

TRIAGE CATEGORY: Enhanced Primary Care Pathway

H. PYLORI

Based on full review of your referral, it has been determined that **management of this patient within the Enhanced Primary Care Pathway is appropriate, without need for specialist consultation at this time.**

This clinical pathway has been developed by the Calgary Zone Primary Care Network in partnership with the Section of Gastroenterology and Alberta Health Services. These local guidelines are based on best available clinical evidence, and are practical in the primary care setting. This package includes:

1. Focused summary of H. pylori relevant to primary care
2. Summary of 2016 Canadian Association of Gastroenterology Guidelines for the treatment of *Helicobacter pylori*
3. Review of your patient's H. pylori treatment history
4. Recommended next-round H. pylori treatment regimen
5. Checklist for your in-clinic follow-up of this patient

If you would like to discuss this referral with a Gastroenterologist, call Specialist LINK available 08:00-17:00 weekdays at 403-910-2551 or toll-free 1-844-962-5465 or submit a Netcare e-Referral Advice Request to Adult Gastroenterology.

If your patient completes the Enhanced Primary Care Pathway and remains symptomatic or if your patient's status or symptoms have changed, a new referral using the QURE guidelines (included in this package) indicating 'completed care pathway' or 'new information' should be faxed to GI Central Access and Triage at 403-944-6540 for prioritized review.

Thank you.



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Section of Gastroenterology

Enhanced Primary Care Pathway: HELICOBACTER PYLORI

1. Focused summary of Hp relevant to primary care

Epidemiology. The overall prevalence of *H. pylori* (Hp) in Canada is about 20-30%, but is considerably higher in First Nations communities and in immigrants from developing countries in South America, Africa, and Asia where prevalence can be 70-90%. Infection most commonly occurs during childhood, likely by oral route. The prevalence of antibiotic resistant strains of Hp is high in certain immigrant populations.

Symptoms. Many humans are asymptomatic carriers of Hp, but those who develop significant gastroduodenitis experience dyspepsia, which is post-prandial epigastric pain or bloating, nausea, belching, early satiety, or loss of appetite. Most studies suggest that Hp does not play a role in gastro-esophageal reflux disease, and patients are understandably disappointed when their GERD does not improve after eradication of co-incidental Hp colonization.

Complications. About 5-15% of patients with Hp will develop duodenal or gastric ulcers, but this is higher in patients who chronically use nonsteroidal anti-inflammatory drugs including low-dose aspirin (e.g. for long-term management of arthritis or other pain conditions). Hp increases the risk of gastric adenocarcinoma and MALT lymphoma but overall the absolute risk of this is very low, less than 1%.

Diagnosis. The *H. pylori* stool antigen (HpSAT) is now the preferred non-invasive test for Hp in Calgary (due to equivalent accuracy, ease of access and collection for the patient, and reduced result turn-around time). The urea breath test (UBT) is now only available for limited indications. False positive results with either test are rare, but false negatives may result from recent use of antibiotics or antisecretory drugs (PPI or H₂-receptor antagonists). Patients should be off antibiotics for at least 4 weeks before the test. CLS suggests stopping PPIs 3 days before the test, but preferably this should be 2 weeks, which may be difficult for some patients who become symptomatic off PPI.

Who to Test. (1) Patients with relevant upper GI symptoms. (2) Patients with a history of peptic ulcer disease or upper GI bleed especially if contemplating use of low dose aspirin and or other antiplatelet agent. (3) Patients who have a first-degree relative with gastric cancer. (4) Hp testing is a consideration in patients who are starting long-term NSAIDs, but in such patients equal consideration should be given to concurrent use of a PPI for gastro-protection. There is no clear evidence-based guideline in Canada for testing asymptomatic individuals based on country of birth or aboriginal status.

