Submission to the Medicines Classification Committee for:

Omeprazole
(Omezol Relief 10 mg Capsules)

Response to Minutes of the 38th Meeting of the Medicines Classification Committee regarding Omeprazole 10 mg Capsules

July 2008

Sponsor: Pacific Pharmaceuticals Ltd.

Executive Summary

In July 2007 Pacific Pharmaceuticals Ltd applied to the Medicines Classification Committee (MCC) to reclassify omeprazole from a Prescription Only Medicine to a Pharmacist Only Medicine. In December 2007 the MCC recommended that there should be no change to the current prescription medicine classification of omeprazole. A response to the issues raised in the minutes of the December 2007 (38th) MCC Meeting is included on the following pages for consideration at the next (40th) MCC meeting scheduled for November 2008.

Response to MCC Queries

Proposed Indication and Dosage

Pacific Pharmaceuticals Ltd confirms that the proposed indication is for the short-term symptomatic relief of reflux-like symptoms in sufferers aged 18 years and over. The claim on the proposed pack stating that Omezol Relief was "for effective long-lasting relief from heartburn and acid reflux" has been removed. The reference to "advanced treatment" has also been removed from the proposed packaging.

Pacific Pharmaceuticals Ltd would like to propose the following more specific dosing regimen: The starting dose is two 10 mg capsules once daily and may need to be taken for three to four days to obtain symptom relief. When symptoms improve the dose can then be reduced to one 10 mg tablet daily, returning to two tablets if symptoms return. The lowest effective dose should always be used.

The revised dosing information is included on the proposed package insert and carton (Annex 1).

Pacific Pharmaceuticals Ltd proposes that the product be taken as required up to a maximum of 14 days.

Packaging

A copy of the revised carton for Omezol Relief is enclosed (Annex 1). Pacific Pharmaceuticals Ltd proposed to include a CMI in the pack and a draft version is enclosed (Annex 2).

A copy of the currently approved UK carton and package insert for Zanprol™ 10 mg Omeprazole Tablets is also enclosed for reference (Annex 3).

Duration of Treatment

Pacific Pharmaceuticals Ltd proposes that the product be taken as required up to a maximum of 14 days.

The Royal Pharmaceutical Society of Great Britain states under its practice guidance for OTC omeprazole states that symptomatic relief may be experienced after one day of treatment, increasing to a maximum effect after three to four days[1]. Patients requiring immediate symptomatic relief can take a simple antacid or antacid/alginate at the same time for the first few days of treatment if necessary.

Omeprazole has been approved as an OTC Medicine in the UK (Zanprol™) for use for up to 4 weeks since 2004 and in the US (Prilosec OTC®) for 14 days since 2003. The British Gastroenterology Society advises that it is acceptable to institute a single course of treatment with an anti-secretory agent for 2-4 weeks in such patients who have troublesome symptoms but without "alarm" symptoms. The above symptoms are easily recognised by the patient. Therefore, consumer self-diagnosis with pharmacist counseling, followed by a short-term treatment with low dose Omezol Relief in such patients would not only be acceptable but also recommended.

In addition, the Intensive Medicines Monitoring Programme reported that "Omeprazole has proved to be very safe and has the lowest adverse reaction rate (2.7 %) of any medicine monitored recently in the IMMP" [2].

One important concern is the potential masking of a more serious disorder with OTC omeprazole treatment. According to the British Society of Gastroenterology Dyspepsia Management Guidelines, the majority of patients with gastric cancer will present with characteristic symptoms (dysphagia, weight loss) and the guidelines quote a rate of less than 3% of gastric cancers occurring in those aged under 45. As Omezol Relief is only to be taken for a maximum of 14 days, such a short delay is unlikely to affect prognosis of more serious conditions. In addition, pharmacists will be trained to counsel patients and to intervene if symptoms imply a more serious condition. For further information on proposed pharmacist training, please refer to the relevant section below.

