

**Proposal for Reclassification**

**of**

**Losec®**

**Tablets**

**Omeprazole 10 mg**

**to**

**General Sales Medicine**

**July 2013**

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**PART A**

The current classification of omeprazole in New Zealand is:-

Pharmacy Only

In divided solid dosage forms for oral use containing 20 milligrams or less with a maximum daily dose of 20 milligrams for the short-term symptomatic relief of gastric reflux-like symptoms in sufferers aged 18 years and over when sold in the manufacturer’s original pack containing not more than 28 dosage units.

Prescription

Except when specified elsewhere in this schedule.

This submission to the Medicines Classification Committee proposes changing this current classification to:-

***General Sales***

***In divided solid dosage forms for oral use containing 10 milligrams or less with a maximum daily dose of 20 milligrams for the short-term symptomatic relief of gastric reflux-like symptoms in sufferers aged 18 years and over when sold in the manufacturer’s original pack containing not more than 14 dosage units.***

Pharmacy Only

In divided solid dosage forms for oral use containing 20 milligrams or less with a maximum daily dose of 20 milligrams for the short-term symptomatic relief of gastric reflux-like symptoms in sufferers aged 18 years and over when sold in the manufacturer’s original pack containing not more than 28 dosage units, ***except for divided solid dosage forms for oral use containing 10 milligrams or less when sold in the manufacturer’s original pack containing not more than 14 dosage units.***

Prescription

Except when specified elsewhere in this schedule.

Reclassification of Losec 10 mg tablets to General Sales is considered safe and appropriate in New Zealand for the following reasons:-

***Improved consumer choice of effective treatments*** - the availability of omeprazole 10 mg as a General Sales Medicine will improve the choice of effective treatments available to consumers for self-selection at any outlet.

***Safety Profile/Toxicity*** – omeprazole has an excellent safety record, with few serious or frequent side-effects or medicinal interactions.

***New Zealand Precedent*** – treatment of reflux/heartburn is already well established in New Zealand as being suitable for consumer self-selection of treatment options at all types of retail outlets, with a number of classes of medications already available in the General Sales category.

***International Precedents*** – in the last decade omeprazole has been reclassified to an over-the-counter medicine (to General Sales or Pharmacy Medicine level) in many countries, without subsequent adverse events of any consequence.

***Encourage Selfcare*** – reclassification of omeprazole 10 mg to General Sales Medicine would empower patients to independently address their health care needs for reflux/heartburn treatments.

***Consumer Convenience/Accessability*** – omeprazole at the lowest strength is suitable to be added to range of products that can be self-selected at all retail outlets, offering consumers the opportunity to consider and compare at all points of purchase.

**A1. Name of the Medicine**

The International Non-Proprietary Name of the medicine is omeprazole.

The proprietary or brand name of the product is Losec®.

This application is specifically related to the tablet dosage form, containing omeprazole magnesium.

**A2. Name of the Company**

This submission is made by:-

Bayer New Zealand Limited

C. P. O. Box 2825

Auckland

Ph: (09) 443-3093

Contact: Mr. Tom Mayson

 Senior Brand Manager – Losec

Bayer currently markets Losec tablets 10 mg as a Pharmacy Only Medicine in New Zealand.

**A3. Dose Forms, Strengths and Pack Sizes**

As stated above, the current classification of omeprazole is:-

Pharmacy Only

In divided solid dosage forms for oral use containing 20 milligrams or less with a maximum daily dose of 20 milligrams for the short-term symptomatic relief of gastric reflux-like symptoms in sufferers aged 18 years and over when sold in the manufacturer’s original pack containing not more than 28 dosage units.

Prescription

Except when specified elsewhere in this schedule.

Bayer New Zealand Limited currently markets Losec (10 mg tablets, packs of 7 and 14 tablets) and Losec Extra (20 mg tablets, packs of 14 and 28 tablets) within the Pharmacy Only Medicine classification available.

In terms of dose form, strength and pack size, it is proposed that solid dose forms for oral use of Losec (omeprazole 10 mg) be reclassified from Pharmacy Medicine to General Sales Medicine with the pack size limited to 14 tablets for this category.

**A4. Indications**

As per the current classification of omeprazole, the appropriate indication for the compound as a Pharmacy Medicine is:-

Short-term, symptomatic relief of gastric reflux-like symptoms in sufferers aged 18 years and over.

This indication is considered reasonable and appropriate for omeprazole as an over-the-counter medicine, and the same indication is proposed for omeprazole 10 mg tablets as a General Sales Medicine.

***A4.1 Dosage Recommendation***

The current dosage instructions on the carton label for Losec 10 mg tablets approved by Medsafe (see Appendix One) are:-

Take 2 tablets once daily until symptoms improve, then reduce the dose to 1 tablet once daily. If symptoms return, the dose may be increased to 2 tablets once daily.

Use the lowest dose that controls your symptoms.

This same dosage recommendation is proposed for Losec 10 mg tablets as a General Sales Medicine.

**A5. Classification**

The current classification of omeprazole, taken from the Medsafe Web site on 5 July 2013, is:-

Omeprazole, except when specified elsewhere in this Prescription

Schedule

Omeprazole; in divided solid dosage forms for oral use Pharmacy Only

containing 20 mg or less with a maximum daily

dose of 20 mg for the short-term symptomatic

relief of gastric reflux-like symptoms in sufferers

aged 18 years and over sold in the

manufacturer’s original pack containing not more

than 28 dosage units

*The classification sought for omeprazole is:-*

***Omeprazole, except when specified elsewhere in this Prescription***

***Schedule***

***Omeprazole; in divided solid dosage forms for oral use Pharmacy Only***

***containing 20 mg or less with a maximum daily***

***dose of 20 mg for the short-term symptomatic***

***relief of gastric reflux-like symptoms in sufferers***

***aged 18 years and over sold in the manu-***

***facturer’s original pack containing not more than***

***28 dosage units, except for divided solid oral***

***dosage forms for oral use containing 10 mg or***

***less when sold in the manufacturer’s original***

***pack containing not more than 14 dosage units***

***Omeprazole; in divided solid dosage forms for oral use General Sales***

***containing 10 mg or less with a maximum daily***

***dose of 20 mg for the short-term symptomatic***

***relief of gastric reflux-like symptoms in sufferers***

***aged 18 years and over sold in the manu-***

***facturer’s original pack containing not more***

***than 14 dosage units***

Essentially, this submission supports and embraces all of the current restrictions for the non-prescription sale of omeprazole, the proposed change being that the 10 mg strength of the medicine be reclassified to General Sales Medicine.