Treatment. In 2016, the Canadian Association of Gastroenterology made significant changes to guidelines for treating Hp. Due to increased antibiotic resistance, standard triple therapy regimens (e.g. PPI-clarithromycin-amoxicillin; HpPAC™) are no longer part of first-line treatment, being replaced by 14-day quadruple therapies, as detailed below. Although resistance of Hp to metronidazole, clarithromycin, and levofloxacin is increasingly common, resistance is low to amoxicillin (0%) and tetracycline (<3%). Resistance to clarithromycin and levofloxacin is an "all or none" phenomenon, meaning that once a patient harbours a resistant strain there is no point using that antibiotic again. In contrast, resistance to metronidazole is partial, that is, it often can be overcome by leaving metronidazole as part of the next treatment. Unfortunately in most places in Canada, the exact frequency of antibiotic resistance to Hp is not known. The best guidance for treatment therefore is given by knowledge of the success rates of the different therapies in the local area where one practices.

Confirming Eradication. Patients should be retested for Hp, but no sooner than 4 weeks after completing treatment; retesting too soon risks a false negative test. Once eradicated, re-infection is rare. If Hp reappears later it likely is due to recrudescence of the original infection. Transmission to others is unlikely so it is not routinely recommended to test spouses or children of patients with Hp, unless they have pertinent symptoms.

Treatment Failure. This is often due to antibiotic resistance, but certainly intolerance or non-adherence to treatments must be explored with the patient. Recurrence likely represents recrudescence of the original infection, prompting alternative antibiotic regimens. **IMPORTANT: After treatment failure, there is no point in retrying the same regimen.**

2. Hp treatment regimens (Canadian Association of Gastroenterology 2016 Guidelines)

Triple therapy (PPI + clarithromycin + amoxicillin or metronidazole) is no longer recommended, as studies of Hp isolates in Canada suggest 25-30% are resistant to metronidazole and 15-20% are resistant to clarithromycin.

With the exception of the rifabutin-based regimen, **all treatments for Hp should be 14 days duration.**

First Round		
CLAMET Quad for <u>14 days</u> <ul style="list-style-type: none">• PPI standard dose BID• Clarithromycin 500mg BID• Amoxicillin 1000mg BID• Metronidazole 500mg BID	OR	BMT Quad for <u>14 days</u> <ul style="list-style-type: none">• PPI standard dose BID• Bismuth subsalicylate 524mg QID• Metronidazole 375mg QID• Tetracycline 500mg QID
Second Round		
<ul style="list-style-type: none">• If CLAMET Quad was used as initial treatment, then use BMT Quad for second round• If BMT Quad was used as initial treatment, then use CLAMET Quad or consider Levo-Amox		
Third Round		
Levo-Amox for <u>14 days</u> <ul style="list-style-type: none">• PPI standard dose BID• Amoxicillin 1000mg BID• Levofloxacin 250 mg BID		
Fourth Round		
Rif-Amox for <u>10 days</u> <ul style="list-style-type: none">• PPI standard dose BID• Rifabutin 150mg BID• Amoxicillin 1000mg BID	IMPORTANT: This should only be considered after failure or intolerance of the above three regimens. Rifabutin has rarely been associated with potentially serious myelotoxicity, that is, low white cell or platelet count. The pros and cons of giving fourth-line therapy should be decided on a case-by-case basis.	

Patient information sheets for each of these regimens are attached below and are available from your PCN website. These one-page information sheets list important additional information about specific Hp treatment regimens including side effects and warnings. Ideally this should be presented and discussed with your patient during an in-clinic visit.

The patient should be reminded of the **importance of completing the entire treatment exactly as prescribed.** For clarity and convenience, particularly with the Quad therapies, it may be helpful to **have the prescription bubble packed** which is free or a nominal charge at most pharmacies.