There are currently large numbers of people with dyspepsia and heartburn who self-medicate and do not seek medical advice. It could be perceived that there is a potentially large risk of prolonged use of omeprazole. However, it could be argued that a similar risk exists with the use of OTC H_2 antagonists. With the packaging clearly stating that Omezol Relief should only be used for short-term treatment of symptoms (and with Pharmacist assurance) this risk would be minimized.

Finally, while there are other products available on the market that may provide more immediate relief, omeprazole has the advantage of being able to give weeks of remission from recurrent attacks. This makes it suitable for heartburn sufferers who experience relapsing symptoms. Bardhan et al demonstrated the superior efficacy of omeprazole (compared to ranitidine) in resolving symptoms of uncomplicated gastro-oesophageal reflux disease when both were administered over short-term[3].

Overseas Experience

The MCC raised concerns about the in market potential for Omeprazole OTC questioning whether consumers would be interested in the product.

Data from markets within which Omeprazole has been launched as an OTC item point to the potential of the product.

Drug Store News, Feb 16, 2004 notes that " After a little more than three months on the market, Proctor and Gamble's Prilosec OTC rapidly is becoming the best-selling heartburn remedy tablet. The article notes that projecting out for a full year Prilosec sales would reach sales of about $250 million.

Pharmacy Times May 2004, notes that Prilosec products range 1,2 and 3 in the antacid/laxative category. The article also notes that Prilosec is the main reason that gastrointestinal products were one of the fastest growing categories in 2004

International Herald Tribune March 3, 2005 notes that demand for Prilosec OTC has exceed supply - again further indicating consumer demand for the product.

It is Pacific Pharmaceuticals Ltd position that there would be significant patient interest in the supply of Omeprazole in an OTC format.

Pharmacist Training Information

To ensure training information support is given to pharmacists, Pacific Pharmaceuticals Ltd proposes the following strategy:

1. To produce written material similar to that developed by the Royal Pharmaceutical Society of Great Britain in their practice guidance document for OTC omeprazole[1]. This would be further supported by a printed 'Patient Questionnaire & Pharmacist Notes' pad, completed by the pharmacist, when consulting with the patient. Pacific Pharmaceuticals Ltd has had success with this approach in the recent launch of Sumagran Active following the reclassification of sumatriptan 50mg x 2's. A copy of the Question & Answer material, produced for Sumagran Active, is included as Annex 5. To ensure all pharmacies received the material in a timely fashion, Pacific Pharmaceuticals Ltd would arrange delivery to every pharmacy in the country as part of the overall launch strategy.

2. Face to face and regional training would also be conducted with Pharmacists by the Pacific Pharmaceuticals Ltd sales team. The company has a team of four full time sales representatives calling regularly into 85% of all pharmacies throughout New Zealand. The material utilized would be written by the Pacific Pharmaceuticals Ltd Regulatory team and approved via the TAPS process.

3. The Pacific Regulatory team will also be available to support pharmacists who may have questions or seek information outside of that contained in the materials described in Point 1.

Gastroenterology Society Formal Opinion

To address the concern raised by the Medicines Classification Committee that a formal opinion should be sought from the NZ Society of Gastroenterologists, Pacific Pharmaceuticals Ltd has been in contact with their President Dr John Wyeth.

Dr Wyeth and the Executive Committee of the Society have responded to the effect that the Society would be very open to detailing an opinion. They have indicated, in response to Pacific's inquiry, that direct contact from the Medicines Classification Committee would be the next step to facilitate the process of a formal opinion being set down.

References

1. Royal Pharmaceutical Society of Great Britain Practice Guidance: OTC Omeprazole. 2004 (refer to Annex 4).

2. Coulter DM. Reactions to omeprazole obscured by aging process. *NZ Family Physician* 1998;25(3): 18-20.

3. Bardhan KD, Muller-Lissner S, Bigard MA, Bianchi Porro G, Ponce J, Hosie J, et al. symptomatic gastro-oesophageal reflux disease: double blind controlled study of intermittent treatment with omeprazole or ranitidine. The European Studyy Group. *BMJ* 1999;318(7182):502-7.