The Safety of Appropriate Use of Over-the-Counter Proton Pump Inhibitors: An Evidence-Based Review and Delphi Consensus

Supplementary material for submission to *Drugs.*

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Online Resource 2

Table 1. Results of consensus voting

1. When taken in accordance with label instructions, PPIs have not been shown to mask the symptoms of early esophageal cancer or meaningfully delay presentation. Available OTC PPIs would not be expected to differ.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
78%	22%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Very Low Agree: 100% Disagree: 0%
2. When taken in accordance with label instructions, it is unlikely that OTC PPIs produce achlorhydria.						

Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
89%	11%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	High Agree: 100% Disagree: 0%
3. When taken in accordance with label instructions, PPIs have not been shown to meaningfully delay the presentation of early gastric cancer. Available OTC PPIs would not be expected to differ.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
78%	22%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Low Agree: 100% Disagree: 0%

4. When taken in accordance with label instructions, OTC PPIs may improve symptoms of peptic ulcer or GERD but are extremely unlikely to adversely affect the natural history of the conditions. Individuals with persistent (>1 month) or recurrent symptoms after use of an OTC PPI should consult a physician.						
Agree Strongly 56%	**Agree With Reservation** 33%	**Undecided** 0%	**Disagree** 11%	**Disagree Strongly** 0%	**Strength of Recommendation** Strong Agree: 89% Disagree: 11%	**Quality of Evidence** Very Low Agree: 78% Disagree: 22%
5. Patients with upper gastrointestinal alarm features should be referred for endoscopy.						

Agree Strongly	Agree With Reservation	Undecided	Disagree	Disagree Strongly	Strength of Recommendation	Quality of Evidence
100%	0%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Low Agree: 89% Disagree: 11%
6. Baseline or routine monitoring of iron, calcium, magnesium, and vitamin B_{12} levels in those taking OTC PPIs is not necessary.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
100%	0%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Moderate Agree: 100% Disagree: 0%
7. Patients requiring repeated courses of OTC PPIs do not need baseline bone density measurement or bone density monitoring unless other clinical risk factors are present.						

Agree Strongly	Agree With Reservation	Undecided	Disagree	Disagree Strongly	Strength of Recommendation	Quality of Evidence
100%	0%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Moderate Agree: 100% Disagree: 0%
8. There are rare idiosyncratic drug reactions that may be associated with PPIs.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
78%	22%	0%	0%	0%	Strong Agree: 78% Disagree: 22%	Low Agree: 67% Disagree: 33%

9. Patients who have ascites secondary to cirrhosis should be advised to consult a physician about the slightly increased risk for spontaneous bacterial peritonitis. Although this association has been reported for only prescribed PPIs, the relative risk with OTC PPIs use has not been studied. A risk/benefit assessment for any PPI use in these patients, with close monitoring, is warranted.						
Agree Strongly 56%	**Agree With Reservation** 44%	**Undecided** 0%	**Disagree** 0%	**Disagree Strongly** 0%	**Strength of Recommendation** Strong Agree: 89% Disagree: 11%	**Quality of Evidence** Very Low Agree: 89% Disagree: 11%
10. It is extremely unlikely that OTC PPI therapy leads to an increased risk of community-acquired pneumonia.						

Agree Strongly	Agree With Reservation	Undecided	Disagree	Disagree Strongly	Strength of Recommendation	Quality of Evidence
78%	22%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Low Agree: 100% Disagree: 0%
11. Use of OTC PPIs may increase risk of infectious diarrhea.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
67%	33%	0%	0%	0%	Strong Agree: 89% Disagree: 11%	Moderate Agree: 89% Disagree: 11%
12. The use of OTC PPIS is not strongly associated with increased risk of *C difficile* infection. There is insufficient evidence to determine an associated causal risk of relapsing *C difficile* infection.						

Agree Strongly	Agree With Reservation	Undecided	Disagree	Disagree Strongly	Strength of Recommendation	Quality of Evidence
33%	67%	0%	0%	0%	Strong Agree: 78% Disagree: 22%	Moderate Agree: 89% Disagree: 11%
13. Patients taking medication, the absorption, metabolism, or effect of which may be affected significantly by PPI therapy, should be advised to consult with a healthcare professional before starting OTC PPI therapy.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
100%	0%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Very Low Agree: 100% Disagree: 0%

14. The pharmacodynamic interaction of clopidogrel with omeprazole and esomeprazole has not been shown to have clinically meaningful adverse cardiovascular effects. Individuals being treated with clopidogrel may continue using OTC PPIs.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
33%	56%	11%	0%	0%	Strong Agree: 78% Disagree: 22%	High Agree: 100% Disagree: 0%
15. It is extremely unlikely that PPIs increase risk for myocardial infarction. OTC PPIs would not be expected to differ.						
Agree Strongly	**Agree With Reservation**	**Undecided**	**Disagree**	**Disagree Strongly**	**Strength of Recommendation**	**Quality of Evidence**
89%	11%	0%	0%	0%	Strong Agree: 100% Disagree: 0%	Very Low Agree: 100% Disagree: 0%

16. There is no contraindication for the use of category B OTC PPIs for heartburn during pregnancy.						
Agree Strongly 56%	**Agree With Reservation** 44%	**Undecided** 0%	**Disagree** 0%	**Disagree Strongly** 0%	**Strength of Recommendation** Strong Agree: 78% Disagree: 22%	**Quality of Evidence** Moderate Agree: 89% Disagree: 11%
17. There is a rapid treatment response for heartburn with OTC PPIs, which begins on day 1 for many patients.						
Agree Strongly 78%	**Agree With Reservation** 22%	**Undecided** 0%	**Disagree** 0%	**Disagree Strongly** 0%	**Strength of Recommendation** Strong Agree: 89% Disagree: 11%	**Quality of Evidence** High Agree: 100% Disagree: 0%

18. As there is a rapid treatment response for heartburn-related sleep impairment with PPIs, which begins on day 1 in many patients, OTC PPIs are likely to have the same effect.						
Agree Strongly 67%	**Agree With Reservation** 33%	**Undecided** 0%	**Disagree** 0%	**Disagree Strongly** 0%	**Strength of Recommendation** Strong Agree: 89% Disagree: 11%	**Quality of Evidence** Moderate Agree: 100% Disagree: 0%

GERD gastroesophageal reflux disease, *OTC* over-the-counter, *PPIs* proton pump inhibitors