postpartum. Concentrations of pertussis-specific anti-PT IgA and IgG were increased in breast milk of vaccinated mothers, and this was observed for both term and preterm deliveries (Orije 2021). According to the manufacturer, the decision to breastfeed following immunization should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of vaccination to the mother; however, breastfeeding is not a contraindication to vaccine

	administration. Patients who have not previously had a dose of Tdap should receive a dose postpartum to help prevent pertussis in infants <12 months of age. Administration does not affect the safety of breastfeeding for the mother or the infant. Breastfeeding infants should be vaccinated according to the recommended schedules.
Contraindications	Hypersensitivity to diphtheria toxoid-, tetanus toxoid-, or pertussis-containing vaccine, or any component of the formulation; progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy (postpone until condition stabilized) (Infanrix only); encephalopathy occurring within 7 days of a previous dose of a pertussis-containing vaccine and not attributable to another cause; administration to children and adults ≥7 years of age (Daptacel only). Canadian labeling: Additional contraindications (not in US labeling; Boostrix only): Transient thrombocytopenia or neurological complications following a previous dose of diphtheria and/or tetanus vaccine.
Monitoring Requirements	Monitor for hypersensitivity and syncope for 15 minutes following administration. If seizure-like activity associated with syncope occurs, maintain patient in supine or Trendelenburg position to reestablish adequate cerebral perfusion.
Precautions	**Concerns related to adverse effects:** • Anaphylactoid/Hypersensitivity reactions: Immediate treatment (including epinephrine 1 mg/mL) for anaphylactoid and/or

	hypersensitivity reactions should be available during vaccine use. • Arthus-type hypersensitivity: Patients with a history of severe local reaction (Arthus-type) following a previous diphtheria toxoid or tetanus toxoid-containing vaccine dose should not be given further routine or emergency doses of Td unless ≥10 years since most recent dose, even if using for wound management with wounds that are not clean or minor; these patients generally have high serum antitoxin levels. • Reactions from previous dose: Carefully consider use in patients with history of any of the following effects from previous administration of any pertussis-containing vaccine: Fever ≥105°F (40.5°C) within 48 hours of unknown cause; seizures with or without fever occurring within 3 days; persistent, inconsolable crying episodes lasting ≥3 hours and occurring within 48 hours; collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours. • Shoulder injury related to vaccine administration: Vaccine administration that is too high on the upper arm may cause shoulder injury (eg, shoulder bursitis or tendinopathy) resulting in shoulder pain and reduced range of motion following injection. Use proper injection technique for vaccines

	administered in the deltoid muscle (eg, injecting in the central, thickest part of the muscle) to reduce the risk of shoulder injury related to vaccine administration. • Syncope: Syncope has been reported with use of injectable vaccines and may result in serious secondary injury (eg, skull fracture, cerebral hemorrhage); typically reported in adolescents and young adults and within 15 minutes after vaccination. Procedures should be in place to avoid injuries from falling and to restore cerebral perfusion if syncope occurs. **Disease-related concerns:** • Acute illness: The decision to administer or delay vaccination because of current or recent febrile illness depends on the severity of symptoms and the etiology of the disease. Postpone administration in patients with moderate or severe acute illness (with or without fever); vaccination should not be delayed for patients with mild acute illness. • Bleeding disorders: Use with caution in patients with bleeding disorders (including thrombocytopenia); bleeding/hematoma may occur from IM administration; if the patient receives antihemophilia or other similar therapy, IM injection can be scheduled

