

GASTRO-OESOPHAGEAL REFLUX DISEASE

CHI Formulary Indication Review



INDICATION UPDATE

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**ADDENDUM to the CHI Original
Gastro-esophageal reflux disease
Clinical Guidance - Issued November
2019**

Contents

Related Documents	4
List of Tables.....	4
List of Figures.....	4
Abbreviations.....	5
Executive Summary	7
Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence	16
1.1 Revised Guidelines.....	16
1.1.1 American College of Gastroenterology (ACG) Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease 2022	16
1.2 Additional Guidelines	19
1.2.1 Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Guidelines for the Surgical Treatment of Gastroesophageal Reflux (2021).....	20
1.2.2 American Gastroenterological Association (AGA) Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease (2023)	21
1.2.3 American Gastroenterological Association (AGA) Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett’s Esophagus (2022)	21
1.2.4 American Gastroenterological Association (AGA) Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors (2022)	22
1.2.5 American Gastroenterological Association (AGA) Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD (2022).....	23
1.2.6 American College of Gastroenterology (ACG) Guidelines on the Diagnosis and Management of Barrett’s Esophagus (2022)	23
1.2.7 German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS) S2k Guideline for Gastroesophageal Reflux Disease and Eosinophilic Esophagitis (2023)	25
1.2.8 Saudi Gastroenterology Association Consensus on the Clinical Care Pathway for the Diagnosis and Treatment of GERD (2024)	28
1.2.9 American Gastroenterological Association (AGA) Clinical Practice Update on Integrating Potassium Competitive Acid Blockers into Clinical Practice: Expert Review (2024).....	31
1.2.10 The Consensus of the Asociación Mexicana de Gastroenterología on the Diagnosis and Treatment of Gastroesophageal Reflux and Gastroesophageal Reflux Disease in Infants (2024)	32

1.2.11 Good Clinical Practice Recommendations for the Diagnosis and Treatment of Gastroesophageal Reflux Disease: An Expert Review from the Asociación Mexicana de Gastroenterología (2024).....	34
1.2.12 American Society for Gastrointestinal Endoscopy Guideline on the Diagnosis and Management of GERD: Summary and Recommendations (2025)	36
Section 2.0 Drug Therapy	39
2.1 Additions.....	39
2.2 Modifications	39
2.3 Delisting	40
2.4 Other Drugs.....	40
2.4.1 Vonoprazan	40
Section 3.0 Key Recommendations Synthesis.....	41
Section 4.0 Conclusion	45
Section 5.0 References	46
Section 6.0 Appendices.....	49
Appendix A. Supplementary Appendix	49
Appendix B. Level of Evidence Description	51
A. SAGES Clinical Guidelines Grading/Level of Evidence.....	51
B. ACG Clinical Guidelines Grading/Level of Evidence	51
C. DGVS Clinical Guidelines Grading/Level of Evidence	52
D. ASGE Clinical Guidelines Grading/Level of Evidence	52
Appendix C. PubMed Search	53
Appendix D. Treatment Algorithm	55

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

Table 1. Prescribing Edits Modifications for GERD Medications	10
Table 2. General Recommendations for the Management of Gastroesophageal Reflux Disease (GERD).....	10
Table 3. Guidelines Requiring Revision.....	16
Table 4. 2022 ACG Guideline Recommendations.....	17
Table 5. List of Additional Guidelines.....	19
Table 8. DVGS Recommendations for GERD Management	25
Table 9. Saudi Gastroenterology Association recommendations for GERD diagnosis and treatment.....	28
Table 10. Potassium-Competitive Acid Blocker and Proton Pump Inhibitor Class Comparison.....	32
Table 11. ASGE Summary of Recommendations	37
Table 12. Prescribing Edits (PE) Modifications for GERD Medications.....	39
Table 13. SAGES Clinical Guidelines Grading/Level of Evidence	51
Table 14. ACG Clinical Guidelines Grading/Level of Evidence.....	51
Table 15. DGVS Clinical Guidelines Grading/Level of Evidence	52
Table 16. ASGE Clinical Guidelines Grading/Level of Evidence.....	52

List of Figures

Figure 1. Diagnosis of GERD. Adapted from Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. American Journal of Gastroenterology. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538.....	55
Figure 2. Diagnostic Algorithm for Extraesophageal GERD. Adapted from Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. American Journal of Gastroenterology. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538.....	56
Figure 3. Treatment algorithm for the management of GERD	57

Abbreviations

ACG	American College of Gastroenterology
AGA	American Gastroenterological Association
ASGE	American Society for Gastrointestinal Endoscopy
BE	Barrett's Esophagus
CDA	Canada's Drug Agency
CHI	Council of Health Insurance
COPD	Chronic Obstructive Pulmonary Disease
CPG	Clinical Practice Guideline
DDF	Daman Drug Formulary
DGVS	German Society of Gastroenterology, Digestive and Metabolic Diseases
EAC	Esophageal Adenocarcinoma
EET	Endoscopic Eradication Therapy
EoE	Eosinophilic Esophagitis
FDA	Food and Drug Administration
GERD	Gastro-Esophageal Reflux Disease
HAS	Haute Autorité de Santé
H2RA	H2 Receptor Antagonists
HGD	High-Grade Dysplasia
HTA	Health Technology Assessment
IPF	Idiopathic Pulmonary Fibrosis
IQWiG	Institute for Quality and Efficiency in Healthcare
LGD	Low-Grade Dysplasia
NDBE	Non-dysplastic Barrett's esophagus
NERD	Nonerosive Reflux Disease
NICE	National Institute for Health and Care Excellence
OSAHS	Obstructive Sleep Apnea Hypopnea Syndrome
PAAEs	PPI-Associated Adverse Events

PBAC	Pharmaceutical Benefits Advisory Committee
PPI	Proton Pump Inhibitor
RYGB	Roux-en-Y Gastric Bypass
SFDA	Saudi Food and Drug Authority
TIF	Transoral Incisionless Fundoplication

Executive Summary

Gastroesophageal reflux disease (GERD) is a chronic condition defined by the retrograde flow of gastric contents into the esophagus, leading to troublesome symptoms and/or mucosal damage. This reflux occurs due to the improper closure of the lower esophageal sphincter. It can also involve injury or complications that arise from the backward flow of stomach contents into the esophagus, oropharynx, and/or respiratory tract. Symptoms caused by reflux, the presence of erosive esophagitis, and long-term complications can severely impact daily activities, work efficiency, sleep patterns, and overall quality of life in a detrimental manner^{1,2}.

The hallmark symptoms of GERD include heartburn—a burning sensation in the chest—and regurgitation of acidic stomach contents into the throat or mouth. Other manifestations may involve chest pain, difficulty swallowing (dysphagia), chronic cough, hoarseness, and a sensation of a lump in the throat. In infants and children, GERD can present as recurrent vomiting, coughing, respiratory issues, and feeding difficulties³.

Several factors contribute to the development of GERD. Obesity increases abdominal pressure, promoting reflux. Pregnancy similarly elevates abdominal pressure and alters hormone levels, affecting sphincter function. Smoking can impair the lower esophageal sphincter's ability to function properly. A hiatal hernia, where part of the stomach pushes through the diaphragm, can also facilitate reflux. Additionally, certain medications—including benzodiazepines, calcium channel blockers, tricyclic antidepressants, nonsteroidal anti-inflammatory drugs (NSAIDs), and some asthma treatments—may relax the sphincter or irritate the esophageal lining, exacerbating GERD symptoms⁴.

GERD is typically diagnosed through a combination of clinical evaluation and diagnostic testing. The initial approach often involves assessing characteristic symptoms such as heartburn and regurgitation. In patients presenting with typical symptoms without alarm features (e.g., dysphagia, weight loss, gastrointestinal bleeding), an empirical trial of proton pump inhibitors (PPIs) may be initiated; a positive response can support the diagnosis of GERD. For individuals who do not respond to PPI therapy, or when the diagnosis is uncertain, further diagnostic evaluations are warranted. Upper endoscopy is recommended in patients with alarm symptoms or those at risk for complications like Barrett's esophagus. Esophageal pH monitoring, particularly 24-hour ambulatory pH monitoring, serves as the gold standard for quantifying acid exposure and confirming GERD in patients with persistent symptoms despite therapy. Esophageal manometry may be utilized to assess esophageal motility disorders, especially prior to anti-reflux surgery⁵.

GERD is a prevalent condition globally, affecting approximately 10% to 20% of the population in the Western world. Studies suggest that approximately one-third of

the population experiences GERD, according to the American Gastroenterological Association. The prevalence varies significantly across different regions due to dietary habits, obesity rates, and genetic predispositions. A review study published in the journal *Gut* provides the following GERD prevalence estimates: **North America:** 18–28%, **Europe:** 9–26%, **East Asia:** 3–8%, **Middle East:** 9–33% and **Australia:** 12%⁶. The global pooled prevalence of GERD was 13.98% and varied greatly according to region (12.88% in Latin America and the Caribbean to 19.55% in North America) and country (4.16% in China to 22.40% in Turkey). Using the United Nations 2017 Revision of World Population Prospects, the estimated number of individuals suffering from GERD globally is 1.03 billion⁷.

In Saudi Arabia, based on two studies conducted in the west region and Riyadh using the GERDQ questionnaire with a score of ≥ 8 as the diagnostic criteria of GERD, the prevalence range of GERD was 23.47% - 45.4%⁸.

Data from the National Platform for Health and Insurance Exchange Services (NPHIES), a unified electronic services platform covering the Saudi private sector, shows a 1-year prevalence of GERD of 1,455 per 100,000, and an incidence of 1,242 per 100,000. *The prevalence and incidence estimates extracted from the NPHIES database may be subject to potential errors due to data scrutiny limitations.*

Failure to receive appropriate treatment or incorrect treatment of this condition can result in the development of complications. Esophagitis, an inflammation of the esophageal lining, can cause ulcers and bleeding. Esophageal strictures, or the narrowing of the esophagus due to scar tissue, can result from chronic inflammation, leading to swallowing difficulties. Barrett's esophagus, a condition where the esophageal lining changes to resemble intestinal tissue, increases the risk of developing esophageal adenocarcinoma, a type of cancer³.

GERD imposes a significant burden on healthcare systems and individuals. Economically, it leads to substantial direct costs from medical consultations, diagnostic procedures, and long-term medication use. Indirect costs arise from lost productivity due to work absenteeism and decreased work efficiency. The broad spectrum of GERD symptoms contributes significantly to healthcare costs, as many cases require extensive testing to diagnose or rule out other conditions, such as heart attacks. The expense of excluding cardiac-related conditions alone is particularly high. Socially, GERD can diminish quality of life, affecting dietary choices, sleep patterns, and overall well-being⁶.