In New Zealand omeprazole has been down-scheduled repeatedly over the last few years. Several proposals to move the substance from a Prescription Medicine to over-the-counter status were made, starting in 2001, with the switch to Pharmacist Only Medicine finally being approved for the 10 mg strength in 2009 and the 20 mg strength in 2010. A pack size increase to 28 tablets/capsules was allowed in 2012. Initially, New Zealand was relatively late compared to many other countries in switching the substance but the changes made in the last 4 years have changed the situation, and the New Zealand classification of omeprazole is now generally aligned with that in other countries (see below).

***A5.1 Classification Status in Other Countries***

Over the last fifteen years there has been a world-wide trend towards removing restrictions on the sale of proton pump inhibitor medicines, in recognition of their favourable efficacy and safety profiles. The table below lists the movement of omeprazole from prescription medicine to OTC medicine in various countries, and provides information on the nature of the OTC status in countries of interest i.e. those with regulatory agencies that Medsafe considers recognisable.

**Switch Status of Omeprazole Oral Presentations**

|  |  |  |
| --- | --- | --- |
| **Country** | **Current Classification** | **Year of Switch from Prescription** |
| Sweden | Omeprazole 10 mg, 20 mg – classification equivalent to Pharmacy Only Medicine | April 2000 |
| United States of America | Omeprazole 20 mg – classification equivalent to General Sales Medicine (available in all stores, with or without pharmacist presence) | June 2003 |
| Mexico | Omeprazole 10 mg, 20 mg – classification equivalent to General Sales Medicine | June 2003 |
| United Kingdom | Omeprazole 10 mg, max. pack size 28 tablets/capsules, max. treatment period 4 weeks – classification equivalent to Pharmacy Only Medicine.***A proposal for omeprazole 10 mg, max. pack size 28 tablets/capsules, max. treatment period 2 weeks to become a General Sales Medicine is currently being assessed in the UK – see Section B4.*** | January 2004 |
| China | Omeprazole 10 mg | December 2004 |
| Argentina |  | 2005 |
| Croatia | Omeprazole 10 mg | March 2005 |
| Norway | Omeprazole 10 mg | May 2006 |
| Denmark | Omeprazole 10 mg | December 2006 |
| Estonia, Latvia, Lithuania, Czech republic | Omeprazole 10 mg | 2007 |
| Portugal | Omeprazole 10 mg | 2008 |
| Netherlands | Omeprazole 10 mg – classification equivalent to Pharmacy Only Medicine Medicine  | 2008 |
| Germany | Omeprazole 20 mg, max. pack size 14 tablets/capsules - classification equivalent to Pharmacy Only Medicine. | August 2009 |
| Spain | Omeprazole 10 mg, max. treatment period 4 weeks. | 2003 |
| France | Omeprazole 20 mg, max. pack size 14 tablets/capsules - classification equivalent to Pharmacy Only Medicine. | May 2010 |
| Australia | Omeprazole 20 mg – S3 (equivalent to Pharmacist Only or Restricted Medicine) | September 2010. |

Table adapted from AESGP/WSMI publications http://www.aesgp.eu status 5 July 2013 and data on file.

Cleary, since the turn of this century there has been a world-wide trend towards reducing restriction on the availability of omeprazole. This trend has embraced an OTC classification that favours consumer self-selection of the medicine anddoes not require the direct involvement of a pharmacist in each and every sale i.e. in most countries omeprazole has an OTC status equivalent to Pharmacy Medicine or less.

Furthermore, many markets have several years of experience with omeprazole as an OTC medicine. Of particular note are the United States with 10 years’ experience and the United Kingdom with 9 years. Neither of these two populous countries have reported concerns with the OTC availability of omeprazole, demonstrating that consumers can safely and effectively self-select omeprazole for the treatment of reflux-like symptoms.

**A6. Extent of Usage**

It is well-known that patient exposure to omeprazole as a prescription medicine has been extensive. In recent years the same has become true for the medicine in the over-the-counter market. Prilosec (omeprazole) OTC was first approved for marketing in the United States on 20 June 2003 for the treatment of frequent heartburn in patients aged 18 years and older. From its introduction as an OTC product until 2007, around 144.7 million courses of treatment had been sold, each course being a 14 day regimen of 1 tablet per day. More recently the medicine has been sold without prescription in many other countries, and this exposure continues to increase.

In New Zealand, Losec 10 mg tablets have been marketed as a Pharmacist Only Medicine since August 2009, and Losec Extra 20 mg tablets have been marketed as a Pharmacist Only Medicine since October 2010. Both strengths of the product were reclassified to Pharmacy Medicine in February 2011. Sales volumes of these products ex-pharmacy over the last 3 years were:-

 **MAT►19/06/11 MAT►17/06/12 MAT►16/06/13**

Losec Extra 20mg 14’s 14,540 45,180 44,930

Losec Extra 20mg 28’s 0 0 7,320

Losec 10mg 14’s 23,140 15,220 13,590

Losec 10mg 7’s 16,390 16,990 16,240

Bayer has received four adverse event reports for Losec over this period, and none for Losec Extra. There were no adverse events in 2011, 3 in 2012 (allergic rash, lack of efficacy and increase in serum clozapine level) and one in 2013 (nose bleed).

Market research has shown that consumers tend to treat their reflux-like symptoms on an as-needed basis. Nonetheless, assuming that each pack represents a course of treatment apart from the 28 pack which represents two course of treatment, the rates of adverse event reporting are extremely low being conservatively estimated at less than 0.005% per patient exposure.

**A7. Labelling**

See Appendix One for the currently approved labelling (7 tablet pack) for Losec 10 mg tablets. These labels meet all of the requirements for omeprazole 10 mg as a Pharmacy Only Medicine, and were submitted to Medsafe on 22 November 2012.