	shortly after such therapy is administered. • Brachial neuritis: Has occurred following tetanus toxoid-containing vaccines; use with caution. • Guillain-Barré syndrome: Use with caution if Guillain-Barré syndrome occurred within 6 weeks of prior tetanus toxoid-containing vaccine. • Neurologic disorders: Use with caution in patients with progressive neurologic disease including infantile spasms, uncontrolled seizure, or a progressive encephalopathy, or conditions predisposing to seizures; the Advisory Committee on Immunization Practices (ACIP) guidelines recommend deferring immunization until health status can be assessed and condition stabilized. **Concurrent drug therapy issues:** • Anticoagulant therapy: Use with caution in patients receiving anticoagulant therapy; bleeding/hematoma may occur from IM administration; vaccinations should be administered prior to initiation of anticoagulation therapy if possible. • Vaccines: In order to maximize vaccination rates, the ACIP recommends simultaneous administration (ie, >1 vaccine on the same day at different anatomic sites) of all age-appropriate vaccines (live or

	nonlive) for which a person is eligible at a single clinic visit, unless contraindications exist. The use of combination vaccines is generally preferred over separate injections, taking into consideration provider assessment, patient preference, and adverse events. When using combination vaccines, the minimum age for administration is the oldest minimum age for any individual component; the minimum interval between dosing is the greatest minimum interval between any individual component. The ACIP prefers each dose of a specific vaccine in a series come from the same manufacturer when possible; however, vaccination should not be deferred because a specific brand name is unavailable. Administration of Menactra (meningococcal MenACWY-D conjugate vaccine) one month after Daptacel has been shown to have reduced meningococcal antibody responses in children 4 to 6 years; these vaccines should be administered simultaneously or Menactra should be administered prior to Daptacel.
Black Box Warning	N/A
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 Diphtheria and tetanus toxoids and acellular pertussis vaccines (Tdap/dTap) for the prevention of pertussis (whooping cough) in COPD.**

Conclusion Statement – Diphtheria and tetanus toxoids and acellular pertussis vaccines (Tdap/dTap)

The CDC recommends the Tdap vaccination (dTaP/dTPa; pertussis, tetanus and diptheria) for COPD patients who were not vaccinated in adolescence in all COPD patients. It is important to note that there is currently no available data or recommendations from HTA bodies specifically addressing the use of dTap/Tdap in the prevention of pertussis (whooping cough) in COPD patients, however, dTap/Tdap is recommended to be added to CHI formulary.

2.2 Modifications

No modifications have been made since February 2020.

2.3 Delisting

The medications below are no longer SFDA registered (SFDA Drug List, June 2023), therefore, it is advisable to delist the following drugs from CHI formulary.

- Clavulanic acid
- Influenza vaccine surface antigen NYMC X-181, NYMC X-187, and NYMC BX-35

2.4 Other Drugs

There are two respiratory syncytial virus (RSV) vaccines that are approved by the FDA and recommended by the CDC for individuals over 60 years and or with chronic lung disease:

1. Arexvy (GSK adjuvanted RSV vaccine)
2. Abrysvo (Pfizer RSV vaccine)

Both vaccines are recombinant protein vaccines that stimulate the immune system to generate RSV antibodies.

Both are currently authorized for a single dose and have demonstrated efficacy in clinical trials in safeguarding against symptomatic lower respiratory tract disease

caused by RSV in individuals aged 60 and above, exhibiting over 80% effectiveness during the initial RSV season post-vaccination.

GSK's vaccine incorporates an adjuvant (the same adjuvant present in GSK's recombinant zoster vaccine, Shingrix), designed to enhance the immune response to vaccination. In contrast, Pfizer's vaccine lacks an adjuvant.

The CDC does not express a preference for either vaccine, allowing individuals aged 60 and older to receive whichever vaccine is available.

Currently, the RSV vaccine series consists of a **single dose**. Studies are ongoing to determine whether older adults might benefit from receiving additional RSV vaccines in the future[3].

- ✓ SARS-COV-2 (COVID-19) Vaccines have been approved by FDA since 2021 and are now available on the NUPCO list. They are recommended by the CDC in people with COPD in line with national recommendations[1].