The primary objectives in managing GERD are to alleviate symptoms, heal esophageal inflammation, prevent complications, and improve the patient's quality of life. Achieving these goals involves a combination of lifestyle modifications, pharmacological interventions, and, in certain cases, surgical procedures. The current medical approach involves the utilization of medications, such as proton pump inhibitors (PPIs), which function by reducing the production of stomach acid.

Additionally, surgical interventions are employed with the objective of increasing pressure in the lower esophageal sphincter to prevent reflux⁹. Treatment also includes simple antacids and H2 blockers⁴.

There are certain preventive measures that can assist in reducing the discomfort associated with GERD. These include avoiding food and beverages that can trigger the burning sensation, quitting smoking, and maintaining a healthy weight. Making lifestyle changes can also help alleviate symptoms. These changes may involve clothing and from lying down immediately after eating, consuming meals 2-3 hours before bedtime, opting for smaller and spaced-out meals throughout the day, avoiding tight-fitting clothing, and elevating the head of the bed by 15-20 centimeters¹⁰.

CHI issued GERD clinical 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 GERD clinical guidance and seeks to offer guidance for the effective management of GERD. It provides an **update on the GERD Guidelines** for CHI Formulary with the ultimate objective of updating the DDF (Daman Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies**. This formulary is intended to assist in coverage decisions and does not replace the clinical judgment of treating healthcare providers but complements their decision-making process. It is a dynamic resource, updated regularly based on emerging evidence.

Main triggers for the update are summarized, being the addition of **new guidelines to the report** such as **2023** S2k guideline Gastroesophageal reflux disease and eosinophilic esophagitis of the **German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS)**; **2024** The **Saudi Gastroenterology Association** consensus on the clinical care pathway for the diagnosis and treatment of GERD; **2024 AGA** Clinical Practice Update on Integrating Potassium-Competitive Acid Blockers Into Clinical Practice: Expert Review; **2024** The consensus of the **Asociación Mexicana de Gastroenterología** on the diagnosis and treatment of gastroesophageal reflux and gastroesophageal reflux disease in infants; **2024** Good clinical practice recommendations for the diagnosis and treatment of gastroesophageal reflux disease. An expert review from the **Asociación Mexicana de Gastroenterología** and the **2025 American Society for Gastrointestinal Endoscopy** guideline on the diagnosis and management of GERD: summary and recommendations.

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is important to note that there has been **withdrawal** of the following drug: Cimetidine.

Main recommendations issued by different Health Technology Assessment (HTA) bodies on the use of the current medications in GERD were reviewed and summarized. These include the National Institute for Health and Care Excellence (NICE), Canada’s Drug Agency (CDA), Haute Autorité de Santé (HAS), the Institute for Quality and Efficiency in Healthcare (IQWiG), and the Pharmaceutical Benefits Advisory Committee (PBAC).

Additionally, there have been **updates** regarding previously mentioned drugs in terms of drug information and prescribing edits since June 2023:

Table 1. Prescribing Edits Modifications for GERD Medications

Drugs	Prescribing Edits Modifications
Famotidine	Removed CU Added ST: H2RAs are second-line treatment for GERD in patients intolerant to PPIs
Metoclopramide	Removed CU
Nizatidine	Removed CU Added ST: H2RAs are second-line treatment for GERD in patients intolerant to PPIs

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) reflecting specific drug class role in the management of GERD.

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

Table 2. General Recommendations for the Management of Gastroesophageal Reflux Disease (GERD)

Management of GERD		
General Recommendations	Level of Evidence/Grade of Recommendation	Reference
In patients with symptomatic and confirmed GERD with predominant heartburn symptoms, the ASGE recommends medical management with PPI at the lowest possible dose	Strong recommendation, moderate quality of evidence ⁵	ASGE ⁵

for the shortest period of time possible while initiating discussion about long-term management options.		
According to Saudi guidelines, in patients with classic GERD symptoms who have no alarm features, the physician should start 6–8 weeks of treatment with a standard dose of PPI or potassium-competitive acid blocker (P-CAB). If there is an adequate response, PPIs should be discontinued or reduced to the lowest effective dose	Not graded ¹²	Saudi Gastroenterology Association ¹²
In cases of confirmed or probable GERD, PPI therapy should be given for at least 4 to 8 weeks. PPI dosage should be based on the phenotype of GERD and the approval status of the selected PPI.	Strong consensus ¹³	DGVS ¹³
Treatment with PPIs is recommended over H2RA for maintenance of healing for EE. PPIs are more effective in the treatment of proven GERD and healing esophagitis. P-CABs are an alternative when available. Other adjunctive pharmacotherapy should be tailored to the GERD phenotype. Adjunctive medications include H2RAs, which can be used for nocturnal symptoms, alginate antacids, which can be used for breakthrough symptoms, and baclofen, which can be used for regurgitation or belching	Not graded ^{12, 14}	Saudi Gastroenterology Association ¹² Asociación Mexicana de Gastroenterología ¹⁴
For patients with GERD who do not have EE or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, an attempt should be made to discontinue PPIs or to switch to on-demand therapy in which PPIs	Conditional recommendation, low level of evidence Strong recommendation	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵

are taken only when symptoms occur and discontinued when they are relieved.	n, Strong consensus ¹³	DGVS ¹³
The guideline does not recommend baclofen in the absence of objective evidence of GERD.	Strong recommendation, moderate level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵
The guideline recommends against treatment with a prokinetic agent of any kind for GERD therapy unless there is objective evidence of gastroparesis.	Strong recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵
The guideline does not recommend sucralfate for GERD therapy except during pregnancy .	Strong recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵
PPIs (except omeprazole) are considered safe during pregnancy	Not graded ¹²	Saudi Gastroenterology Association ¹²
Standard-dose PPI therapy is recommended for GERD management in pregnant patients	Not graded ¹⁴	Asociación Mexicana de Gastroenterología ¹⁴
The guideline suggests on-demand or intermittent PPI therapy for heartburn symptom control in patients with NERD .	Conditional recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵
In cases of confirmed or probable GERD and inadequate response to a standard dose of a PPI, switching to another PPI, doubling the dose of the PPI (1-0-1), or combination therapy	Strong consensus ¹³	DGVS ¹³

with another active principle may be used.		
For patients who have both extraesophageal and typical GERD symptoms, the guideline suggests considering a trial of twice-daily PPI therapy for 8–12 weeks before additional testing.	Conditional recommendation, low level of evidence. Strong recommendation ¹³ Not graded ¹⁴	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵ DGVs ¹³ Asociación Mexicana de Gastroenterología ¹⁴
For patients who have regurgitation as their primary PPI- refractory symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF.	Conditional recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵
Antireflux surgery should be offered in cases of long-standing confirmed reflux and complicated GERD (e.g., LA grade C/D, peptic stricture). The indication for antireflux surgery should be evaluated if the patient cannot tolerate long-term medication.	Strong consensus ¹³	DGVs ¹³
Laparoscopic fundoplication should be performed as first-line surgical therapy. The procedure is effective and has only a few complications.	Strong recommendation, strong consensus ¹³ Not graded ¹²	DGVs ¹³ Saudi Gastroenterology Association ¹²
The guideline suggests consideration of Roux-en-Y gastric bypass (RYGB) as an option to treat GERD in obese patients who are candidates for this procedure and who are willing to accept its risks and requirements for lifestyle alterations.	Conditional recommendation, low level of evidence.	2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease ¹⁵

1. Surgical (fundoplication) versus medical (PPI) management in adult and pediatric patients with chronic or refractory GERD 1a. The panel suggests managing adult patients with confirmed chronic or chronic refractory gastroesophageal reflux with surgical fundoplication rather than continued medical treatment. 1b. No recommendation was made regarding pediatric patients.	Conditional recommendation based on very low certainty in the evidence of effects	2021 Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD)¹⁶
Testing can be considered for those with an established objective diagnosis of GERD who do not respond to high doses of acid suppression. Testing can include pH-impedance monitoring while on acid suppression to evaluate the role of ongoing acid or non-acid reflux.	Not graded	2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease¹⁷
All patients with BE should be placed on at least daily proton pump inhibitor therapy.	Not graded	2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review¹⁸
Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.	Not graded	2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review¹⁹
Patients with complicated GERD, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally	Not graded	2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump

not be considered for PPI discontinuation.		Inhibitors: Expert Review ¹⁹
Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing.	Not graded	2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review ¹⁹
In patients with proven GERD, Roux-en-Y gastric bypass is an effective primary anti-reflux intervention in obese patients, and a salvage option in non-obese patients, whereas sleeve gastrectomy has potential to worsen GERD.	Not graded	2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review ²⁰
Clinicians should provide patients presenting with troublesome heartburn, regurgitation, and/ or non-cardiac chest pain without alarm symptoms a 4- to 8-week trial of single-dose PPI therapy. With inadequate response, dosing can be increased to twice a day or switched to a more effective acid suppressive agent once a day. When there is adequate response, PPI should be tapered to the lowest effective dose.	Not graded	2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review ²⁰
In symptomatic GERD patients, lifestyle changes should be recommended, including weight reduction, avoiding meals within 2–3 hours of bedtime, elevating the head of the bed during sleep, and smoking/alcohol cessation.	Not graded ¹² Strong recommendation, low quality of evidence ⁵	ASGE ⁵ Saudi Gastroenterology Association ¹² Asociación Mexicana de Gastroenterología ¹⁴

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

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts: one part includes recommendations from **updated versions of guidelines** mentioned in the previous CHI GERD report, and one part includes **newly added guidelines** that have helped generate this report.

Table 3. Guidelines Requiring Revision

Guidelines requiring revision	
Old versions	Updated versions
American College of Gastroenterology Guidelines for the Diagnosis and Management of Gastroesophageal Reflux Disease	ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease 2022 ¹⁵
NICE Guidelines on Managing gastro-esophageal reflux disease in adults 2019	N/A*
European Association of Endoscopic Surgery Guidelines for the management of gastroesophageal reflux disease 2014	N/A*
World Gastroenterology Organization Global Guidelines 2017	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)

1.1 Revised Guidelines

This part contains the updated versions of the guidelines mentioned in the 2019 CHI GERD Report and the corresponding recommendations.

1.1.1 American College of Gastroenterology (ACG) Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease 2022

(Please refer to section 1.1 of the 2019 CHI report on GERD)

Please refer to Appendix B for the Grades of Recommendation/Level of Evidence interpretation for this guideline.