Virtually identical packs are envisaged for Losec 10 mg packs as a General Sales Medicine, apart from the necessary removal of the classification statement.

The pack insert would be a copy of the proposed Consumer Medicine Information provided in Appendix Two.

**A8. Proposed Warnings**

Medsafe requires the following warnings to be applied to proton pump inhibitors sold as over-the-counter medicines with any classification (Label Statements Database as of 8 July 2013):-

|  |  |
| --- | --- |
| **Proton pump inhibitors**Includes:* [Lansoprazole](http://www.medsafe.govt.nz/regulatory/labelling.asp#Lansoprazole)
* [Omeprazole](http://www.medsafe.govt.nz/regulatory/labelling.asp#Omeprazole)
* [Pantoprazole](http://www.medsafe.govt.nz/regulatory/labelling.asp#Pantoprazole)
 | * Do not use if you are experiencing weight loss, persistent regurgitation of food or vomiting, difficulty swallowing or symptoms of gastro-intestinal bleeding, except on medical advice.
* This product is for temporary use only. [or] For short term use only.
* Do not use this medicine for any purpose other than that specified on the pack, except on doctor's advice.
* Do not use if you are pregnant except on the advice of a healthcare professional.
* Consult a doctor if symptoms/condition persist(s), worsens or recur.
* Consult a doctor if new or additional symptoms occur.
 |

Bayer considers these requirements reasonable and appropriate for omeprazole, and that they apply would equally appropriately to omeprazole 10 mg tablets as a General Sales Medicine. Note that in the proposed pack insert some of these statements have been elaborated on – for example, the symptoms of gastro-intestinal bleeding are explained. This additional information is considered valuable to the consumer, and Bayer recommends that for the product as a General Sales Medicine this additional information should be added to the carton label.

Apart from the point above, additional labelling requirements are not considered necessary for the product as a General Sales Medicine.

**A9. Other Products**

In addition to the Losec 10 mg tablets that are the subject of this submission, there are a small number of other omeprazole products registered to be sold and classified as available in the New Zealand market as Pharmacy Only Medicines at the time of this submission. These are:-

|  |  |  |
| --- | --- | --- |
| **Brand Name** | **Strength and Pack Size** | **Sponsor Company** |
| Losec Extra | Tablets 20mg | Bayer New Zealand Limited |
| Dr. Reddy’s Omeprazole Modified Release Capsule | Capsule 10 mg | Dr Reddy’s New Zealand Limited |
| Dr. Reddy’s Omeprazole Modified Release Capsule | Capsule 20 mg | Dr Reddy’s New Zealand Limited |

The Dr. Reddy’s 10 mg capsule presentation above would be affected by the proposed reclassification of omeprazole 10 mg to General Sales Medicine.

**PART B**

This proposal to reclassify omeprazole 10 mg capsules or tablets to General Sale Medicine, including the restrictions as outlined in Part A, is based on and essentially similar to the current conditions for omeprazole 10 mg and 20 mg as Pharmacy Medicines. Reclassification of Losec 10 mg tablets to a General Sale Medicine offers:-

***Improved Consumer Choice of Effective Treatments*** - some consumers have troublesome heartburn that is not adequately relieved by antacids, antacid /alginate mixtures or H2-receptor antagonists. Omeprazole 10 mg as a General Sale Medicine will improve access to effective treatment, and will make available the recommended treatment for reflux and heartburn for self-selection in all retail outlets.

***Suitable Safety Profile*** – omeprazole has an excellent safety record, with few serious or frequent side-effects. Omeprazole’s safety record is comparable to that of ranitidine, which is already available as a General Sales Medicine at a low strength for similar indications.

***Parity with Similar Treatments (New Zealand Precedent)*** – treatment of reflux/heartburn is already well established in New Zealand as being suitable for consumer self-selection of treatment options at all types of retail outlet, with both ranitidine and a full range of antacids and antacid/alginate mixtures being available as general sale medicines.

***Parity with International Precedents*** – in the last fifteen or so years omeprazole has been reclassified to an over-the-counter medicine in many countries, effectively sold as a General Sales or Pharmacy Medicine. International experience to date has endorsed such classification, as the availability of omeprazole to consumers has been relatively incident-free. No regulators have reviewed the availability of omeprazole as an OTC medicine due to increased adverse events.

***Encouragement for Selfcare*** – reclassification of omeprazole 10 mg to General Sales Medicine would empower patients to further address their health care needs for reflux/heartburn treatments.

***Consumer Convenience*** – generally, consumers seeking a reflux/heartburn treatment can self-select a product from the shelf in a pharmacy or supermarket. Bayer wishes to add omeprazole to the range of products that can be self-selected in all retail outlets, offering consumer’s the ability to consider and compare all options available at the point of purchase, and potentially reducing cost. Increased consumer involvement in product choice is like to encourage compliance.

Furthermore, a large proportion of people suffering from reflux-type symptoms more than once a week currently only purchase their medication from supermarket-type outlets, mainly because they perceive their condition is not serious enough to warrant a solution restricted to pharmacies. Reclassifying Losec 10 mg tablets to General Sales Medicine would place this recognised first-line treatment in the type of outlet where these consumers expect to purchase their medication, and so has the potential to introduce a significant number of heartburn/reflux sufferers to a new and superior treatment option.

Many of the usual considerations taken into account for reclassification of a medicine, such as the suitability of the indication, ease of self-diagnosis, possibility of resistance, etc. have already been resolved for omeprazole or have been resolved for heartburn/reflux medications at the General Sales level. Consequently they are not discussed further in this submission.

Reclassification of Losec 10 mg tablets to General Sales Medicine has the potential to offer consumers improved choice and convenience with little increase in the risk of unwanted side effects, medicinal interactions or masking of serious disease. It would offer consumers the opportunity to directly access best practice medication for the treatment of reflux and heartburn at all retail locations.

Risk to benefit analysis favours the proposed reclassification.