3. Review of previously tried Hp treatment(s) for patient:

Date HpSAT positive	Twice daily PPI + listed antibiotics	Duration (days)	Correctly prescribed/dispensed?
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

A = amoxicillin, B = bismuth, C = clarithromycin, L = levofloxacin, M = metronidazole, T = tetracycline, R = rifabutin

4. Suggested subsequent Hp treatment for patient:

14 day PPI + clarithromycin + amoxicillin + metronidazole **CLAMET**

14 day PPI + bismuth subsalicylate + metronidazole + tetracycline **BMT**

14 day PPI + levofloxacin + amoxicillin **Levo-Amox**

10 day PPI + rifabutin + amoxicillin **Rif-Amox**

Attached is a one-page information sheet for your patient about this regimen

5. Checklist to guide your in-clinic review of this patient after treatment of Hp

- Recheck HpSAT (off antibiotics ≥ 4 weeks; off PPI ≥ 3 days but preferably ≥ 2 weeks)
- If HpSAT remains positive, use an alternative treatment and recheck HpSAT. Refer to above treatment guidelines. If questions, please call GI Specialist Link at 403-910-2551 or toll-free 1-855-387-3151 or use a Netcare GI E-referral Advice Request.
- If HpSAT negative but persistent symptoms, follow the DYSPEPSIA enhanced primary clinical care pathway.
- If HpSAT negative but family history of gastric cancer in a first-degree relative, send in a new referral to GI triage re: screening endoscopy

IMPORTANT INFORMATION REGARDING YOUR RECENT REFERRAL

To ensure that your referral is triaged appropriately, please review this quality referral checklist as you create the referral. Free pocket sized copies of this checklist are available through Quality Referral Evolution (QuRE) at www.ahs.ca/QuRE.

PATIENT INFORMATION

Name, DOB, PHN, Address, Phone, Alternate contact, Translator required

PRIMARY CARE PROVIDER INFORMATION

Name, Phone, Fax, cc/Indicate if different from family physician

REFERRING PHYSICIAN INFORMATION

Name, Phone, Fax

TIPS

REASON FOR REFERRAL

Diagnosis, management and/or treatment
Procedure issue / care transfer

Assist with patient communication by indicating patient's preferred method of contact and if they will be unavailable (holiday, etc)

PATIENT'S CURRENT STATUS

Stable, worsening or urgent/emergent
Understanding of situation
Key symptoms and findings
Symptom onset / duration
Red flags

Don't forget that the referring physician isn't always the family physician. Keep everyone in the loop with a cc.

Make sure to express clear expectations for the consult and, when possible, outline a specific question.

FINDINGS AND/OR INVESTIGATIONS

(RELEVANT RESULTS ATTACHED)

What has been done & is available
What has been ordered & is pending

Current status is must-know clinical information that has direct impact on triage of the referral.

CURRENT & PAST MANAGEMENT

(LIST WITH OUTCOMES)

None
Unsuccessful / successful treatment(s)
Previous or concurrent consultations for this issue

Ensure you have listed all ordered tests so the receiving consultant does not unknowingly order the same tests again.

COMORBIDITIES

Medical history
Pertinent concurrent medical problems
Current & recent medications (name, dosage, PRN basis)
Allergies
Warnings & challenges

Provide information on what has been tried previously and why a consult is required.

A complete medical history can help the consultant determine the complexity and urgency of the referral.

Taking CLAMET-PPI Treatment

What is CLAMET-PPI?

- Your doctor has prescribed CLAMET-PPI treatment because you have an infection of the stomach (*H. pylori*). CLAMET-PPI treatment gets its name from the medicine in it (**cl**arithromycin, **a**moxicillin, **met**ronidazole, and a **p**roton **p**ump **i**nhibitor).

How do I take CLAMET-PPI?

- Most people take CLAMET-PPI treatment without having any problems. If you're pregnant or breastfeeding, you can't take CLAMET-PPI treatment.
- You'll need to take the medicine listed below for **14 days**. To make it easier, ask your pharmacist to put your prescriptions in a bubble pack. CLAMET-PPI treatment costs about \$160 if generic medicine is used.
- If you don't take the treatment as recommended, it will not work as well.