The 2022 American College of Gastroenterology (ACG) Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease listed the recommendations below¹⁵:

Table 4. 2022 ACG Guideline Recommendations

Indication	Recommendation	Class of Evidence
GERD	A recently approved device for evaluation of GERD uses a catheter-based balloon lined by sensors that measure mucosal impedance during endoscopy. This technique has shown promise for differentiating GERD from EoE and may develop to be a useful adjunct to endoscopy in the diagnosis of GERD.	Not graded
GERD	The guideline suggests avoiding meals within 2–3 hours of bedtime.	Conditional recommendation, low level of evidence.
GERD	For patients with GERD who do not have EE or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, an attempt should be made to discontinue PPIs or to switch to on-demand therapy in which PPIs are taken only when symptoms occur and discontinued when they are relieved.	Conditional recommendation, low level of evidence.
GERD	The guideline recommends maintenance PPI therapy indefinitely or antireflux surgery for patients with LA grade C or D esophagitis.	Strong recommendation, moderate level of evidence.
GERD	The guideline does not recommend baclofen in the absence of objective evidence of GERD.	Strong recommendation, moderate level of evidence.
GERD	The guideline recommends against treatment with a prokinetic agent of any kind for GERD therapy unless there is objective evidence of gastroparesis.	Strong recommendation, low level of evidence.
GERD	Antacids are used exclusively for on-demand symptom relief with little evidence to favor 1 type over another. Studies with an alginic acid	Not graded.

	preparation manufactured in the United Kingdom suggest potential efficacy in symptom relief compared with other products, but alginate content of preparations sold in other countries is variable.	
GERD	The guideline does not recommend sucralfate for GERD therapy except during pregnancy.	Strong recommendation, low level of evidence.
GERD	The guideline suggests on-demand or intermittent PPI therapy for heartburn symptom control in patients with NERD.	Conditional recommendation, low level of evidence.
Extra-esophageal GERD	The guideline recommends that patients who have extraesophageal manifestations of GERD without typical GERD symptoms (e.g., heartburn and regurgitation) undergo reflux testing for evaluation before PPI therapy.	Strong recommendation, moderate level of evidence.
Extra-esophageal GERD	For patients who have both extraesophageal and typical GERD symptoms, the guideline suggests considering a trial of twice-daily PPI therapy for 8–12 weeks before additional testing.	Conditional recommendation, low level of evidence.
Extra-esophageal GERD	In patients treated for extraesophageal reflux disease, surgical or endoscopic antireflux procedures are only recommended in patients with objective evidence of reflux.	Conditional recommendation, low level of evidence.
Refractory GERD	The guideline recommends optimization of PPI therapy as the first step in management of refractory GERD.	Strong recommendation, moderate level of evidence.
Refractory GERD	For patients who have regurgitation as their primary PPI-refractory symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF.	Conditional recommendation, low level of evidence.
Surgical and endoscopic	The guideline suggests consideration of TIF for patients with troublesome regurgitation or heartburn who do not wish to undergo	Conditional recommendation,

options for GERD	antireflux surgery and who do not have severe reflux esophagitis (LA grade C or D) or hiatal hernias > 2 cm.	low level of evidence.
Surgical and endoscopic options for GERD	The guideline suggests consideration of Roux-en-Y gastric bypass (RYGB) as an option to treat GERD in obese patients who are candidates for this procedure and who are willing to accept its risks and requirements for lifestyle alterations.	Conditional recommendation, low level of evidence.
Surgical and endoscopic options for GERD	The guideline recommends antireflux surgery performed by an experienced surgeon as an option for long-term treatment of patients with objective evidence of GERD, especially those who have severe reflux esophagitis (LA grade C or D), large hiatal hernias, and/or persistent, troublesome GERD symptoms.	Strong recommendation, moderate level of evidence.

Figure 1 (Appendix D) details the algorithm for the diagnosis of **GERD**¹⁵.

Figure 2 (Appendix D) represents the steps for the diagnosis of **extraesophageal** reflux disease¹⁵.

1.2 Additional Guidelines

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

Table 5. List of Additional Guidelines

Additional Guidelines
2021 SAGES Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD) ¹⁶
2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease: Expert Review ¹⁷
2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review ¹⁸
2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review ¹⁹
2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review ²⁰
2022 ACG Guidelines on the Diagnosis and Management of Barrett's Esophagus ²¹

2023 S2k guideline Gastroesophageal reflux disease and eosinophilic esophagitis of the German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS)¹³

2024 The Saudi Gastroenterology Association consensus on the clinical care pathway for the diagnosis and treatment of GERD¹²

2024 AGA Clinical Practice Update on Integrating Potassium Competitive Acid Blockers Into Clinical Practice: Expert Review²²

2024 The consensus of the Asociación Mexicana de Gastroenterología on the diagnosis and treatment of gastroesophageal reflux and gastroesophageal reflux disease in infants²³

2024 Good clinical practice recommendations for the diagnosis and treatment of gastroesophageal reflux disease. An expert review from the Asociación Mexicana de Gastroenterología¹⁴

2025 American Society for Gastrointestinal Endoscopy guideline on the diagnosis and management of GERD: summary and recommendations⁵

1.2.1 Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Guidelines for the Surgical Treatment of Gastroesophageal Reflux (2021)

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) published in 2021 their clinical guidelines for the surgical treatment of gastroesophageal reflux (GERD). The main recommendations are detailed below¹⁶:

1- Surgical (fundoplication) versus medical (PPI) management in adult and pediatric patients with chronic or refractory GERD

1a. The panel suggests managing adult patients with confirmed chronic or chronic refractory gastroesophageal reflux with surgical fundoplication rather than continued medical treatment (conditional recommendation based on very low certainty in the evidence of effects).

1b. No recommendation was made regarding pediatric patients.

2- Robotic versus laparoscopic fundoplication in adult and pediatric patients with GERD requiring surgery.

2a. The panel suggests that adult patients with gastroesophageal reflux who are candidates for surgery be treated with either robotic or laparoscopic fundoplication based on surgeon and patient's shared decision-making (conditional recommendation based on low certainty in the evidence of effects).

2b. The panel suggests that children with gastroesophageal reflux who are candidates for surgery be treated with either robotic or laparoscopic fundoplication

based on surgeon and patient's shared decision-making and feasibility (conditional recommendation based on very low certainty in the evidence of effects).

3- Complete versus partial fundoplication in adult and pediatric patients with GERD who are candidates for surgery.

3a. The panel suggests that adult patients with GERD who are candidates for surgery be treated with either partial or complete fundoplication based on patients' values (conditional recommendations based on low certainty in the evidence of effects).

3b. For pediatric patients without large hiatal hernia, the panel suggests either partial or complete fundoplication approaches guided by shared surgeon-patient decision-making (conditional recommendations based on low certainty in the evidence of effects).

1.2.2 American Gastroenterological Association (AGA) Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease (2023)

The recommendations of 2023 AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease: Expert Review are listed below¹⁷:

- Initial testing to evaluate reflux should be tailored to patients' clinical presentation and can include upper endoscopy and ambulatory reflux monitoring studies of acid suppressive therapy.
- Testing can be considered for those with an established objective diagnosis of GERD who do not respond to high doses of acid suppression. Testing can include pH-impedance monitoring while on acid suppression to evaluate the role of ongoing acid or non-acid reflux.
- Alternative treatment methods to acid suppressive therapy (e.g., lifestyle modifications, alginate containing antacids, external upper esophageal sphincter compression device, cognitive behavioral therapy, neuromodulators) may serve a role in management of EER symptoms.

1.2.3 American Gastroenterological Association (AGA) Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus (2022)

The recommendations of 2022 AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review are listed below¹⁸:

- All patients with BE should be placed on at least daily proton pump inhibitor therapy.
- Patients with nondysplastic BE should undergo surveillance endoscopy in 3 to 5 years.
- In patients undergoing surveillance after endoscopic eradication therapy, random biopsies should be taken of the esophagogastric junction, gastric cardia, and the distal 2 cm of the neo squamous epithelium as well as from all visible lesions, independent of the length of the original BE segment.

1.2.4 American Gastroenterological Association (AGA) Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors (2022)

The recommendations of 2022 AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors are listed below¹⁹:

- Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.
- Patients with complicated GERD, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.
- Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing.
- PPI users should be assessed for upper GI bleeding risk using an evidence-based strategy before de-prescribing.
- Patients at high risk for upper GI bleeding should not be considered for PPI deprescribing.
- Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper GI symptoms due to rebound acid hypersecretion.
- When de-prescribing PPIs, either dose tapering, or abrupt discontinuation can be considered.
- The decision to discontinue PPIs should be based solely on the lack of an indication for PPI use, and not because of concern for PPI associated adverse events (PAAEs). The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.

1.2.5 American Gastroenterological Association (AGA) Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD (2022)

The recommendations of 2022 AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD are listed below²⁰:

- In patients with proven GERD, Roux-en-Y gastric bypass is an effective primary anti-reflux intervention in obese patients, and a salvage option in non-obese patients, whereas sleeve gastrectomy has potential to worsen GERD.
- In patients with proven GERD, laparoscopic fundoplication and magnetic sphincter augmentation are effective surgical options, and transoral incisionless fundoplication is an effective endoscopic option in carefully selected patients.
- Clinicians should personalize adjunctive pharmacotherapy to the GERD phenotype, in contrast to empiric use of these agents. Adjunctive agents include alginate antacids for breakthrough symptoms, nighttime H2 receptor antagonists for nocturnal symptoms, baclofen for regurgitation or belch predominant symptoms, and prokinetics for coexistent gastroparesis.
- Clinicians should provide patients presenting with troublesome heartburn, regurgitation, and/ or non-cardiac chest pain without alarm symptoms a 4- to 8-week trial of single-dose PPI therapy. With inadequate response, dosing can be increased to twice a day or switched to a more effective acid suppressive agent once a day. When there is adequate response, PPI should be tapered to the lowest effective dose.

1.2.6 American College of Gastroenterology (ACG) Guidelines on the Diagnosis and Management of Barrett's Esophagus (2022)

Please refer to Appendix B for the Grades of Recommendation/Level of Evidence interpretation for this guideline.

The recommendations of the 2022 ACG guidelines on the diagnosis and management of Barrett's esophagus (BE) are listed below:²¹

Screening of BE:

- The guideline suggests a single screening endoscopy for patients with chronic GERD symptoms and 3 or more additional risk factors for BE, including male sex, age > 50 years, White race, tobacco smoking, obesity, and family history of BE or esophageal adenocarcinoma (EAC) in a first-degree relative (strength of recommendation: conditional; quality of evidence: very low).

- The guideline suggests that a swallowable, nonendoscopic capsule sponge device combined with a biomarker is an acceptable alternative to endoscopy for screening for BE in those with chronic reflux symptoms and other risk factors (strength of recommendation: conditional; quality of evidence: very low).
- Repeat endoscopic screening in patients who have undergone an initial negative screening examination by endoscopy is not recommended (strength of recommendation: conditional; quality of evidence: low).