1. ***Efficacy of Losec 10 mg Tablets***

The efficacy of omeprazole has been studied extensively, and reported to the Medicines Classification Committee in previous submissions. The efficacy of the compound is without question. As such, a summary is considered sufficient for the purposes of this submission.

A recent (2006) meta-analysis conducted by the Cochrane Collaboration1 summarised the results of 31 randomised controlled trials focussing on the symptomatic outcome after short-term treatment for Gastro-Oesophageal Reflux Disease (GORD) using proton pump inhibitors, H2-receptor antagonists or prokinetic agents. The studies in the meta-analysis were those where the participants could be classed in the empirical treatment group (no endoscopy used in treatment allocation) or in the endoscopy negative reflux disease group (ENRD, no endoscopic signs of erosive oesophagitis). Thirty-one trials (9457 participants) were included: fifteen in the empirical treatment group, twelve in the ENRD group and four in both. In empirical treatment of GORD, the relative risk (RR) for heartburn remission (the primary efficacy variable) in placebo-controlled trials for proton pump inhibitors was 0.37 (two trials, 95% confidence interval (CI) 0.32 to 0.44), for H2-antagonists 0.77 (two trials, 95% CI 0.60 to 0.99) and for prokinetics 0.86 (one trial, 95% CI 0.73 to 1.01).

In a direct comparison proton pump inhibitors were more effective than H2-antagonists (seven trials, RR 0.66, 95% CI 0.60 to 0.73) and prokinetics (two trials, RR 0.53, 95% CI 0.32 to 0.87). According to this data, proton pump inhibitors are more effective than H2-antagonists in relieving heartburn in patients with GORD who are treated empirically. Analysis confirmed that this was also true for those with ENRD, although the magnitude of benefit is greater for those treated empirically.

The current United Kingdom NHS Clinical Knowledge Summary (CKS, formerly Prodigy guideline)2 and NICE guidelines3 for dyspepsia now recommend that empirical treatment with a proton pump inhibitor should be the first line treatment in patients with typical dyspepsia without alarm symptoms. When symptoms resolve, the lowest dose should be used to maintain patients symptom free. The New Zealand Guidelines Group Best Practice Guidelines default to those of the British Medical Journal as recommended in the United Kingdom. This recommendation is also reflected in the New Zealand Guidelines Group – Management of Dyspepsia and Heartburn4. Thus, the recommendation above applies equally in New Zealand.

More recently Holtmann et al.23 developed guidance on the use of over-the-counter proton pump inhibitors. They noted that:-

* Sufferers taking OTC omeprazole use it responsibly and take it as directed. Patients generally seek the advice of a doctor when symptoms are persistent.
* Based on experience with H2-antagonsists switching from prescription to self-medication, the number of doctor visits does not decrease because of over-the-counter availability. This is likely to be true for proton pump inhibitors switching from prescription to OTC status in New Zealand also, and the proposed change from Pharmacy Medicine to General Sales for the 10 mg presentation is considered unlikely to affect this variable.
* PPI’s are more effective than H2-antagonists
* Misuse in the form of continuous administration is only of concern in the presence of alarm symptoms. The proposed warnings regarding alarm signals and continuous use are considered appropriate to protect the consumer from misuse.

The group concluded that “Effective self-management of GERD with……omeprazole could lead to lasting freedom from symptoms and improved quality of life for GERD sufferers”. The findings of this group are considered of particular interest because of their geographic diversity, with representation from Australia, France, Germany and London.

The availability of omeprazole 10 mg as a General Sales Medicine will allow consumers convenient, direct and broad access to the recognized best, recommended first-line treatment for heartburn and reflux.

1. ***Safety Profile***

Omeprazole has a broad therapeutic window and the safety profile for the approved over-the-counter indications is both well established and satisfactory. The safety and tolerability of omeprazole when self-administered is demonstrated by its record of safe use in the pharmacy environment, both in New Zealand and in many other countries since 20035.

* 1. ***Ability to Mask Serious Disease***

In the event that there is incorrect self-diagnosis, the patient would not unduly aggravate the condition as the label instructs the patient to seek medical advice if symptoms persist for more than 14 days. This reflects a balance between dosing for long enough to achieve an effect and avoiding the risk of masking or delaying diagnosis and treatment of a more serious condition. This balance has already been accepted by MCC for omeprazole 10 mg and 20 mg as Pharmacy Only Medicines, and is considered to apply equally well to the proposed General Sales Medicine classification for Losec 10 mg tablets. Holtmann et al.23 concluded that patient’s seeks advice when they have persistent complaints, initial empirical treatment would only result in a short delay and this delay is not considered significant in the prognosis of an advanced neoplasm. They also concluded that generally PPI use did not increase the risk of infectious disorders.

***2.2 Potential for Misuse or Abuse***

Misuse has not been observed with omeprazole during more than 20 years of sale and supply6. Furthermore, omeprazole has no psychotropic or narcotic characteristics. There are no reports of abusive use of omeprazole as an addictive substance or intoxicant. This very low potential for misuse or abuse has already been recognized for omeprazole in New Zealand, and applies equally well to the proposed General Sales Medicine classification.

***2.3 Adverse Effects***

According to several comparative studies, the profile of adverse effects during short-term omeprazole therapy (for between 2 and 12 weeks) does not differ significantly from H2-antagonists or from placebo regarding either severity or frequency6,7.

Adverse events (AEs) that may occur with use of 10 mg or 20 mg omeprazole as a single daily dose are mainly mild and reversible. More serious reactions occur rarely or very rarely. The most common adverse events involve the gastrointestinal tract (such as abdominal pain, diarrhoea, constipation, flatulence, nausea and vomiting) or appear as non-specific symptoms such as headache. The occurrence of adverse reactions does not show any dose-dependent increase. Dose adaptation is not required with daily doses of up to 20 mg in patients with diminished liver function.

Interstitial nephritis is a very rare, but serious, side effect of omeprazole. The current pack insert for Losec has the following warning statement:-

**See your doctor if:**

* you experience fever, nausea, a generally unwell feeling, tiredness, blood in the urine or weight loss. These are symptoms of interstitial nephritis, a rare side effect of omeprazole.