CLAMET-PPI Treatment		
Medicine	Dose	How Often
Clarithromycin	500 mg (take 1 capsule)	2 times a day
Amoxicillin	1000 mg (take 2 capsules)	2 times a day
Metronidazole	500 mg (take 1 tablet)	2 times a day
Proton pump inhibitor	take 1 pill	2 times a day

- **Clarithromycin** (Biaxin®): This antibiotic is often used to treat lung and ear infections, but works well to treat *H. pylori*. Common side effects include making things taste different, loose stools, and nausea.
- **Amoxicillin** (generic): This antibiotic is often used to treat lung and bladder infections, but works well against *H. pylori*. Common side effects include loose stools and a rash. If you get a rash while taking this medicine, stop taking it right away and contact your doctor. If you've ever had a reaction to penicillin, tell your doctor before you start taking this medicine.
- **Metronidazole** (Flagyl®): This antibiotic is used for many gastrointestinal infections. Common side effects include nausea, a metal taste in the mouth, and loose stools. Don't drink alcohol when you take this drug because it can cause bad side effects (e.g. low blood pressure, heart palpitations, chest pain).
- **Proton pump inhibitor**: This medicine blocks the stomach from making acid, which helps the antibiotics work better. All proton pump inhibitors work the same whether they're brand name or generic.

Do I need to know anything else about taking antibiotics?

- Antibiotics can cause bad diarrhea and may interact with some types of medicine like warfarin (Coumadin®). If you take other medicine, talk to your prescribing doctor or pharmacist before you take CLAMET-PPI.
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Taking BMT-PPI Treatment

What is BMT-PPI?

- Your doctor has prescribed BMT-PPI treatment because you have an infection of the stomach (*H. pylori*). BMT-PPI treatment gets its name from the medicine in it (**b**ismuth subsalicylate, **m**etronidazole, **t**etracycline, and a **p**roton **p**ump **i**nhibitor).

How do I take BMT-PPI?

- Most people take BMT-PPI treatment without having any problems. If you're pregnant or breastfeeding, you can't take BMT-PPI treatment.
- You'll need to take the medicine listed below for **14 days**. To make it easier, ask your pharmacist to put your prescriptions in a bubble pack. BMT-PPI treatment costs about \$95 if generic medicine is used.
- If you don't take the treatment as recommended, it will not work as well.

BMT-PPI Treatment		
Medicine	Dose	How Often
Bismuth subsalicylate (Pepto-Bismol®)	524 mg (take 2 caplets)	4 times a day
Metronidazole	375 mg (take 1½ tablets)	4 times a day
Tetracycline	500 mg (take 1 capsule)	4 times a day
Proton pump inhibitor	take 1 pill	2 times a day

- Bismuth subsalicylate** (Pepto-Bismol®): This is an over-the-counter medicine to treat indigestion, which works well to treat *H. pylori*. Common side effects include making your bowel movements a dark colour and it can also make the tongue look black—these effects go away after the medicine is stopped. Tell your doctor if you have kidney problems before you start taking this medicine.
- Metronidazole** (Flagyl®): This antibiotic is used for many gastrointestinal infections. Common side effects include nausea, a metal taste in the mouth, and loose stools. Don't drink alcohol when you take this medicine because it can cause bad side effects (e.g. low blood pressure, heart palpitations, chest pain).
- Tetracycline**: This medicine is used for lung and skin infections, but it works well to *treat H. pylori*. Most people have no side effects, but some people get nausea, vomiting, loose stools, and a rash. This medicine makes people more sensitive to UV light, so stay out of the sun while taking it.
- Proton pump inhibitor**: This medicine blocks the stomach from making acid, which helps the antibiotics work better. All proton pump inhibitors work the same whether they're brand name or generic.

Do I need to know anything else about taking antibiotics?

- Antibiotics can cause bad diarrhea and may interact with some types of medicine like warfarin (Coumadin®). If you take other medicine, talk to your prescribing doctor or pharmacist before you take BMT-PPI.

Taking LevoAmox-PPI Treatment

What is LevoAmox-PPI?

- Your doctor has prescribed LevoAmox-PPI treatment because you have an infection of the stomach (*H. pylori*). LevoAmox-PPI treatment gets its name from the medicine in it (**levofloxacin**, **amoxicillin**, and a **proton pump inhibitor**).