Management of BE with low grade dysplasia vs high grade dysplasia:

- The guideline recommends that length of the non-dysplastic Barrett's esophagus (NDBE) segment be considered when assigning surveillance intervals such that longer segments of BE (≥ 3 cm) are surveyed on a 3-year interval and shorter segments of BE (< 3 cm) are surveyed on a 5-year interval (quality of evidence: moderate; strength of recommendation: strong).

Non endoscopic treatment of BE:

- The guideline suggests at least once-a-day PPI therapy in patients with BE without allergy or other contraindication to PPI use (strength of recommendation: conditional; quality of evidence: very low).
- The use of antireflux surgery as an antineoplastic measure in patients with BE is not recommended (strength of recommendation: conditional; quality of evidence: low).
- The guideline could not make a recommendation on combination therapy with ASA and PPI in patients with BE to reduce the risk of progression to HGD/EAC.

Endoscopic treatment of BE:

- The guideline recommends endoscopic eradication therapy (EET) compared with esophagectomy in patients with BE with high-grade dysplasia (HGD) (strength of recommendation: strong; quality of evidence: moderate).
- The guideline suggests endoscopic therapy in patients with BE with confirmed low-grade dysplasia (LGD) to reduce the risk of progression to HGD/EAC, with endoscopic surveillance of confirmed LGD as an acceptable alternative (strength of recommendation: conditional; quality of evidence: moderate).
- The guideline recommends an endoscopic surveillance program in patients with BE who have completed successful EET (strength of recommendation: strong; quality of evidence: moderate).

1.2.7 German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS) S2k Guideline for Gastroesophageal Reflux Disease and Eosinophilic Esophagitis (2023)

Please refer to Appendix B for the Grades of Recommendation/Level of Evidence interpretation for this guideline.

The DGVC has issued recommendations below¹³:

Table 6. DVGS Recommendations for GERD Management

Therapeutic Recommendation	Target Population	LoE	GoR
A distinction should be made between therapy for reflux symptoms (without confirmed GERD) and that for confirmed GERD.	Children and adults	Recommendation	Strong consensus
Patients with reflux symptoms and those with confirmed GERD should be counseled about the importance of general measures in the therapeutic concept.	Children and adults	Strong recommendation	Strong consensus
A standard-dose PPI should be prescribed for typical reflux symptoms with no alarm symptoms, no positive family history of upper gastrointestinal tract malignancy, and no risk factors for complications.	Children and adults	Recommendation	Strong consensus
In typical reflux symptoms without alarm symptoms, without a positive family history for malignancies of the upper digestive tract and without risk factors for complications, other antireflux preparations (e.g., H2 receptor antagonists, alginates, antacids) can also be used on a trial basis if symptom control is sufficient.	Children and adults	Recommendation	Open, strong consensus

In case of inadequate or absent response of typical reflux symptoms without previous diagnosis to PPI therapy adequately performed for at least 8 weeks, further clarification should be performed.	Children and adults	Recommendation	Strong consensus
In cases of confirmed or probable GERD, PPI therapy should be given for at least 4 to 8 weeks. PPI dosage should be based on the phenotype of GERD and the approval status of the selected PPI.	Children and adults	Strong recommendation	Strong consensus
In cases of confirmed or probable GERD and inadequate response to a standard dose of a PPI, switching to another PPI, doubling the dose of the PPI (1-0-1), or combination therapy with another active principle may be used.	Children and adults	Recommendation	Open, strong consensus
In refractory GERD, defined as inadequate response to at least 8 weeks of therapy with twice the dose of a PPI (1-0-1), further evaluation should be performed.	Children and adults	Strong recommendation	Strong consensus
In uncomplicated GERD (NERD, mild Los Angeles reflux esophagitis grade A/B), long-term medical management should be based on symptoms. Overtreatment should be avoided.	Children and adults	Recommendation	Strong consensus
In complicated GERD (reflux esophagitis grade C/D, peptic stricture), PPI continuous therapy should be given.	Children and adults	Recommendation	Strong consensus
If an extraesophageal manifestation of GERD is suspected in adults, PPI therapy should be given at twice the	Adults	Strong recommendation	Consensus

standard dose (1-0-1) for 12 weeks. Children and adolescents should be diagnosed first.			
If reflux thoracic pain syndrome is clinically suspected, therapy with twice the standard dose of a PPI (1-0-1) should be given for 8 weeks.	Children and adults	Recommendation	Strong consensus
Patients with sleep disturbances in the setting of GERD may be treated with a PPI and/or an alginate at night.	Children and adults	Recommendation	Open, strong consensus
Step-up management should be used for reflux symptoms in pregnancy: General measures, antacid, alginate, sucralfate, H2-receptor antagonist, PPI.	Pregnancy	Recommendation	Strong consensus
If PPI therapy is no longer necessary, treatment should be discontinued. This can be done gradually with the addition of an on-demand medication in case of breakthrough symptoms.	Children and adults	Strong recommendation	Strong consensus
The absolute risk of side effects for PPI is low. In GERD, the benefit outweighs the risk.	Children and adults	Strong consensus	Consensus
If long-term therapy with PPI is necessary, <i>Helicobacter pylori</i> diagnostics and therapy should be performed according to the currently valid S2k guideline of the DGVS.	Children and adults	Recommendation	Strong consensus
Antireflux surgery should be offered in cases of long-standing confirmed reflux and complicated GERD (e.g., LA grade C/D, peptic stricture). The indication for antireflux surgery should be evaluated if the patient cannot tolerate long-term medication.	Children and adults	Recommendation	Strong consensus

Laparoscopic fundoplication should be performed as first-line surgical therapy. The procedure is effective and has only a few complications.	Children and adults	Strong recommendation	Strong consensus
Surgical alternatives to fundoplication, such as magnetic sphincter augmentation, have shown promising results in current studies, and may be considered if the indication is precise.	Children and adults	Recommendation	Open, strong consensus
Reflux recurrences without diagnostically proven anatomic/morphologic complications should initially be treated again with PPI.	-	Recommendation	Strong consensus

1.2.8 Saudi Gastroenterology Association Consensus on the Clinical Care Pathway for the Diagnosis and Treatment of GERD (2024)

The Saudi Gastroenterology Association has issued recommendations below¹²:

Table 7. Saudi Gastroenterology Association recommendations for GERD diagnosis and treatment

Category	Statement
Definition of GERD	GERD is defined as objective evidence of GERD by mucosal damage on endoscopy and/or abnormal pH monitoring in the presence of compatible troublesome symptoms.
Clinical assessment and role of PPI	Two terms are used in the evaluation of symptomatic patients with GERD: unproven and proven. The term “unproven GERD” refers to patients in whom endoscopy and/or ambulatory pH monitoring have not revealed conclusive evidence of GERD. In contrast, the term “proven GERD” is used when there is conclusive evidence for GERD on endoscopy and/or ambulatory pH monitoring.
	Classic GERD symptoms include heartburn, regurgitation, and noncardiac chest pain, while extraesophageal

	manifestations include globus sensation, asthma, chronic cough, laryngitis, and dental erosions.
	In patients with classic GERD symptoms who have no alarm features, the physician should start 6–8 weeks of treatment with a standard dose of PPI or potassium-competitive acid blocker (P-CAB) . If there is an adequate response, PPIs should be discontinued or reduced to the lowest effective dose.
	In patients with extraesophageal GERD manifestations without classic GERD symptoms, the physician should consider a diagnostic GERD workup before initiating PPI therapy.
Upper GI Endoscopy	Endoscopy is recommended as a first step in the evaluation of patients with alarm symptoms (dysphagia, loss of weight, anemia) and in patients with multiple risk factors for Barrett's esophagus.
	For unproven GERD, discontinuation of PPI for a minimum of 2 weeks before upper GI endoscopy is recommended.
	For upper GI endoscopic examination, the physician should use the LA classification for grading esophagitis, measure the length of the axial hiatal hernia, and use the AFS endoscopic classification of esophagogastric junction integrity and the Prague classification for grading Barrett's esophagus.
	Mucosal damage on upper GI endoscopy (LA grade B, C, and D esophagitis, peptic stricture, and Barrett's esophagus) is conclusive evidence of GERD (proven GERD).
Ambulatory pH Monitoring	For unproven GERD, ambulatory pH monitoring should be performed off PPI therapy. If available, wireless pH monitoring for 72–92 hours is preferred.
	In proven GERD with persistent symptoms despite the standard dose of PPI therapy, ambulatory pH impedance monitoring should be performed on PPI therapy to identify the mechanism of persistent GERD symptoms.
HREM (High-Resolution Esophageal Manometry)	HREM is recommended in the evaluation of patients with proven GERD and persistent symptoms to identify the mechanism of refractoriness, in patients with persistent GERD symptoms and negative testing to rule out the alternative diagnosis, in patients with regurgitation and negative EGD and pH monitoring testing to rule out

	achalasia, rumination/belching disorders, and before antireflux surgical and endoscopic treatment to rule out achalasia and absent contractility.
Barium Esophagram	Barium esophagogram is not recommended for the diagnosis of GERD, but can be used to assess structural abnormalities of the esophagus before endoscopic treatment and antireflux surgery.
Medical Treatment	In symptomatic GERD patients, lifestyle changes should be recommended, including weight reduction, avoiding meals within 2–3 hours of bedtime, elevating the head of the bed during sleep, and smoking/alcohol cessation. PPIs are more effective in the treatment of proven GERD and healing esophagitis. P-CABs are an alternative when available. Other adjunctive pharmacotherapy should be tailored to the GERD phenotype. Adjunctive medications include H2RAs, which can be used for nocturnal symptoms, alginate antacids, which can be used for breakthrough symptoms, and baclofen, which can be used for regurgitation or belching.
Endoscopic Treatment	TIF may be considered an effective minimal-invasive option in selected patients with proven GERD or who have refused antireflux surgery. TIF should not be recommended for patients with severe esophagitis LA grades C and D, hiatal hernias >2 cm in length, a peptic stricture, and Barrett's esophagus. Due to limited data, ARMS, ARMA, and Stretta may be considered as alternative options in patients with proven GERD who are not candidates for antireflux surgery or who refuse antireflux surgery and TIF.
Surgical Treatment	Antireflux surgery (laparoscopic fundoplication and MSA) is recommended as an effective treatment for objectively proven GERD.
GERD and Bariatric Surgery	RYGB is considered as a treatment option for proven GERD in obese patients.
GERD Treatment in Pregnancy	Lifestyle changes are recommended for pregnant women with GERD symptoms. If lifestyle changes fail, antacids and sucralfate are the first choice of treatment.