Section 3.0 Key Recommendations Synthesis

- Individuals diagnosed with COPD are recommended to get the influenza vaccine (Evidence B)[1].
- Both the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) support COVID-19 vaccination for individuals with a COPD diagnosis (Evidence B)[1].
- According to the CDC, individuals with COPD should be administered either a single dose of the 20-valent pneumococcal conjugate vaccine (PCV20) or one dose of the 15-valent pneumococcal conjugate vaccine (PCV15) followed by the 23-valent pneumococcal polysaccharide vaccine (PPSV23) (Evidence B)[1].
- Research has shown that pneumococcal vaccination can reduce the occurrence of community-acquired pneumonia and COPD exacerbations in individuals with a COPD diagnosis (Evidence B)[1].
- The CDC recommends that individuals with COPD who did not receive the Tdap (dTAP/dTPa) vaccination during adolescence consider it to protect against pertussis (whooping cough) (Evidence B). Additionally, individuals with COPD aged 50 and above are advised to receive the Zoster vaccine to guard against shingles (Evidence B)[1].
- In individuals with moderate to severe COPD who experience frequent exacerbations, the extended use of macrolide antibiotics could potentially decrease the occurrence of exacerbations[4].

- The evidence indicates that preventive antibiotics can lower the risk of individuals experiencing a COPD exacerbation and can reduce the annual frequency of exacerbations in people with COPD who have sputum production[9].
- Administering azithromycin (250 mg/day or 500 mg three times per week) or erythromycin (250 mg twice a day) for one year to patients prone to exacerbations resulted in a reduced risk of exacerbations when compared to standard care[1].
- Using pulse therapy involving moxifloxacin (400 mg/day for 5 days every 8 weeks) in individuals with chronic bronchitis who frequently experience exacerbations did not yield a beneficial effect on the overall exacerbation rate[1].
- Exacerbations displaying indications of infection, such as elevated sputum volume, alterations in color, and/or the presence of a fever, experience advantages from antibiotic treatment (I, Strong)[4].
- For all patients with COPD exacerbations necessitating admission to the intensive care unit (ICU), antibiotics are recommended (Strong, moderate)[5].
- The suggested duration for antibiotic treatment is 5-7 days[1].
- For the outpatient management of COPD exacerbations, we advise a treatment duration of ≤ 5 days[1].
- Antibiotics, when deemed necessary, can expedite recovery, lower the risk of early relapse, prevent treatment failure, and reduce the length of hospitalization. The typical duration of therapy should be 5 days (Evidence B)[1].
- The selection of the antibiotic should be influenced by the bacterial resistance patterns prevalent in the local area[1].
- Typically, the initial empiric treatment consists of an aminopenicillin with clavulanic acid, a macrolide, tetracycline, or, in specific cases, a quinolone[1].
- It is recommended to use oral corticosteroids for individuals undergoing severe exacerbations (Strong, moderate)[5].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing report** and aims to provide recommendations to aid in the management of Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing report. 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 Chronic Obstructive Pulmonary Disease: Antimicrobial

Prescribing report. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

Section 5.0 References

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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. Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing Scope

2020	Changes	2023	Rationale
Section 1.0 Chronic Obstructive Pulmonary Disease: Antimicrobial Prescribing Clinical Guidelines			
Global strategy for the diagnosis, management and prevention of Chronic obstructive pulmonary disease [2019]	Updated	GOLD Guidelines [2023][1]	**Vaccinations** • Vaccines required: Influenza, pneumonia vaccine (PCV20 OR PCV15 followed by PPSV23), dTaP and COVID-19. **Antibiotics** • antibiotics should be given to patients with exacerbations of COPD who have three cardinal symptoms: increase in dyspnea, sputum volume, and sputum purulence; have two of the cardinal symptoms, if increased purulence of sputum is one of the two symptoms; or require mechanical ventilation (invasive or noninvasive). • Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should normally be 5 days (Evidence B). • Usually, initial empirical treatment is an aminopenicillin with clavulanic acid, macrolide, tetracycline or, in selected patients, quinolone. • For individuals experiencing frequent exacerbations, severe airflow obstruction, or those who have required mechanical ventilation during exacerbations, it is advisable to conduct cultures

