

CONFIRMATION: Referral Received
TRIAGE CATEGORY: Enhanced Primary Care Pathway
REFERRAL STATUS: **CLOSED**

H.PYLORI

Dear Colleague,

The above-named patient was referred to GI-CAT for further assessment of refractory *Helicobacter pylori* (Hp) infection of the stomach and relevant GI symptoms. Based on full review of your referral, it has been determined that **management of this patient within an Enhanced Primary Care Pathway is appropriate, without need for specialist consultation at this time.**

This clinical pathway has been developed by the Division of Gastroenterology in partnership with the South Island and Victoria Divisions of Family Practice. 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. Checklist to guide your in-clinic patient review
3. Links to additional resources for this specific condition
4. Clinical flow diagram with expanded detail

This referral is CLOSED.

If you would like to discuss this referral, one of our Gastroenterologists is available for phone advice via the South Island RACE program 08:00-17:00 weekdays. This service is accessible by downloading the RACEApp+ on your smart phone.

If your patient completes the Enhanced Primary Care Pathway and remains symptomatic or if your patient's status or symptoms change, a new referral indicating 'completed care pathway' or 'new information' should be faxed to 1-888-398-7091.

Thank you.



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Enhanced Primary Care Pathway: HELICOBACTER PYLORI

1. Focused summary of Hp relevant to primary care

Epidemiology. The overall prevalence of 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 gastro-duodenitis 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-incident 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 urea breath test (UBT) and stool Hp antigen test are the most commonly used non-invasive tests for Hp in Victoria. False positive results 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. The UBT costs about \$45 and takes about one hour for the patient to complete.

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 always be retested for Hp at least 4 weeks after 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. 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 Hp 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. Options for 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 UBT or Hp stool antigen (off antibiotics ≥ 4 weeks; off PPI ≥ 7 days but preferably ≥ 2 weeks)

If Hp remains positive, use an alternative treatment and recheck. Refer to above treatment guidelines. If questions, please contact GI via RACEApp+.

If Hp negative but persistent symptoms, send in a new referral with full details to GI CAT re: diagnostic endoscopy.

If Hp negative but family history of gastric cancer in a first-degree relative, send in a new referral re: screening endoscopy

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.

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 (**levo**floxacin, **amox**icillin, 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.

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.