With several years of international OTC experience with omeprazole, interstitial nephritis has not emerged as a cause for concern, sufficient to consider up-scheduling, in any market. Naturally, this warning would be retained in the pack insert for Losec 10 mg as a General Sales Medicine.

Recent concerns have arisen regarding hypomagnesaemia. Deficiency of magnesium causes weakness, muscle cramps, [cardiac arrhythmia](http://en.wikipedia.org/wiki/Cardiac_arrhythmia), increased irritability of the [nervous system](http://en.wikipedia.org/wiki/Nervous_system) with tremors, [athetosis](http://en.wikipedia.org/wiki/Athetosis), jerking, [nystagmus](http://en.wikipedia.org/wiki/Pathologic_nystagmus) and an extensor [plantar reflex](http://en.wikipedia.org/wiki/Plantar_reflex). In addition, there may be confusion, disorientation, [hallucinations](http://en.wikipedia.org/wiki/Hallucinations), [depression](http://en.wikipedia.org/wiki/Depression_%28mood%29), epileptic [fits](http://en.wikipedia.org/wiki/Convulsion), [hypertension](http://en.wikipedia.org/wiki/Hypertension), [tachycardia](http://en.wikipedia.org/wiki/Tachycardia) and [tetany](http://en.wikipedia.org/wiki/Tetany_%28medical_sign%29).

The current pack insert states:-

**Tell your doctor if you notice any of the following:**

* skin rash
* muscle pain, cramping or weakness
* dizziness
* "pins and needles"
* changes in sleep patterns, restlessness
* mood changes or confusion
* increase in breast size (males)
* fever
* increased bruising

 **These side effects are less common but can be serious and may need medical attention.**

Hypomagesaemia causes a range of symptoms that are difficult to fully describe to the consumer. The list of symptoms above is considered to adequately include the possibility of hypomagnesaemia, which is recognised as an effect of long-term use and is highly unlikely at OTC dosages providing directions are followed by the consumer. This list is retained in the proposed pack insert for Losec 10 mg as a General Sales Medicine.

***2.4 Medicinal Interactions***

Although the absorption of some medicines might be altered due to decreased intragastric acidity caused by omeprazole, clinically relevant adverse drug reactions (ADRs) based on interactions have seldom been observed with omeprazole. Of especial importance, there are no reports of interactions between omeprazole and other substances used for self-medication, such as antacids or analgesics.

Dose adjustment may be required for some prescription medicines, when combined with omeprazole, in some circumstances. In such cases, however, the patient and the drug therapy is already being monitored by a physician. All relevant interactions are listed in the patient information leaflet, and patients who are taking these medications will be advised they should first consult with either their pharmacist or doctor before taking omeprazole.

The potential for drug/drug interactions with omeprazole may be grouped as follows:

1. *Based on gastric pH effects:* The higher stomach pH with omeprazole treatment may interfere with the absorption of some drugs (nelfinavir, atazanavir, ketoconazole, itraconazole) while potentially increasing the bioavailability of others (e.g. digoxin).
2. *Based on metabolic effects:* Omeprazole is, to a major extent, metabolised in the liver via the cytochrome P450 isoenzyme CYP2C19. It is also, in therapeutic doses, an inhibitor of CYP2C19 and therefore has the potential to interact with drugs handled by the same enzyme systems:
* Omeprazole may delay the elimination of certain drugs and increase their plasma levels (e.g. digoxin, R-warfarin, other Vitamin K antagonists, diazepam, phenytoin)
* Omeprazole may decrease the efficacy of some drugs that serve as prodrugs and are activated by the CYP 2C19 system (e.g. clopidogrel).
* Some drugs may increase levels of omeprazole through inhibition of CYP2C19 or CYP 3A4 (clarithomycin, voriconazole)
* Drugs that induce liver enzymes may decrease levels of omeprazole (rifampicin)
1. Unknown mechanisms (tacrolimus, saquinavir plasma levels may be increased when co-administered with omeprazole).

Empirically, interactions that increase or decrease plasma levels of omeprazole are unlikely to produce adverse events due to direct toxicity. Omeprazole may compromise the efficacy of some co-administered drugs by interference with absorption or through effects on metabolism. Interactions that raise the levels of co-administered drugs have been the focus of particular attention in surveys of prescription use, and data presented to the FDA confirms that such interactions are reassuringly rare.

A summary of adverse events and drug interactions occurring during therapy with proton pump inhibitors – which were reported to the Food and Drug Administration – was published by Labenz and co-workers8 in 2003. The study involved a search of the Food and Drug Administration’s database for adverse events and drug interactions with omeprazole, lansoprazole or pantoprazole as the primary or secondary suspect drug. An estimate of the amount of drug dispensed during the adverse event collection period (from US drug launch) was obtained from the International Medical Statistics health database. Of the suspected drug interactions recorded, vitamin K antagonist interactions, although rare, were the most common. The frequency of vitamin K antagonist interactions was 0.09 per million packages for omeprazole and 0.11 per million packages for lansoprazole and pantoprazole respectively. Interactions with benzodiazepines or phenytoin were even rarer, being reported in less than 10 patients treated with each proton pump inhibitor.

Clearly, the incidence of drug interactions over all dosage regimes (including prescription) is exceptionally low, and is likely to be lower for the low-dose short-term therapy associated with over-the-counter use of omeprazole. Nonetheless, the following statement is currently included in the pack insert for Losec 10 mg, and is proposed to be maintained for the product as a General Sales Medicine:-

**Before taking Losec, you should seek extra advice if you are taking any other medicines, including any you have bought without a prescription from a pharmacy, supermarket or health food shop.**

***3. New Zealand Precedent***

***3.1 Ranitidine***

Treatment of reflux and heartburn is well-established in New Zealand as being suitable for consumer self-care. A large range of antacids and antacid/alginate mixtures have been available as general sales medicines for many years. Over the last 10 – 15 years more effective medicines such as H2 antagonists and proton pump inhibitors have become available over the counter as pharmacist only, pharmacy or general sales medicines.

When considering reclassification of omeprazole 10 mg to General Sales Medicine, the most appropriate compound for comparison is ranitidine, which is indicated for the same symptoms and has been the subject of progressive down-scheduling in New Zealand.