	PPIs (except omeprazole) are considered safe during pregnancy.
AFS = American Foregut Society, ARMA = antireflux mucosal ablation, ARMS = antireflux mucosectomy, GERD = gastroesophageal reflux disease, GI = gastrointestinal, H2RA = histamine type-2 receptor antagonist, HREM = high-resolution esophageal manometry, MSA = magnetic sphincter augmentation, P-CAB = potassium-competitive acid blocker, PPI = proton pump inhibitor, RYGB = Roux-en-Y gastric bypass, TIF = transoral incisionless fundoplication.	

1.2.9 American Gastroenterological Association (AGA) Clinical Practice Update on Integrating Potassium Competitive Acid Blockers into Clinical Practice: Expert Review (2024)

The AGA has issued recommendations below²²:

- Based on nonclinical factors (including cost, greater obstacles to obtaining medication, and fewer long-term safety data), clinicians should generally not use P-CABs as initial therapy for acid-related conditions in which clinical superiority has not been shown.
- Based on current costs in the United States, even modest clinical superiority of P-CABs over double-dose proton pump inhibitors (PPIs) may not make P-CABs cost-effective as first-line therapy.
- Clinicians should generally not use P-CABs as first-line therapy for patients with uninvestigated heartburn symptoms or nonerosive reflux disease. Clinicians may use P-CABs in selected patients with documented acid-related reflux who fail therapy with twice-daily PPIs.
- Although there is currently insufficient evidence for clinicians to use P-CABs as first-line on-demand therapy for patients with heartburn symptoms who have previously responded to antisecretory therapy, their rapid onset of acid inhibition raises the possibility of their utility in this population.
- Clinicians should generally not use P-CABs as first-line therapy in patients with milder erosive esophagitis (EE) (Los Angeles classification of erosive esophagitis grade A/B EE). Clinicians may use P-CABs in selected patients with documented acid-related reflux who fail therapy with twice-daily PPIs.
- Clinicians may use P-CABs as a therapeutic option for the healing and maintenance of healing in patients with more severe EE (Los Angeles classification of erosive esophagitis grade C/D EE). However, given the markedly higher costs of the P-CAB presently available in the United States and the lack of randomized comparisons with double-dose PPIs, it is not clear

that the benefits in endoscopic outcomes over standard-dose PPIs justify the routine use of P-CABs as first-line therapy.

Table 8. Potassium-Competitive Acid Blocker and Proton Pump Inhibitor Class Comparison

Variable	P-CAB	PPI
Effect of Gastric Acid	Acid-stable	Acid-labile (note enteric coating)
Prodrug	No	Yes (converted to sulfonamide compounds in acidic environment)
Binding to Proton Pump	Ionic (reversible) binding (blocks access of K ⁺ to potassium-binding site of pump)	Binds covalently (irreversible) to cysteines on active pumps (blocks exchange of H ⁺ and K ⁺)
Half-life estimates, h	5–7	6–9
Timing of Administration	Independent of mealtimes (not restricted, given longer half-life)	30–60 min before meals (so presence in secretory canaliculus coincides with postprandial peak in active pumps)
Dosing Range, d, for Maximal Acid Suppression	1	3–5
Examples	Revaprazan, vonoprazan, tegoprazan, fexuprazan, linaprazan, zastaprazan, keverprazan	Dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole

1.2.10 The Consensus of the Asociación Mexicana de Gastroenterología on the Diagnosis and Treatment of Gastroesophageal Reflux and Gastroesophageal Reflux Disease in Infants (2024)

The Asociación Mexicana de Gastroenterología has issued recommendations below²³:

Non-Pharmacological Treatment

- Infant regurgitation management should prioritize parental education and support.

- In children with regurgitation and GERD, exclusive breastfeeding should be encouraged, and its discontinuation should be avoided.
- In bottle-fed infants (whether receiving breast milk or formula), weight gain assessment is recommended before adjusting feeding volume or frequency. In breastfed infants, mothers should be guided in responsive feeding to recognize hunger and thirst cues, as overfeeding may increase regurgitation episodes.
- Proper breastfeeding technique should be carefully observed in breastfed infants with regurgitation.
- In formula-fed infants, the use of thickened formulas may help reduce visible regurgitation.
- Routine use of extensively hydrolyzed or amino acid-based formulas is not recommended for managing physiological reflux (regurgitation) in infants.
- Routine position changes are not recommended as a strategy to improve regurgitation.

Pharmacological Treatment

- Alginates may be considered as an alternative to formula thickening for breastfed infants or as a therapeutic trial for those with persistent symptoms despite non-pharmacological management.
- Routine use of prokinetic agents is not recommended for treating regurgitation in infants.
- PPIs and histamine H₂ receptor antagonists (H₂RAs) should not be used in otherwise healthy infants presenting with crying or irritability, with or without regurgitation.
- PPIs are recommended as the first-line treatment for reflux associated with erosive esophagitis.
- H₂RAs may be considered when PPIs are unavailable or contraindicated.

Surgical Treatment and Emerging Therapeutic Options

- Before proceeding with antireflux surgery, a thorough assessment using additional diagnostic tools is suggested to exclude complications or GERD secondary to another underlying condition.
- In patients with GERD unresponsive to medical therapy, referral to a pediatric gastroenterologist is advised to explore alternative treatments, such as transpyloric tube feeding, before considering surgery.

- Surgical intervention should be reserved for patients with refractory symptoms, life-threatening complications, or chronic conditions that pose a high risk of GERD-related complications despite optimal medical therapy.
- Referral to a pediatric gastroenterologist is recommended for children with GERD in the following cases:
 - Presence of alarm signs and symptoms suggestive of an underlying gastrointestinal disorder
 - Lack of response to optimal medical treatment
 - Inability to discontinue pharmacologic therapy after 6 to 12 months

1.2.11 Good Clinical Practice Recommendations for the Diagnosis and Treatment of Gastroesophageal Reflux Disease: An Expert Review from the Asociación Mexicana de Gastroenterología (2024)

The expert review from the Asociación Mexicana de Gastroenterología has issued recommendations below¹⁴:

Lifestyle Modifications

- Lifestyle modifications should be advised for all patients with GERD, including weight loss for those with overweight or obesity, early dinner consumption, bed head elevation, sleeping on the left side, and smoking cessation.

Proton Pump Inhibitors

- PPIs are the preferred treatment for GERD. A standard dose should be administered for four weeks in NERD and eight weeks in EE. In cases of severe esophagitis (Los Angeles classification C or D), a double-dose PPI for eight weeks is recommended.
- On-demand therapy is recommended for NERD and mild esophagitis (LA classification A and B), while continuous PPI therapy is preferred for severe esophagitis (C and D). The lowest effective dose should be used to control symptoms and maintain esophagitis healing.

Potassium-Competitive Acid Blockers

- P-CABs are a first-line treatment for GERD, with a standard dose recommended for four weeks in NERD and eight weeks in EE, regardless of severity. A reduced dose of P-CAB may be used for maintenance therapy, whether on-demand or continuous.

Adjuvant Treatments in Gastroesophageal Reflux Disease

- Antacids, alginates, and mucosal protective agents may be combined with antisecretory drugs for symptom relief in GERD. H2RAs can be used short-

term (two weeks) for nocturnal symptoms uncontrolled by PPIs. Prokinetics are indicated only for GERD patients with symptoms suggestive of delayed gastric emptying, such as early satiety and fullness.

Medical Treatment of Non-Erosive Gastroesophageal Reflux Disease

- In NERD, initial therapy should consist of a standard dose of PPI or P-CAB for four weeks. Maintenance therapy should follow an on-demand or intermittent approach, using the lowest effective dose of PPI or P-CAB to control symptoms.

Medical Treatment of Erosive Gastroesophageal Reflux Disease

- In EE, initial therapy should include a standard dose of PPI or P-CAB for eight weeks. For severe esophagitis (LA classification C or D), a double-dose PPI for eight weeks is advised. Maintenance therapy for mild esophagitis (LA classification A and B) should involve an on-demand regimen with a standard-dose PPI or half-dose P-CAB. For severe esophagitis, continuous maintenance therapy with a standard-dose PPI or half-dose P-CAB is recommended.

Treatment of Refractory Gastroesophageal Reflux Disease

- Antisecretory therapy should be optimized in refractory GERD symptoms through the following strategies:
 - a. Ensuring treatment adherence and appropriate PPI dosing relative to meals
 - b. Doubling the PPI dose
 - c. Switching to a different PPI
 - d. Transitioning from PPI to P-CAB
 - e. Adding adjuvant therapy
- Patients with persistent or treatment-refractory GERD symptoms should undergo ambulatory reflux monitoring to assess potential overlap with esophageal functional disorders.
- In functional heartburn, antisecretory therapy should be discontinued, and neuromodulators with psychological therapies should be used. For acid hypersensitivity or GERD overlap with functional disorders, antisecretory therapy should be optimized alongside neuromodulators and psychological therapies.

Treatment of Extraesophageal Manifestations

- Double-dose PPI therapy for 12 weeks is advised in patients with extraesophageal manifestations and objective evidence of GERD.

Endoscopic and Surgical Treatment

- Antireflux surgery should be considered for patients with objective GERD evidence, predominant regurgitation symptoms, large hiatal hernia, no severe esophageal motility disorder, and no significant dyspepsia or IBS symptoms. The procedure should be performed by an experienced surgeon, particularly in patients unwilling to undergo long-term medical treatment.

GERD in Special Populations: Pregnant Patients, Older Adults, and Obese Patients

- Standard-dose PPI therapy is recommended for GERD management in pregnant patients.
- Endoscopy should be performed in older adults with GERD symptoms due to the higher prevalence of severe disease.
- In obese patients with GERD eligible for bariatric surgery, gastrojejunal bypass is the preferred surgical approach. Sleeve gastrectomy and adjustable gastric banding are not recommended due to their potential to exacerbate reflux.

1.2.12 American Society for Gastrointestinal Endoscopy Guideline on the Diagnosis and Management of GERD: Summary and Recommendations (2025)

Please refer to Appendix B for the Grades of Recommendation/Level of Evidence interpretation for this guideline.