How do I take LevoAmox-PPI?

- Most people take LevoAmox-PPI treatment without having any problems. If you're pregnant or breastfeeding, you can't take LevoAmox-PPI treatment.
- You'll need to take the medicine listed below for **14 days**. To make it easier, ask your pharmacist to put your prescriptions in a bubble pack. LevoAmox-PPI treatment costs about \$110 if generic medicine is used.
- If you don't take the treatment as recommended, it will not work as well.

LevoAmox-PPI Treatment		
Medicine	Dose	How Often
Levofloxacin	250 mg (take 1 tablet)	2 times a day
Amoxicillin	1000 mg (take 2 capsules)	2 times a day
Proton pump inhibitor	take 1 pill	2 times a day

- **Levofloxacin** (Levaquin®): This antibiotic is often used to treat lung, bladder, sinus, and skin infections, but works well to treat *H. pylori* that hasn't responded to other treatment. Common side effects include headaches, nausea, and diarrhea. If you have liver or kidney problems, tell your doctor before you start taking this medicine. Don't take this medicine if you have an allergy to antibiotics like ciprofloxacin.
- **Amoxicillin** (generic): This antibiotic is often used to treat lung and bladder infections, but works well against *H. pylori*. Common side effects include loose stools and a rash. If you get a rash while taking this medicine, stop taking it right away and contact your doctor. If you've ever had a reaction to penicillin, tell your doctor before you start taking this medicine.
- **Proton pump inhibitor**: This medicine blocks the stomach from making acid, which helps the antibiotics work better. All proton pump inhibitors work the same whether they're brand name or generic.

Do I need to know anything else about taking antibiotics?

- Antibiotics can cause bad diarrhea and may interact with some types of medicine like warfarin (Coumadin®). If you take other medicine, talk to your prescribing doctor or pharmacist before you take LevoAmox-PPI.
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Taking RifAmox-PPI Treatment

What is RifAmox-PPI?

- Your doctor has prescribed RifAmox-PPI treatment because you have an infection of the stomach (*H. pylori*). RifAmox-PPI treatment gets its name from the medicine in it (**rif**abutin, **amox**icillin, and a **p**roton **p**ump **i**nhibitor).

How do I take RifAmox-PPI?

- Most people take RifAmox-PPI treatment without having any problems. If you're pregnant or breastfeeding, you can't take RifAmox-PPI treatment.
- You'll need to take the medicine listed below for **10 days**. To make it easier, ask your pharmacist to put your prescriptions in a bubble pack. RifAmox-PPI treatment costs about \$170 if generic medicine is used.
- If you don't take the treatment as recommended, it will not work as well.

RifAmox-PPI Treatment		
Medicine	Dose	How Often
Rifabutin	150 mg (take 1 tablet)	2 times a day
Amoxicillin	1000 mg (take 2 capsules)	2 times a day
Proton pump inhibitor	take 1 pill	2 times a day

- **Rifabutin** (Mycobutin®): This antibiotic is often used to treat tuberculosis, but works well to treat *H. pylori*. Rifabutin is expensive and it may take a few days for your drugstore to get. It causes a metal taste in the mouth and makes your urine orange or red. Side effects include headaches, nausea, diarrhea, rash, or muscle/joint pain. Rarely, people can have liver or bone marrow problems.
- **Amoxicillin** (generic): This antibiotic is often used to treat lung and bladder infections, but works well against *H. pylori*. Common side effects include loose stools and a rash. If you get a rash while taking this medicine, stop taking it right away and contact your doctor. If you've ever had a reaction to penicillin, tell your doctor before you start taking this medicine.
- **Proton pump inhibitor**: This medicine blocks the stomach from making acid, which helps the antibiotics work better. All proton pump inhibitors work the same whether they're brand name or generic.

Do I need to know anything else about taking antibiotics?

- Antibiotics can cause bad diarrhea and may interact with some types of medicine like warfarin (Coumadin®). If you take other medicine, talk to your prescribing doctor or pharmacist before you take RifAmox-PPI.
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