			from sputum or other lung materials. This is important because gram-negative bacteria, such as Pseudomonas species, or antibiotic-resistant pathogens that may not respond to the antibiotics mentioned earlier could be present. • The choice between oral and intravenous administration of antibiotics should be determined based on the patient's ability to eat and the pharmacokinetics of the antibiotic, although oral administration is preferred when possible.
National institute for health and care excellence guidelines for COPD in over 16s: Diagnosis and management [2018]	N/A		
National institute for health and care excellence guidelines for Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing [2018]	N/A		
The Saudi Guidelines for the Diagnosis and Management of COPD 2014	N/A		

	Missing	The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2023[4]	**Prevention** • Vaccination lowers the likelihood of experiencing complications related to influenza and pneumococcal infections (I, Strong). **Management of COPD exacerbations** • Antibiotics are prescribed when dealing with purulent sputum to address both common and uncommon microorganisms. • Exacerbations with signs of infection (such as increased sputum volume, change in color, and/or fever) benefit from antibiotic therapy (I, Strong). • Typically, a course of antibiotics should be five days. • Initial empiric antibiotic therapy should be tailored according to clinical and radiographic criteria.
	Missing	Spanish COPD Guidelines (GesEPOC) 2021 Update. Diagnosis and Treatment of COPD Exacerbation Syndrome[5]	• Antibiotics are recommended for individuals experiencing an outpatient COPD exacerbation (Weak, low). • Antibiotics are suggested for patients with COPD exacerbation who require hospital admission (Weak, low). • Antibiotics are recommended for all patients who have COPD exacerbation and require ICU admission (Strong, moderate). • Antibiotics are recommended when there is a shift in sputum color (from clear to dark) in individuals experiencing a COPD exacerbation (Weak, very low). • It is recommended to consider antibiotic therapy based on CRP (C-reactive protein) levels in patients

			with COPD exacerbation when evaluating the change in sputum color is inconclusive. Antibiotic treatment should be indicated in patients with elevated CRP (≥20 mg/L). This biomarker can be used in both hospital and outpatient settings (capillary CRP) (Weak, low). • The regular use of procalcitonin to determine antibiotic usage in COPD exacerbations is discouraged (Weak, low). • Using oral corticosteroids is advisable for patients experiencing severe exacerbations (Strong, moderate). • The suggested dosage of oral corticosteroids is 0.5 mg per kilogram of body weight per day, using prednisone or an equivalent, for a duration of up to 5 days in cases of moderate exacerbations and up to 14 days in cases of severe exacerbations. In instances of very severe exacerbations, the preferred administration route is parenteral. • Oral corticosteroids are advised for patients experiencing moderate exacerbations (Weak, moderate). • Oral corticosteroid treatment is recommended for patients with eosinophil counts equal to or exceeding 300 cells/mm^3. The efficacy of oral corticosteroids in COPD exacerbations is higher in patients with eosinophil counts ≥ 300 cells/mm3 (Weak, low).

Appendix C. MeSH Terms PubMed

C.1 Pubmed Search for Chronic Obstructive Pulmonary Disease

The following is the result of the PubMed search conducted for chronic obstructive pulmonary disease guideline search:

Query	Filters	Search Details	Results
((((((((((Pulmonary Disease, Chronic Obstructive[MeSH Terms]) OR (Chronic Obstructive Lung Disease[Title/Abstract])) OR (Chronic Obstructive Pulmonary Diseases[Title/Abstract])) OR (COAD[Title/Abstract])) OR (COPD[Title/Abstract])) OR (Chronic Obstructive Airway Disease[Title/Abstract])) OR (Chronic Obstructive Pulmonary Disease[Title/Abstract])) OR (Airflow Obstruction, Chronic[Title/Abstract])) OR (Airflow Obstructions, Chronic[Title/Abstract])) OR (Chronic Airflow Obstructions[Title/Abstract])) OR (Chronic Airflow Obstruction[Title/Abstract])	Guideline, in the last 5 years	("pulmonary disease, chronic obstructive"[MeSH Terms] OR "chronic obstructive lung disease"[Title/Abstract] OR "chronic obstructive pulmonary diseases"[Title/Abstract] OR "COAD"[Title/Abstract] OR "COPD"[Title/Abstract] OR "chronic obstructive airway disease"[Title/Abstract] OR "chronic obstructive pulmonary disease"[Title/Abstract] OR "airflow obstruction chronic"[Title/Abstract] OR "airflow obstructions chronic"[Title/Abstract] OR "chronic airflow obstructions"[Title/Abstract] OR "chronic airflow obstruction"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	33

Appendix D. Treatment Algorithm

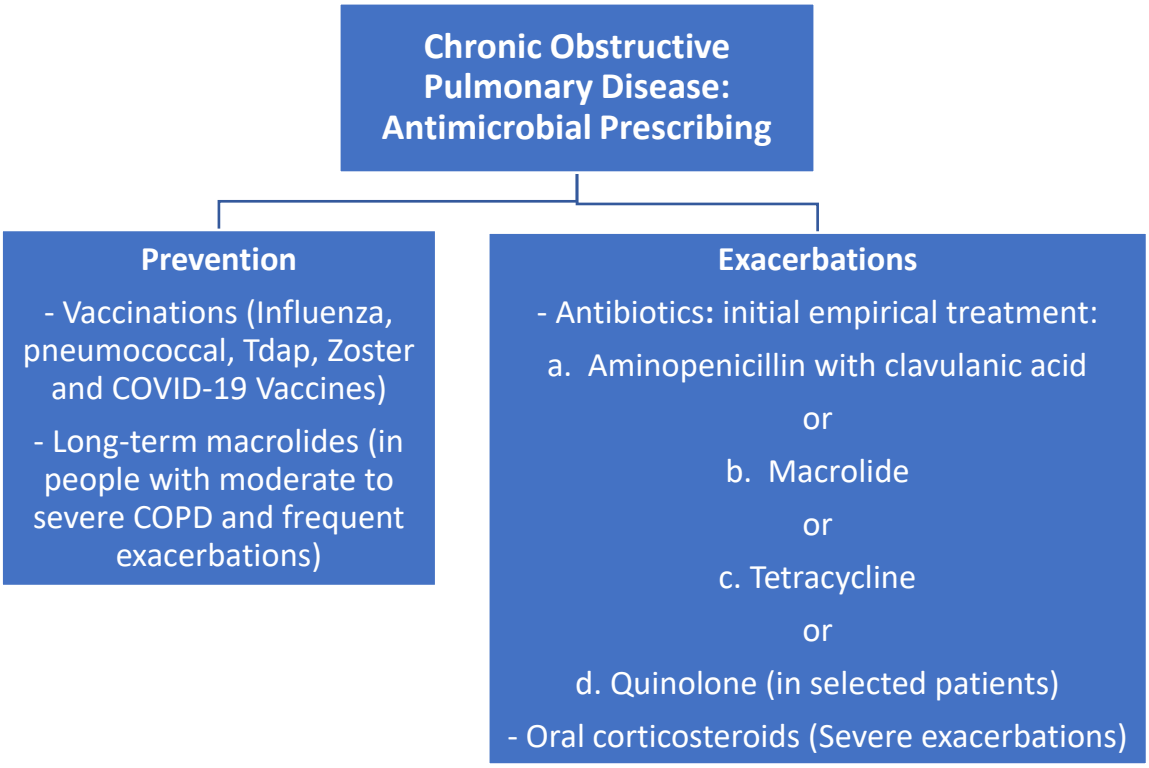

Figure 1. *Treatment algorithm for antimicrobial prescribing in chronic obstructive pulmonary disease*[1,4,5]