The American Society for Gastrointestinal Endoscopy has issued recommendations below⁵:

Table 9. ASGE Summary of Recommendations

Recommendation	Best practice advice	Strength of recommendation	Quality of the evidence
In patients with GERD symptoms, the ASGE recommends lifestyle modifications: • Weight loss for patients who are overweight or obese • Smoking cessation • Elevation of head of bed • Avoiding meals within 3 h of bedtime	–	Strong	Low
In patients with symptomatic and confirmed GERD with predominant heartburn symptoms, the ASGE recommends medical management with PPI at the lowest possible dose for the shortest possible period of time while initiating discussion about long-term management options.	1. Patients who have been on chronic PPI therapy (>6 mo) should be considered for optimization and de-escalation of medical management. 2. Providers should carefully consider the risks, benefits, and alternatives of PPI use with the patient with GERD. 3. Providers prescribing PPI therapy should be aware that adverse events from PPIs in prospective data have been limited to increased risk of enteric infections; however, long-term robust data are needed to prove or disprove any other putative adverse events.	Strong	Moderate

In patients with suboptimal clinical response to PPI therapy, the ASGE suggests testing for CYP2C19 polymorphism and adjusting PPI dosage and selection accordingly.	–	Conditional	Very low
In patients with confirmed GERD with a small hiatal hernia (<2 cm) and Hill grade I or II who meet any of the following criteria, the ASGE suggests evaluation for transoral incisionless fundoplication as an alternative to chronic medical management: • Chronic GERD (at least 6 months) • Chronic PPI use (>6 mo) for management for GERD symptoms • Refractory GERD • Regurgitation-predominant GERD • Patient prefers to avoid long-term PPI use	–	Conditional	Low
In patients with confirmed GERD with a large hiatal hernia (>2 cm) and Hill grade III or IV, the ASGE suggests evaluation for combined hiatal hernia repair and transoral incisionless fundoplication in a multidisciplinary review.	In patients with confirmed GERD and small hiatal hernias (<2 cm) and Hill grade I or II, Stretta can be considered when other alternatives (endoscopic/surgical fundoplication) are not available or feasible.	Conditional	Very low

Section 2.0 Drug Therapy

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

2.1 Additions

After November 2019, there are no new drugs added to the treatment of GERD. The drugs used for the management of GERD are still the same.

2.2 Modifications

Some modifications were made from the previous 2019 CHI report.

Please refer to section 2.1.7 in the previous report to highlight these modifications:

- Metoclopramide does not need prior authorization (PA) as a prescribing edit: it is an old drug, not expensive; tardive dyskinesia as a serious side effect should be monitored²⁴.
- Metoclopramide age limits are not to be used in less than 1 year old, however, it is also not recommended to be used in patients older than 60 years of age²⁴.

Please refer to section 2.2.6 in the previous 2019 CHI report:

- Cimetidine, famotidine and nizatidine do not need prior authorization (PA): they are drugs that have been on the market since decades and used as a second-line treatment option with concurrent use of PPI if symptoms are still present.

Please refer to section 2.7.7 in the previous 2019 CHI report:

- Domperidone does not need PA: it is a drug that has been on the market for decades, and it is only used if a patient has gastroparesis and did not improve while using metoclopramide²⁵.
- Domperidone has an age limit: efficacy has not been demonstrated; use is not recommended in infants and children < 12 years²⁵.

In addition, the following modifications and adjustments have been implemented since the 2023 report:

Table 10. Prescribing Edits (PE) Modifications for GERD Medications

Drugs	Prescribing Edits (PE) Modifications
Famotidine	Removed CU

	Added ST: H2RAS are second-line treatment for GERD in patients intolerant to PPIs
Metoclopramide	Removed CU
Nizatidine	Removed CU Added ST: H2RAS are second-line treatment for GERD in patients intolerant to PPIs

2.3 Delisting

Ranitidine was withdrawn from the market after a request by the FDA in April 2020, and it is no longer registered by the SFDA. The withdrawal was due to the presence of a contaminant known as N-Nitroso dimethylamine (NDMA) in ranitidine medications. NDMA is a probable human carcinogen¹¹. Cimetidine is no longer SFDA²⁶ registered, therefore, it is delisted from the DDF.

2.4 Other Drugs

The drug detailed in this section is a supplement commonly used for GERD, however, **it is not registered by the SFDA**.

2.4.1 Vonoprazan

Vonoprazan is a potassium-competitive acid blocker (P-CAB) approved by the U.S. Food and Drug Administration (FDA) on **November 1, 2023**, for the treatment of erosive gastroesophageal reflux disease (GERD) and relief of associated heartburn in adults. As of April 2025, the European Medicines Agency (EMA) has not approved vonoprazan for use in GERD. In the management of GERD, vonoprazan serves as a **first-line therapy** for healing all grades of erosive esophagitis, maintaining healing, and providing symptomatic relief from heartburn associated with erosive GERD. The recommended oral dosage for adults is **20 mg once daily** for up to 8 weeks to heal erosive esophagitis. For maintenance therapy and relief of heartburn, a dosage of **10 mg once daily** is advised. The safety and efficacy of vonoprazan in individuals under 18 years of age have not been established; therefore, its use in pediatric patients is not recommended. Common adverse reactions reported in clinical trials include gastritis, diarrhea, abdominal distension, abdominal pain, nausea, indigestion, hypertension, and urinary tract infection. Long-term use of vonoprazan may lead to vitamin B12 deficiency, hypomagnesemia, increased risk of *Clostridioides difficile*-associated diarrhea, and potential development of fundic gland polyps. Additionally, vonoprazan may interact with certain medications, such as atazanavir or rilpivirine, due to its potent acid suppression. Therefore, its use requires careful consideration of patient-specific factors and ongoing monitoring by healthcare providers^{27,28}.

Section 3.0 Key Recommendations Synthesis

GERD diagnosis:

- In patients with chest pain who have had adequate evaluation to exclude heart disease, objective testing for GERD (endoscopy and/or reflux monitoring) is recommended. (Conditional recommendation, low level of evidence)
- Endoscopy is recommended as the first test for evaluation of patients presenting with dysphagia or other alarm symptoms (weight loss and GI bleeding) and for patients with multiple risk factors for Barrett's esophagus. (Strong recommendation, low level of evidence)
- In patients for whom the diagnosis of GERD is suspected but not clear, and endoscopy shows no objective evidence of GERD, guidelines recommend reflux monitoring be performed off therapy to establish the diagnosis. (Strong recommendation, low level of evidence)

GERD management:

- In patients with symptomatic and confirmed GERD with predominant heartburn symptoms, the ASGE recommends medical management with PPI at the lowest possible dose for the shortest possible period of time while initiating discussion about long-term management options (Strong recommendation, moderate quality of evidence⁵).
- A standard-dose PPI should be prescribed for typical reflux symptoms with no alarm symptoms, no positive family history of upper gastrointestinal tract malignancy, and no risk factors for complications (Strong consensus¹³).
- According to Saudi guidelines, in patients with classic GERD symptoms who have no alarm features, the physician should start 6–8 weeks of treatment with a **standard dose of PPI** or **potassium-competitive acid blocker (P-CAB)**. If there is an adequate response, PPIs should be discontinued or reduced to the lowest effective dose (Not graded¹²).
- In cases of confirmed or probable GERD, PPI therapy should be given for at least 4 to 8 weeks. PPI dosage should be based on the phenotype of GERD and the approval status of the selected PPI (Strong recommendation, Strong consensus¹³).
- Treatment with PPIs is recommended over H2RA for maintenance of healing for EE. (Strong recommendation, moderate level of evidence). **PPIs are more effective** in the treatment of proven GERD and healing esophagitis. **P-CABs** are an **alternative** when available. Other adjunctive pharmacotherapy should be tailored to the GERD phenotype. Adjunctive medications include **H2RAs**, which can be used for nocturnal symptoms, **alginate antacids**, which can be

used for breakthrough symptoms, and **baclofen**, which can be used for regurgitation or belching (Not graded^{12,14}).

- Clinicians should generally not use P-CABs as first-line therapy for patients with uninvestigated heartburn symptoms or nonerosive reflux disease or patients with milder erosive esophagitis (EE). Clinicians may use P-CABs in selected patients with documented acid-related reflux who fail therapy with twice-daily PPIs (Not graded²²).
- Maintenance PPI therapy is recommended indefinitely or antireflux surgery for patients with LA grade C or D Moderate Strong esophagitis. (Strong recommendation, moderate level of evidence)
- Baclofen is not recommended in the absence of objective evidence of GERD. (Strong recommendation, moderate level of evidence.)
- Treatment with a prokinetic agent is not recommended for any kind for GERD therapy unless there is objective evidence of gastroparesis. (Strong recommendation, low level of evidence.)
- Sucralfate is only recommended in pregnancy GERD. (Strong recommendation, low level of evidence).
- **PPIs (except omeprazole)** are considered safe during pregnancy (Not graded¹²). Standard-dose PPI therapy is recommended for GERD management in pregnant patients (Not graded¹⁴).
- For patients with GERD who do not have EE or Barrett's esophagus, and whose symptoms have resolved with PPI therapy, an attempt should be made to discontinue PPIs or to switch to on-demand therapy in which PPIs are taken only when symptoms occur and discontinued when they are relieved. (Conditional recommendation, low level of evidence; Strong recommendation, Strong consensus¹³).
- In cases of confirmed or probable GERD and inadequate response to a standard dose of a PPI, switching to another PPI, doubling the dose of the PPI (1-0-1), or combination therapy with another active principle may be used (Strong consensus¹³).
- Alginates may be considered as an alternative to formula thickening for breastfed infants or as a therapeutic trial for those with persistent symptoms despite non-pharmacological management (Not graded²³).
- Routine use of prokinetic agents is not recommended for treating regurgitation in infants. PPIs and histamine H2 receptor antagonists (H2RAs) should not be used in otherwise healthy infants presenting with crying or irritability, with or without regurgitation (Not graded²³).

Extraesophageal GERD symptoms:

- Evaluation for non-GERD causes in patients with possible extraesophageal manifestations is recommended before ascribing symptoms to GERD. (Strong recommendation, moderate level of evidence.)
- For patients who have extraesophageal manifestations of GERD without typical GERD symptoms (e.g., heartburn and regurgitation) the guidelines recommend undergoing reflux testing for evaluation before PPI therapy. (Strong recommendation, moderate level of evidence.)
- For patients who have both extraesophageal and typical GERD symptoms, the guideline suggests considering a trial of twice-daily PPI therapy for 8–12 weeks before additional testing. (Conditional recommendation, low level of evidence; Strong recommendation¹³; Not graded¹⁴).

Refractory GERD:

- Optimization of PPI therapy is recommended as the first step in management of refractory GERD. (Strong recommendation, moderate level of evidence.)
- Esophageal pH monitoring (Bravo, catheter-based, or combined impedance-pH monitoring) performed OFF PPIs is recommended if the diagnosis of GERD has not been established by a previous pH monitoring study or an endoscopy showing long-segment Barrett's esophagus or severe reflux esophagitis (LA grade C or D). (Conditional recommendation, low level of evidence)
- Esophageal impedance-pH monitoring performed ON PPIs is recommended for patients with an established diagnosis of GERD whose symptoms have not responded adequately to twice-daily PPI therapy. (Conditional recommendation, low level of evidence).
- For patients who have regurgitation as their primary PPI-refractory symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF. (Conditional recommendation, low level of evidence)

Surgical and endoscopic options for GERD:

- Antireflux surgery performed by an experienced surgeon is recommended as an option for long-term treatment of patients with objective evidence of GERD. Those who have severe reflux esophagitis (LA grade C or D), large hiatal hernias, and/or persistent, troublesome GERD symptoms, are likely to benefit most from surgery. (Strong recommendation, moderate level of evidence; Not graded¹⁴).