The current classification of ranitidine in New Zealand is:-

***Ranitidine, except when specified elsewhere in this Prescription***

***schedule; except in medicines containing 150 milligrams or less per dose unit when sold in the manufacturer's original pack containing not more than 7 days' supply***

***Ranitidine; in medicines for the symptomatic relief of Pharmacy Only***

***heartburn, dyspepsia and hyperacidity or to be used on the recommendation of a registered medical practitioner when sold in the manufacturer's original pack containing not more than 14 days' supply; except in medicines containing 150 milligrams or less per dose unit when are sold in the manufacturer's original pack containing not more than 7 days' supply***

***Ranitidine; in medicines containing 150 mg or less per General Sales***

***dose unit when sold in the manufacturer's original pack containing not more than 7 days' supply***

Generally the Pharmacy Medicine strength is 300 mg ranitidine per dose form.

The Medicines Classification Committee recommended that ranitidine be reclassified from restricted medicine to pharmacy-only medicine when it fulfilled the requirements for sale as an OTC medicine as specified in Volume 1 of the New Zealand Regulatory Guidelines for Medicines at its 23rd meeting on 25 May 2000. Ranitidine was again considered by the Committee at the 37th meeting on 14 December 2007, resulting in ranitidine becoming a general sales medicine when in packs containing 7 days’ supply or less and in tablets or capsules containing not more than 150 milligrams.

New Zealand has almost 13 years’ experience with ranitidine for the treatment of heartburn and dyspepsia as a Pharmacy Medicine, and five years’ experience as a general sales medicine for the lower strength. From 2000, consumers have demonstrated themselves well able to self-diagnose and treat these conditions safely and effectively without the input of a pharmacist at every sale, to the point where the Medicines Classification Committee was willing to entirely remove the input of a pharmacist in some instances seven years later.

***3.1.1 Required Warnings***

The Label Statements Database requires the following warnings for ranitidine, taken from the Medsafe Web site on 24 July 2013:-

| **Medicine/ Group/Class** | **Conditions** | **Statements or requirements** |
| --- | --- | --- |
| **H2 antagonists**Includes:* [Cimetidine](http://www.medsafe.govt.nz/regulatory/labelling.asp#Cimetidine)
* [Famotidine](http://www.medsafe.govt.nz/regulatory/labelling.asp#Famotidine)
* [Nizatidine](http://www.medsafe.govt.nz/regulatory/labelling.asp#Nizatidine)
* [Ranitidine](http://www.medsafe.govt.nz/regulatory/labelling.asp#Ranitidine)\*
 | When sold as a Pharmacy-only Medicine | * Do not use this medicine for any purpose other than that specified on the pack, except on doctor's advice.
* Do not use with aspirin except on doctor's advice.
* Do not use with [other] anti-inflammatory medicines except on doctor's advice.
* Consult a doctor if symptoms/condition persist(s), worsens or recur.
* Consult a doctor if symptoms/condition recur[s] within 2 weeks of completing the treatment.
* Consult a doctor if new or additional symptoms occur.
 |
| If the warning statements are included on a package insert instead of the label | * Read the enclosed package insert before starting to use this product.
 |
| **Ranitidine** | When sold as a General Sale Medicine | * Do not use this medicine for any purpose other than that specified on the pack, except on doctor's advice.
* Do not use with aspirin except on doctor's advice.
* Do not use with [other] anti-inflammatory medicines except on doctor's advice.
* Consult a doctor if symptoms/condition persist(s), worsens or recur.
* Consult a doctor if symptoms/condition recur[s] within 2 weeks of completing the treatment.
* Consult a doctor if new or additional symptoms occur.
 |

Compare with the required warnings for omeprazole, as per Section A8 (similar warnings are highlighted in the same colour):-

|  |  |
| --- | --- |
| **Proton pump inhibitors**Includes:* [Lansoprazole](http://www.medsafe.govt.nz/regulatory/labelling.asp#Lansoprazole)
* [Omeprazole](http://www.medsafe.govt.nz/regulatory/labelling.asp#Omeprazole)
* [Pantoprazole](http://www.medsafe.govt.nz/regulatory/labelling.asp#Pantoprazole)
 | * Do not use if you are experiencing weight loss, persistent regurgitation of food or vomiting, difficulty swallowing or symptoms of gastro-intestinal bleeding, except on medical advice.
* This product is for temporary use only. [or] For short term use only.
* Do not use this medicine for any purpose other than that specified on the pack, except on doctor's advice.
* Do not use if you are pregnant except on the advice of a healthcare professional.
* Consult a doctor if symptoms/condition persist(s), worsens or recur.
* Consult a doctor if new or additional symptoms occur.
 |

Clearly, while the H2-antagonist warnings have more emphasis on interactions and the proton pump inhibitors have more emphasis on alarm signals and pregnancy, the warnings required for both classes of compound are relatively similar. Note that there are no additional warnings required for ranitidine as a General Sales Medicine over and above those required when it is sold as a Pharmacy Medicine. It is appropriate that a similar situation should apply to omeprazole as proposed in Section A8, with no additional warnings proposed for the Losec 10 mg as a General Sales Medicine.

***3.1.2 Comparative Efficacy and Safety***

Omeprazole (up to 20 mg per day) compares well with ranitidine 150 mg or 300 mg in terms of efficacy and safety. In a 4-week comparison11, omeprazole was more effective than ranitidine at 150 mg twice daily. On treatment with omeprazole, patients described a statistically significantly more marked decrease in symptoms, irrespective of dosage. Sixty-one percent and 49% of patients were asymptomatic on treatment with omeprazole 20 mg and 10 mg, respectively, compared to 40% on ranitidine at high dosage. Before treatment 61%, 62% and 58% of patients described their heartburn as moderate and 9%, 13% and 13% as severe; after treatment with omeprazole 20 mg and 10 mg or ranitidine the proportions were only 10%, 13% and 18% (moderate) and 1%, 2% and 2% (severe).

