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GUIDELINES FOR TREATMENT OF HELICOBACTER PYLORI IN ADULTS

Helicobacter pylori testing should be performed in patients with active peptic ulcer disease (PUD), a history of PUD, dyspepsia, low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma, a history of early gastric cancer endoscopic resection, chronic non-steroidal anti-inflammatory drug (NSAID) or aspirin use, unexplained iron deficiency anemia, or idiopathic thrombocytopenic purpura.

All patients who test positive for an active *H. pylori* infection should be offered treatment. Success of *H. pylori* eradication depends on choice of regimen, patient adherence, and susceptibility to antibiotics. Antibiotic susceptibility is significantly dependent on previous exposures, and clarithromycin- or fluoroquinolone- based regimens should be avoided in patients previously exposed to these agents.

Test for eradication after *H. pylori* treatment should be performed with a urea breath test, fecal antigen test, or biopsy-based test at least 4 weeks after completion of treatment and after proton pump inhibitor (PPI) is held for 2 weeks. Susceptibility testing is recommended in patients who fail primary therapy. In such patients, the MiChart order 'Helicobacter Pylori Culture and Susceptibility' should be ordered to confirm *H pylori* culture growth from a fresh gastric biopsy and if so, susceptibility testing will be performed. It typically takes 3-7 days to culture *H pylori*, and an additional 7-28 days for susceptibilities to result. If *H pylori* does not grow, confirm test of cure by performing a urea breath test or stool antigen 4 weeks or more after the end of therapy.

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Initial Therapy	Salvage Therapy	Comments
Previous antibiotic exposure should be considered when selecting a treatment regimen. Avoid regimens containing clarithromycin or levofloxacin in patients with past exposure to macrolides or fluoroquinolones, as past exposure is linked to resistance. Resistance to these agents is associated with treatment failure. Treatment duration of 14 days is preferred due to improved eradication compared to shorter treatment durations. <u>No history of macrolide exposure:</u> **Bismuth quadruple therapy** [1] OR **Concomitant therapy** - Clarithromycin 500 mg BID* - Amoxicillin 1 g BID* - Metronidazole 500 mg BID - PPI standard dose BID OR **Rifabutin triple therapy[1]** <u>History of macrolide exposure:</u> **Bismuth quadruple therapy[1]** OR **Rifabutin triple therapy[1]** <u>Preferred treatment in patients with a **verified** penicillin allergy:</u> *Patients with a reported penicillin allergy should be evaluated by the Beta-Lactam Allergy Evaluation Service (BLAES) (inpatients) or Allergy clinic (outpatients). > 90% of patients with a purported penicillin allergy are NOT allergic.* **Bismuth quadruple therapy[1]** <u>Treatment in patients who are NPO:</u> *Treatment of H pylori is never urgent, and thus intravenous therapy should almost never be considered. Consult Gastroenterology or Antimicrobial Stewardship for questions in special circumstances.*	Select a treatment regimen with different antibiotics than used in initial therapy. Treatment duration of 14 days is preferred. <u>If a clarithromycin-based regimen was used for initial therapy:</u> **Bismuth quadruple therapy**[1] OR **Rifabutin triple therapy**[1] OR **High-dose dual therapy** - Amoxicillin 1 g TID or 750 mg QID* - PPI standard or double dose TID or QID <u>If bismuth quadruple therapy was used for initial therapy:</u> **Concomitant therapy** - Clarithromycin[4] 500 mg BID* - Amoxicillin 1 g BID* - Metronidazole 500 mg BID or TID - PPI standard dose[3] BID OR **Rifabutin triple therapy**[1] OR **High-dose dual therapy** - Amoxicillin 1 g TID or 750 mg QID* - PPI standard or double dose TID or QID <u>Other option (only if no history of fluoroquinolone use):</u> **Levofloxacin triple therapy** - Levofloxacin 500 mg QD* - Amoxicillin 1 g BID* - PPI standard dose BID	- Treatment of H pylori is never urgent, and as such inpatient initiation of treatment is often unnecessary - PPI standard dose: o dexlansoprazole 30 mg o esomeprazole 20 mg o lansoprazole 30 mg o omeprazole 20 mg o pantoprazole 40 mg o rabeprazole 20 mg. - **Clarithromycin and rifabutin have significant drug-drug interaction potential, and interaction screens (e.g., using the Lexi-Comp interaction tool) must be performed before prescribing a regimen containing these agents**. Clarithromycin is a strong CYP3A4, OATP1B1/1B3, and P-glycoprotein/ABCB1 inhibitor. Rifabutin is a weak CYP2C9 and moderate CYP3A4 inducer. Significant drug-drug interactions may exist. - Doxycycline 100 mg BID substitution for tetracycline 500 mg QID in bismuth quadruple therapy has not been robustly studied in the U.S. Limited studies suggest doxycycline may be less effective than tetracycline. - Levofloxacin-based regimens are not a preferred treatment for initial therapy due to high prevalence of levofloxacin resistance. - For patients on antibiotics for a different infection, the following antibiotics are effective *in vitro* but have not been robustly studied *in vivo*: penicillins (ampicillin, piperacillin), cephalosporins (cefixime, cefuroxime, cefotaxime, ceftazidime), carbapenems (imipenem, meropenem). Treatment with a preferred regimen containing 2-3 antibiotics is recommended to increase eradication success. * Dose may need to be adjusted for renal dysfunction. See Michigan Medicine DOSING GUIDELINES

FOOTNOTE 1:

- **Bismuth quadruple therapy** is available as:
    a. Pylera branded product. 3 capsules (bismuth subcitrate 420 mg, metronidazole 375 mg, tetracycline 375 mg) QID with PPI standard dose BID (~$80/day). A generic formulation is also available (~$55/day).
    b. Component regimen: Bismuth subsalicylate (most commonly using Pepto-Bismol) 262mg QID, Metronidazole 250 mg QID or 500 mg TID, Tetracycline 500 mg QID, PPI standard dose BID
    c. Component regimen is an appropriate substitution for combination products and is preferred for inpatient use. However, treatment can almost always be deferred until the patient is discharged.
- **Rifabutin triple therapy** is available as:
    a. Talicia branded product 4 capsules (omeprazole 40 mg, amoxicillin 1000 mg, rifabutin 50 mg) every 8 hours (~$50/day)
    b. Rifabutin 300 mg QD, Amoxicillin 1 g BID*, PPI standard dose BID
    c. Given greater rifabutin intragastric exposure, and higher amoxicillin and PPI doses with Talicia, this product is preferred (see Howden reference) to the component regimen.
- For patients planned to be discharged on a combination product, outpatient coverage should be verified by emailing Pharm-Transitions-of-Care@med.umich.edu.

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