- Antireflux surgery should be offered in cases of long-standing confirmed reflux and complicated GERD (e.g., LA grade C/D, peptic stricture). The indication for antireflux surgery should be evaluated if the patient cannot tolerate long-term medication (Strong consensus¹³).
- Laparoscopic fundoplication should be performed as first-line surgical therapy. The procedure is effective and has only a few complications (Strong recommendation, strong consensus¹³; Not graded¹²).
- The guidelines recommend consideration of MSA (magnetic sphincter augmentation) as an alternative to laparoscopic fundoplication for patients with regurgitation who fail medical management. (Strong recommendation, moderate level of evidence).
- The guidelines suggest consideration of Roux-en-Y gastric bypass (RYGB) as an option to treat GERD in obese patients who are candidates for this procedure and who are willing to accept its risks and requirements for lifestyle alterations. (Conditional recommendation, low level of evidence; Not graded¹²).
- In obese patients, sleeve gastrectomy and adjustable gastric banding are not recommended due to their potential to exacerbate reflux (Not graded¹⁴).
- The guidelines suggest consideration of TIF for patients with troublesome regurgitation or heartburn who do not wish to undergo antireflux surgery and who do not have severe reflux esophagitis (LA grade C or D) or hiatal hernias >2 cm. (Conditional recommendation, low level of evidence)

Lifestyle changes and non-pharmacological treatment of GERD patients

- In symptomatic GERD patients, lifestyle changes should be recommended, including weight reduction, avoiding meals within 2–3 hours of bedtime, elevating the head of the bed during sleep, and smoking/alcohol cessation (Not graded¹²; Strong recommendation, low quality of evidence⁵).
- Lifestyle changes are recommended for pregnant women with GERD symptoms. If lifestyle changes fail, antacids and sucralfate are the first choice of treatment (Not graded¹²).
- In children with regurgitation and GERD, exclusive breastfeeding should be encouraged, and its discontinuation should be avoided (Not graded²³).

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI GERD report** and aims to provide recommendations to aid in the management of gastro-esophageal reflux disease. 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 GERD. 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. Supplementary Appendix

I. Prescribing Edits

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

Table 7. Indications for Proton Pump Inhibitors

This table from the AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors summarizes the indications for PPI:¹⁹

Indications					
Definitely indicated for long-term use (>8 wk)	Conditionally indicated for long-term use	Not indicated for long-term use	Definitely indicated for acute/short-term use (≤8 wk)	Conditionally indicated for acute/short-term use	Not indicated for acute/short-term use
Barrett's esophagus Clinically significant (LA Classification grade C/D) erosive esophagitis Esophageal strictures from GERD (ie, peptic strictures) Zollinger-Ellison syndrome Eosinophilic esophagitis Gastroprotection in users of ASA/nonsteroidal anti-inflammatory drug at high risk for GI bleeding Prevention of progression of idiopathic pulmonary fibrosis	PPI-responsive endoscopy-negative reflux disease, with recurrence on PPI cessation PPI-responsive functional dyspepsia, with recurrence on PPI cessation PPI-responsive upper airway symptoms ascribed to laryngopharyngeal reflux, with recurrence on PPI cessation Refractory steatorrhea in chronic pancreatic insufficiency with enzyme replacement Secondary prevention of gastric and duodenal peptic ulcers with no concomitant antiplatelet drugs	Symptoms of nonerosive reflux disease with no sustained response to high-dose PPI therapy Functional dyspepsia with no sustained response to PPI therapy Steroid therapy in the absence of ASA/nonsteroidal anti-inflammatory drug therapy Prevention of recurrent upper GI bleeding from causes other than: Peptic ulcer disease, including gastric and duodenal erosions Erosive esophagitis	<i>Helicobacter pylori</i> eradication Stress ulcer prophylaxis for ICU patients with risk factors Uninvestigated GERD/dyspepsia Treatment of NSAID-related gastric and duodenal peptic ulcers	Initial or on-demand treatment of endoscopy-negative reflux disease Initial treatment of functional dyspepsia Uninvestigated dyspepsia Ulcer prevention after sclerotherapy or band ligation treatment of esophageal varices Prevention of rebleeding from Mallory-Weiss tears	Empiric treatment of laryngopharyngeal symptomatology Acute undifferentiated abdominal pain Acute nausea and vomiting not believed to be related to GERD/esophagitis Any isolated lower GI symptomatology

Table 8. Lifestyle Modifications for the Management of GERD

This table from the ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease 2022 represents the lifestyle modifications that alleviate the symptoms of GERD:¹⁵

Lifestyle modification	Strength of scientific evidence	Pathophysiologically conclusive?	Recommendable?
Avoid fatty meals	Equivocal	Equivocal	Yes
Avoid carbonated beverages	Moderate	Yes	Yes
Select decaffeinated beverages	Equivocal	Equivocal	Not generally
Avoid citrus	Weak	Yes	Yes, if citrus triggers symptoms
Eat smaller meals	Weak	Yes	Yes
Lose weight	Equivocal	Equivocal	Yes ^a
Avoid alcoholic beverages	Weak	Mechanisms not understood; different alcoholic beverages have different effects	Not generally
Stop smoking	Weak	Yes	Yes ^a
Avoid excessive exercise	Weak	Yes	Yes
Sleep with head elevated	Equivocal	Equivocal	Yes
Sleep on the left side	Unequivocal	Yes	Yes

^aObesity and smoking seem to be risk factors for cancer of the distal esophagus.

Appendix B. Level of Evidence Description

A. SAGES Clinical Guidelines Grading/Level of Evidence

Table 11. SAGES Clinical Guidelines Grading/Level of Evidence

Strength	Definition
Strong	Indicates high confidence that the benefits clearly outweigh the risks or burdens (or vice versa).
Conditional	Indicates that the benefits are closely balanced with risks, or uncertainty remains. Decisions may vary depending on patient circumstances or values.
Quality	Definition
High	Very confident that the true effect lies close to that of the estimate of the effect.
Moderate	Moderately confident; the true effect is likely to be close but may be substantially different.
Low	Limited confidence; the true effect may be substantially different from the estimate.
Very Low	Very little confidence in the effect estimate; the true effect is likely to be substantially different.

B. ACG Clinical Guidelines Grading/Level of Evidence

Table 12. ACG Clinical Guidelines Grading/Level of Evidence

Category	Definition
Quality of Evidence (LOE)	
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.
Strength of Recommendations (GOE)	

Strong	The desirable effects of an intervention clearly outweigh the undesirable effects, or vice versa.
Weak (Conditional)	The desirable effects of an intervention probably outweigh the undesirable effects, or vice versa, but the balance is close or uncertain.

C. DGVS Clinical Guidelines Grading/Level of Evidence

Table 13. DGVS Clinical Guidelines Grading/Level of Evidence

Category	Definition
Quality of Evidence (LOE)	
Recommendation	General advice based on the evidence.
Strong Recommendation	High confidence in the evidence supporting the recommendation.
Strength of Recommendations (GoR)	
Strong Consensus	Agreement among more than 95% of the guideline committee members.
Open Strong Consensus	Agreement among 75-95% of the guideline committee members.

D. ASGE Clinical Guidelines Grading/Level of Evidence

Table 14. ASGE Clinical Guidelines Grading/Level of Evidence

Grade	Definition
Strong	Benefits clearly outweigh risks and burden, or vice versa.
Conditional	Benefits closely balanced with risks and burden; decision may vary by context.
Level	Definition
High	High confidence that the evidence reflects the true effect; further research unlikely to change it.
Moderate	Moderate confidence in the effect estimate; further research may change the result.
Low	Limited confidence in the effect estimate; further research likely to impact the result.

Appendix C. PubMed Search

Query	Filters	Search Details	Results
((((((((((((((Gastroesophageal Reflux[MeSH Terms]) OR (Esophageal Reflux[Title/Abstract])) OR (Gastric Acid Reflux[Title/Abstract])) OR (Acid Reflux, Gastric[Title/Abstract])) OR (Reflux, Gastric Acid[Title/Abstract])) OR (Gastric Acid Reflux Disease[Title/Abstract])) OR (Gastro-Esophageal Reflux[Title/Abstract])) OR (Gastro Esophageal Reflux[Title/Abstract])) OR (Reflux, Gastro-Esophageal[Title/Abstract])) OR (Gastro-oesophageal Reflux[Title/Abstract])) OR (Gastro oesophageal Reflux[Title/Abstract])) OR (Reflux, Gastro-oesophageal[Title/Abstract])) OR (Gastroesophageal Reflux Disease[Title/Abstract])) OR (GERD[Title/Abstract])) OR (Reflux, Gastroesophageal[Title/Abstract])) OR (Gastro-Esophageal Reflux Disease[Title/Abstract])) OR (Gastro Esophageal Reflux Disease[Title/Abstract])) OR (Gastro-Esophageal Reflux Diseases[Title/Abstract])) OR (Reflux Disease, Gastro-Esophageal[Title/Abstract]))	Guideline, in the last 5 years	("gastroesophageal reflux"[MeSH Terms] OR "esophageal reflux"[Title/Abstract] OR "gastric acid reflux"[Title/Abstract] OR "acid reflux gastric"[Title/Abstract] OR "reflux gastric acid"[Title/Abstract] OR "gastric acid reflux disease"[Title/Abstract] OR "gastro esophageal reflux"[Title/Abstract] OR "gastro esophageal reflux"[Title/Abstract] OR "reflux gastro esophageal"[Title/Abstract] OR "gastro oesophageal reflux"[Title/Abstract] OR "gastro oesophageal reflux"[Title/Abstract] OR "reflux gastro oesophageal"[Title/Abstract] OR "gastroesophageal reflux disease"[Title/Abstract] OR "GERD"[Title/Abstract] OR "reflux gastroesophageal"[Title/Abstract] OR "gastro esophageal reflux disease"[Title/Abstract] OR "gastro esophageal reflux disease"[Title/Abstract] OR "gastro esophageal reflux diseases"[Title/Abstract] OR ("Reflux"[All Fields] OR "refluxant"[All Fields] OR "refluxate"[All Fields] OR "refluxates"[All Fields] OR "refluxed"[All Fields] OR "refluxers"[All Fields] OR "refluxes"[All Fields] OR	27 results