During intermittent treatment over a 12-month period, omeprazole 20 mg and 10 mg daily were again superior to ranitidine 150 mg twice daily, 55% and 40% of patients achieving freedom from symptoms after only 2 weeks, compared to 26% on ranitidine12. The further course of follow-up did not differ between the treatment groups. Half of all singly treated patients remained symptom-free in the follow-up period, regardless of the chosen medication. On the other hand, 27% of patients on ranitidine and 22% on omeprazole required long-term treatment with a PPI to achieve freedom from symptoms. Patients already asymptomatic after 2 rather than 4 weeks were less likely to require further treatment. Adequate symptom control after a 14-day course – the maximum treatment duration claimed in the present application for OTC use – was therefore rated as a strong prognostic factor for treatment success.

Superior improvement in quality of life for patients with heartburn and acid-related symptoms has also been demonstrated in comparison with ranitidine. After 14 days of use in patients with moderate or severe heartburn, omeprazole, at dosages of both 20 mg and 10 mg daily, was able to improve quality of life, as measured by the Psychological General Well-Being (PGWB) index, to a significantly greater extent than ranitidine 150 mg twice daily13. Similar results were obtained by Festen et al.14, who used the surrogate parameter Gastrointestinal Symptom Rating Scale (GSRS) to study the effect on quality of life. Compared to ranitidine 300 mg twice daily, quality of life again improved to a significantly greater extent on omeprazole 20 mg once daily.

Armstrong et al.15 showed in 2005 that the mean time to complete symptom relief was only 3 days on omeprazole 20 mg, but 8 days on treatment with ranitidine at a dosage of 150 mg twice daily. The distinct time advantage is attributable to the sustained effect of omeprazole on heartburn (> 24 hours) and to the resultant non-recurrence of symptoms within this period. This is particularly true after omeprazole reaches its maximum pharmacological efficacy after 3 to 5 days. This example clearly shows how important sustainability of effect and the associated duration of freedom from symptoms are in assessing efficacy.

This is of particular interest in the OTC field because marked reduction of acid suppression, consistent with habituation, has been observed during repeated administration of H2-antagonsists for 14 days. pH metry in healthy volunteers showed comparable effects on acid suppression after the first dose of omeprazole 40 mg and ranitidine 300 mg. On repeated administration of omeprazole the acid-reducing effect increased to a maximum and thereafter remained consistently high throughout the 14-day treatment period. On ranitidine 300 mg, however, only half the initial effect was observable on days 7 and 1416. This explains the patient dissatisfaction reported after prolonged treatment with H2-antagonsists.

These results demonstrate the superior efficacy, both immediate and sustained, of omeprazole compared to ranitidtine. Proton pump inhibitors are recognized as “best practice” first-line treatment of reflux and heartburn without alarm symptoms, and therefore omeprazole should be available to consumers on the same basis as other treatments such as ranitidine, unless there are compelling reasons for not doing so.

Omeprazole and H2-antagonsists have similar tolerability profiles during short-term use. A review article summarises data on more than 19,000 patients from clinical studies, most of them comparative studies with ranitidine. The side effects of omeprazole and H2-antagonsists occurred at incidences of the same order of magnitude and displayed similar profiles. During short-term omeprazole use, the analysis likewise showed no differences in the severity and nature of symptoms compared to the side effects of placebo17,18. Similar results emerged from a meta-analysis of 1057 patients conducted by Bamberg et al.19. The very similar side effect profiles of omeprazole and ranitidine suggest these two medicines merit the same classification.

At therapeutic doses, ranitidine has little or no influence on the effect of drugs activated by the hepatic cytochrome P450-dependent mono-oxygenase system (e.g. diazepam, warfarin, propranolol). As with omeprazole, however, interactions such as elevated plasma levels of phenytoin or an increase in the bioavailability of midazolam have been reported with ranitidine in isolated cases20. By raising intragastric pH, H2-antagonsists – like proton pump inhibitors – can modify the uptake of drugs, such as itraconazole, ketoconazole or quinolones, whose absorption depends on gastric acidity. With ranitidine, unlike omeprazole, dose adjustment may be required in renal impairment as the daily dose is recommended not to exceed 150 mg in patients with severe renal impairment. Close monitoring of prothrombin time is recommended for concurrent treatment with ranitidine and warfarin (Zantac Data Sheet) – an interaction between omeprazole and warfarin is also recognized, although a need for close monitoring is not perceived (Losec tablets Data Sheet).

Omeprazole interacts with antiretrovirals and concomitant use is not recommended. However, patients on antiretroviral drugs are under the care of a specialist physician and likely to be intensively monitored.

Omeprazole and ranitidine appear relatively similar in terms of medicine-medicine interactions. Of prime importance is that neither medicine interacts with other over-the-counter medicines, and so a medicinal interaction occurring in a patient not under medical supervision is highly unlikely. Both medicines exhibit some interaction with prescription medicines, but these are relatively rare and although sometimes different are of similar severity. The most prescribed prescription medicine affected appears be warfarin (as demonstrated in the USA, see section 2.4) and both omeprazole and ranitidine are affected.

Both omeprazole and ranitidine can be used in pregnancy, although omeprazole has a specific pregnancy warning required on the labeling. However, both products tend to take a conservative approach for over-the-counter availability, recommending that the advice of a doctor be taken before using the product during pregnancy or breastfeeding.

Omeprazole is characterised by marked overall superiority to H2-antagonsists during short-term use for the treatment of heartburn and acid-related symptoms due to its greater efficacy, while being similarly well tolerated. Since patients experience any symptom recurrence that necessitates renewed medication as a clear quality of life deficit, the primary goal of improving quality of life can be achieved particularly well by taking a long-acting proton pump inhibitor such as omeprazole. While omeprazole appears to have a greater interaction potential than ranitidine, most of the interactions described are common to both medicines. Most of these are, moreover, purely pharmacokinetic in nature, with no particular clinical relevance. Caution with use during pregnancy and lactation is recommended for both medicines.

The discussion above demonstrates that omeprazole and ranitidine are relatively similar medicines – overall, omeprazole offers superior effectiveness but with slightly more interaction potential and a warning against use in pregnancy. On all other parameters the two medicines are equivalent. With five years of experience with ranitidine as a General Sales Medicine, the Medicines Classification Committee can be confident that consumers successfully manage the use of such medicines without supervision. Losec 10 mg tablets constitute a suitable parallel to ranitidine 150 mg tablets, and are considered just as suitable to be classified General Sales Medicine.

