



## Therapeutic Class Review<sup>SM</sup>

### GI – metronidazole, bismuth and tetracycline (Pylera<sup>®</sup>)

September 2007

#### New Product for Review:

bismuth subcitrate potassium, metronidazole and tetracycline (Pylera<sup>®</sup>) [Axcand]

#### Dossier Provided by Manufacturer: No

#### Dossier Evaluation: N/A

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

#### Executive Summary

- Metronidazole/bismuth/tetracycline (Pylera) *in combination with* omeprazole are indicated for the treatment of patients with *Helicobacter pylori* (*H. pylori*) infection and duodenal ulcer disease (active or history of within the last 5 years) to eradicate *H. pylori*.
- Peptic ulcer disease is the cause for dyspepsia in about 10% of patients. Ninety-five percent of duodenal and 70% of gastric ulcers are associated with *H. pylori*.<sup>[11]</sup>
- Metronidazole/bismuth/tetracycline (Pylera) is a rational combination of products. The highest *H. pylori* eradication rates are achieved with the following regimens:<sup>[4]</sup>
  - A proton pump inhibitor (PPI), clarithromycin, and either amoxicillin or metronidazole for 2 weeks.
  - Ranitidine, bismuth citrate, clarithromycin, and either amoxicillin, metronidazole, or tetracycline for 2 weeks.
  - A PPI, bismuth, metronidazole, and tetracycline for 1 to 2 weeks.
- Total pill burden is 14 capsules a day: 3 Pylera QID plus 2 omeprazole 20mg BID, for a total of 10 days.
- Off-label use is unlikely.
- Medical value relative to other treatment options that exist:
  - Metronidazole/bismuth/tetracycline (Pylera) is essentially the same as bismuth subsalicylate/metronidazole/tetracycline (Helidac), but it replaces the histamine (H<sub>2</sub>) antagonist with a PPI, both of which are available generically and over the counter.
  - Metronidazole/bismuth/tetracycline (Pylera) is less expensive than bismuth subsalicylate/metronidazole/tetracycline (Helidac), and significantly less expensive than lansoprazole/amoxicillin/clarithromycin (Prevpac).
  - Metronidazole/bismuth/tetracycline (Pylera) is the only 10 day treatment course (others are a 14 day treatment course).

- Metronidazole/bismuth/tetracycline (Pylera) and bismuth subsalicylate/metronidazole/tetracycline (Helidac) are QID regimens versus the BID regimen of lansoprazole/amoxicillin/clarithromycin (Prevpac).

## Evidence

- The evidence is not reliable in drawing conclusions about the value of metronidazole/bismuth/tetracycline (Pylera).
- The evidence is not useful in drawing conclusions that metronidazole/bismuth/tetracycline (Pylera) has improved efficacy and/or safety over current formulary alternatives.
- The single trial was designed to show that it was at least as good as the combination of omeprazole/amoxicillin/clarithromycin given two times daily for 14 days.
- Metronidazole/bismuth/tetracycline (Pylera) therapy is contraindicated in patients with renal or hepatic impairment.
- No conclusions can be drawn regarding the rates of emerging resistance to with either OMBT (omeprazole/metronidazole/bismuth/tetracycline) or OAC (omeprazole/amoxicillin/ clarithromycin) due to the few numbers of patients with culture results available post treatment.<sup>1</sup>
- Safety issues are no different than the individual components. Metronidazole/bismuth/tetracycline (Pylera) should not be used by pediatric patients or pregnant women.
- FDA approval of Pylera was supported by previous findings for safety and efficacy of Helidac.<sup>1</sup>

## Decision

Metronidazole/bismuth/tetracycline (Pylera) is non-preferred/non-formulary because there is not reliable evidence of its safety and efficacy relative to existing preferred/formulary alternatives.

## Products

Drug Products	FDA approval <sup>a</sup>	Patent Expirations	Size/Qty	FDA approved indications	Usual Dose/Route/Duration	Potential Off-label Uses
Helidac bismuth, metronidazole and tetracycline	8/1996	N/A	14 day pack	In combination with a H <sub>2</sub> antagonist, for eradication of <i>H. pylori</i> , duodenal ulcer (active or history)	oral, 4 capsules QID x 14 days	-
famotidine 20mg			28		BID x 14 days	
Prevpac lansoprazole, amoxicillin, clarithromycin	12/1997	N/A	14 day pack	<i>H. pylori</i> infection, duodenal ulcer (active or 1 year history)	oral, BID x 14 days	-
Pylera bismuth, metronidazole and tetracycline	9/2006	N/A	120 caps	<i>H. pylori</i> infection, duodenal ulcer (active or 5 year history)	oral, 3 caps QID x 10 days	-
omeprazole 20mg			20		1 BID x 10 days	

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

## References

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3. Drug Facts and Comparisons. Drug Facts and Comparisons 4.0 [online]. 2006. Available from Wolters Kluwer Health, Inc. at: <http://online.factsandcomparisons.com/index.aspx?> Accessed November 16, 2006.
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11. Ford AC, Delaney BC, Forman D, Moayyedi P. Eradication therapy for peptic ulcer disease in *Helicobacter pylori* positive patients. *Cochrane Database of Systematic Reviews* 2006, Issue 2. Art. No.: CD003840. DOI: 10.1002/14651858.CD003840.pub4.
12. Biaxin<sup>®</sup> (clarithromycin) Prescribing Information. 2006. Abbott Laboratories, North Chicago, IL.
13. Amoxil<sup>®</sup> (amoxicillin) Prescribing Information. 2006. GlaxoSmithKline, Research Triangle Park, NC.