		"refluxing"[All Fields] OR "refluxive"[All Fields]) AND "disease gastro esophageal"[Title/Abstract])) AND ((y_5[Filter]) AND (guideline[Filter]))	
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Appendix D. Treatment Algorithm

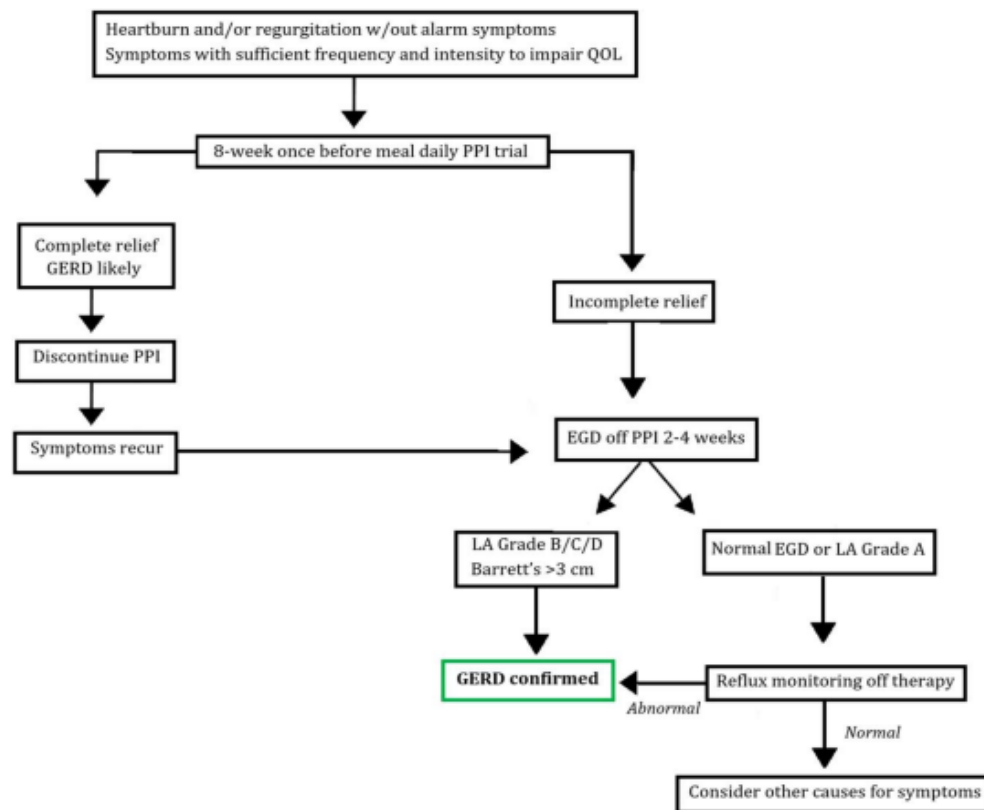


Figure 1. Diagnosis of GERD. Adapted from Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. American Journal of Gastroenterology. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538¹⁵.

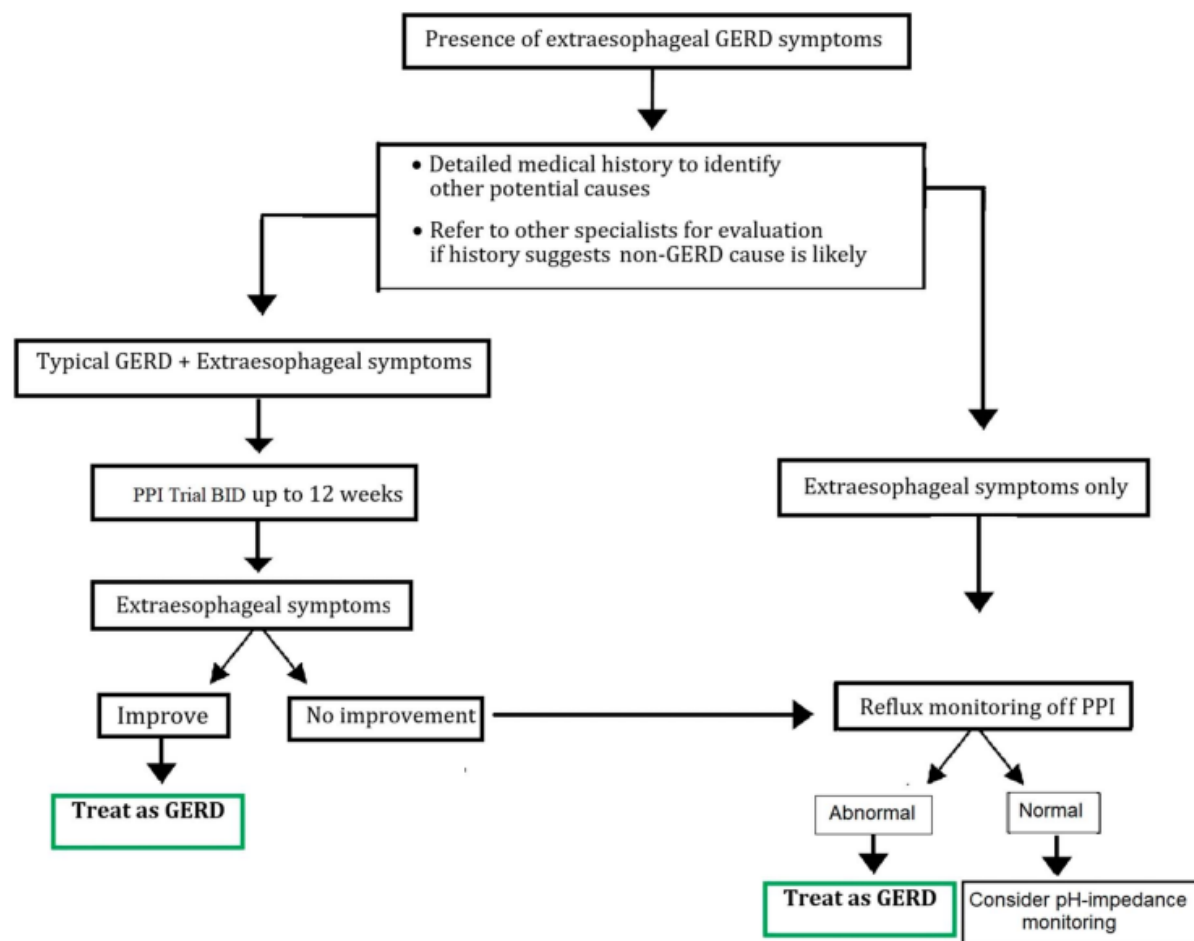


Figure 2. Diagnostic Algorithm for Extraesophageal GERD. Adapted from Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. American Journal of Gastroenterology. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538¹⁵

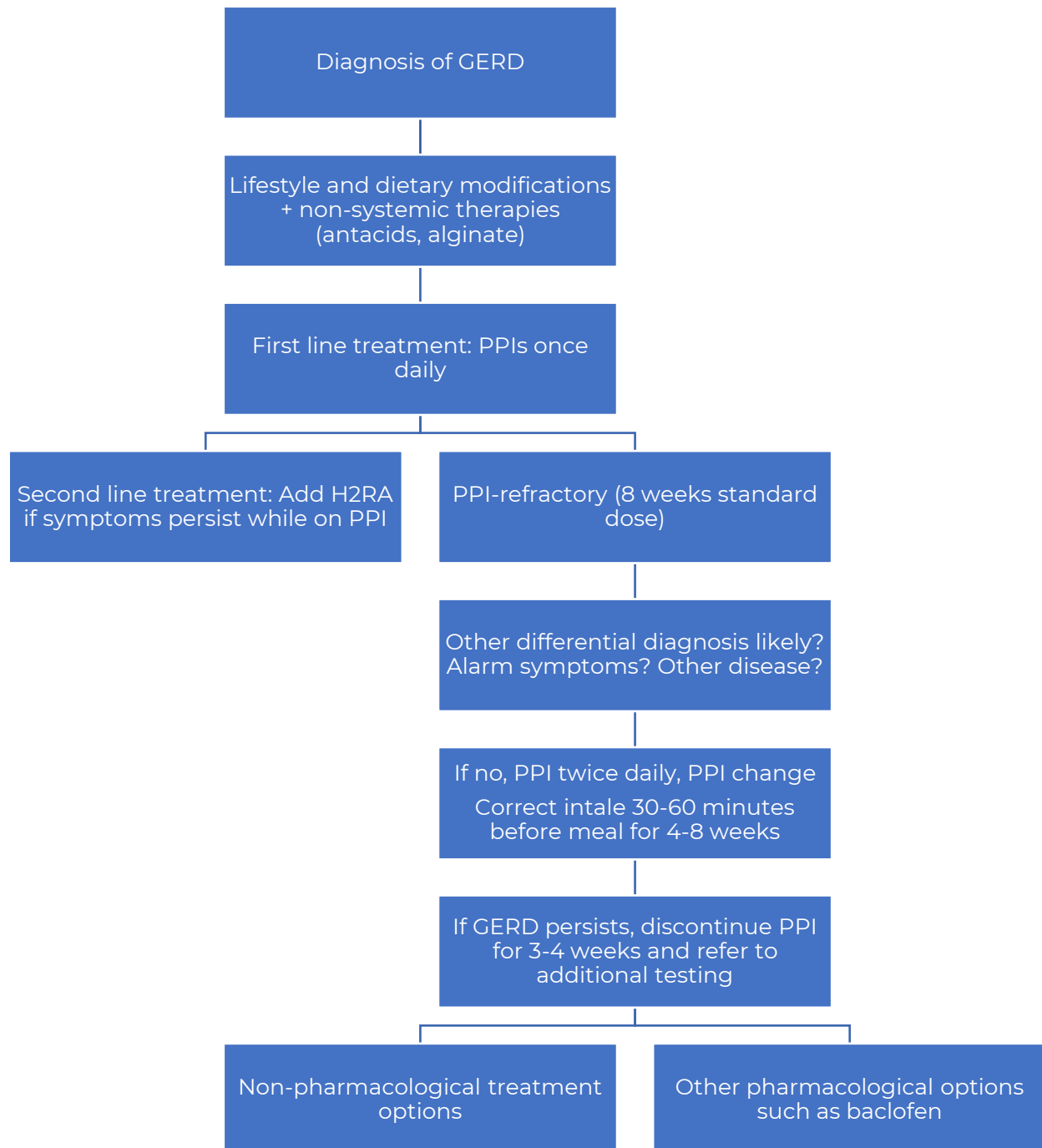


Figure 3. Treatment algorithm for the management of GERD