Expert peer review on application for Antiulcer medicines (ranitidine deletion and addition of parenteral omeprazole)

The conclusions of the application for ranitidine are clear and straightforward: Ranitidine (and other H2RAs) should not be deleted. PPIs are more effective than H2RAs in the management of gastro-oesophageal reflux disease (GERD) and or non-ulcer dyspepsia (NUD). However, H2RAs have advantages (some of which are particularly important for patients in developing countries): faster onset of action, no need to time administration before meals, lower cost, no fear of interaction with clopidogrel, probably safer in pregnancy. Furthermore they can be used in patients who cannot tolerate PPIs because of side effects

The statement on non-ulcer dyspepsia is probably debatable given the substantial lack of effect of any drug in improving symptoms (more than placebo) except for pyrosis/heartburn - so this comment is minor and relates to the interpretation of available evidence.

In the rest of the peer review we'll comment the request to introduce a parenteral PPI in EML.

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes No ✓ (if no, please provide reference and information)
      The application refers to esomeprazole as a reference for PPI parenteral preparation with an indication for GERD with erosive esophagitis without presenting available evidence on the benefits and risks of parenteral PPP for this indication.

   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      Available evidence shows modest benefits on certain outcomes for the treatment of GI bleeding (with no effect on survival benefit which is detrimental in some studies)

   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes No (if no, please provide reference and information)

   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
   a. Have all relevant data on safety provided
      Yes ☑ No ❌ (if no, please provide reference and information)

   b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      No data on parenteral PPI was provided

   c. Please provide any additional relevant information with reference

   d. Is the product available in several low and middle income countries?

4. Assessment of public health need
   a. Please provide the public health need for this product (1-2 sentences)

      The most important aspect from a public health perspective for gastrointestinal bleeding is the immediate access to endoscopy for stopping bleeding. The use of PPI has shown modest benefits with no beneficial effect on reducing mortality.

   b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable

      Yes, for bleeding after endoscopy is performed

5. Are there special requirements for use or training needed for safe/effective use?
   If yes, please provide details in 1-2 sentences

6. Is the proposed product registered by a stringent regulatory authority?
   Yes ☑ No

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)

Ranitidine (and other H2RAs) should not be deleted from EML.

On the basis of the present application the recommendation to the Panel is to reject the inclusion of a parenteral PPI "for gastroesophageal reflux disease (GORD) in patients with erosive reflux esophagitis and/or severe symptoms of reflux"

The inclusion of a parenteral PPI for upper gastrointestinal bleeding (not mentioned in the present application) could be discussed by the Panel though it is not supported at the moment by adequate evidence of benefits.