***3.2 Antacids/Alginates***

Antacids and antacid/alginate combinations have been available as General Sales Medicines for the treatment of heartburn and acid regurgitation for many years. They are mainly sold through supermarkets.

In terms of value, the heartburn/regurgitation treatment market is worth approximately $12 million and is roughly equally split between pharmacies and supermarkets21. However, the products available in supermarkets are generally less expensive and it is thought that a much larger proportion of sufferers source their treatments from supermarkets. It appears a majority of heartburn/acid regurgitation sufferers that treat themselves currently select their treatments without the potential for input from a healthcare professional.

Pouchain et al.24 compared the short-term efficacy of omeprazole and an antacid/alginate combination (Gaviscon) over a maximum 14 day treatment period. They found that the mean time to onset of the first 24 hour heartburn-free period after initial dosing was 2.0 (± 2.2) days for Gaviscon and 2.0 (± 2.3) days for omeprazole (p = 0.93). The mean number of heartburn-free days by day 7 was significantly greater in the omeprazole group: 3.7 ± 2.3 days vs. 3.1 ± 2.1 (p = 0.02). On day 7, overall quality of pain relief was slightly in favour of omeprazole (p = 0.049). There was no significant difference in the reduction in pain intensity between groups by day 7 (p = 0.11) or day 14 (p = 0.08). Tolerance and safety were good and comparable in both groups. While the trial was primarily designed to demonstrate the non-inferiority of Gaviscon, it is apparent from the results that omeprazole is an equivalent or superior medicine on all variables measured. The authors concluded that Gaviscon was non-inferior to omeprazole 20 mg/day. However, the trial made no allowances for the different treatment regimes (four times per day for Gavison vs. once a day for omeprazole) and did not discuss the likely effects of these different regimes in practice on compliance and subsequent efficacy, which almost certainly would favour the omeprazole outcomes.

Tran et al.25 found, using a meta-analysis of trials conducted between 1972 and 2005, that compared to placebo response, the relative benefit increase for H2-antagonists was up to 41%, for alginate/antacid combinations up to 60% and for antacids alone up to 11%. This suggests that antacid/alginate combinations are at least as good as, and possibly better than, H2-antagonists.

Manabe et al.26 found that complete resolution of heartburn for at least 7 consecutive days by the end of a 4 week treatment period was significantly more common in a group treated for NERD with omeprazole and sodium alginate (56.7%) that in a group treated with omeprazole alone (25.7%). However, overall efficacy for heartburn was not significantly different between the two groups. The authors concluded that omeprazole combined with sodium alginate was better than omeprazole alone. The authors did not discuss compliance with the treatment regime or the practical implications of the sodium alginate therapy, which required dosing four times a day, versus the convenience of once-a-day therapy with omeprazole.

In summary, the results discussed above suggest that while there may be some question regarding the efficacy of antacids alone, the efficacy of antacid/alginate mixtures and H2-antogonists is established. Thus, consumers in New Zealand sourcing their treatments for reflux-like symptoms within the supermarket environment already have access to efficacious medicines. However, proton pump inhibitors are recognized as the first-line treatment for people suffering more than once a week (but not every day) – in the absence of serious safety concerns, it is appropriate that a medicine such as Losec 10 mg should also be available at outlets where over 50% of heartburn/regurgitation sufferers currently source their medication.

***4. International Precedents***

Please refer to Section A5.1 for a complete listing of the overseas classification status for omeprazole. It can be seen that in all major reference countries except Canada, omeprazole 10 mg or 20 mg has now been switched to an over-the-counter medicine. Furthermore, in all countries except Australia omeprazole 10 mg or 20 mg is equivalent to a classification in New Zealand of Pharmacy Medicine or General Sales Medicine.

Currently a proposal to reclassify omeprazole 10 mg to General Sales Medicine is being considered in the United Kingdom. The proposal has been through a first assessment, and a request for further information received and responded to – relevant documentation is provided as Reference 27, and all documentation is available on request. The proposed General Sales Medicine CMI/pack insert has been reviewed and compared with the questions posed by the MHRA, and is considered to adequately address the points raised. A further evaluation outcome is expected to be received from MHRA in August 2013, and the Medicines Classification Committee will be kept informed of further developments on this proposal as they become available.

In summary, all major European countries and the United States have assessed omeprazole as being suitable for consumer self-selection. Such international confidence in this medicine suggests the same situation would be appropriate for the New Zealand public. A classification of General Sales Medicine for omeprazole 10 mg would offer New Zealander’s convenient access to a recognized ‘best practice’ medicine for first line treatment of reflux and heartburn.

***5. Encouraging Self-Care***

Today there is a world-wide trend encouraging consumers towards self-care when possible, promoting personal responsibility for the symptomatic treatment of short-term conditions with an aim to reducing health care expenditure for both the consumer and the Government. Reclassification of omeprazole 10 mg to General Sales Medicine would empower patients to address their treatment needs for reflux or heartburn by making the “best practice” first-line treatment readily available at the retail outlets where currently more than 50% of sufferers purchase their treatments. The demonstrated superior efficacy of omeprazole, when compared to H2-antagonists, promotes consumer satisfaction with the treatment and adds significantly to their quality of life.

While it is true that consumers can currently access omeprazole 10 mg relatively readily as a Pharmacy Medicine, this classification does raise barriers to access in that pharmacies are not part of normal shopping activities for many people and as such require a particular visit to be made. For those consumers currently purchasing through supermarkets, market research21 suggests that they expect to find suitable medication within this environment. Frequently they believe their symptoms are not serious enough to warrant deviation from normal shopping practices even though quality of life may be considerably affected.

Furthermore, with a common and easily identified condition such as reflux or heartburn consumers more often than not have previous experience with their symptoms and have established behaviour patterns in dealing with them. Reclassification of Losec 10 mg to General Sales Medicine would allow this recognised first-line treatment to be offered to appropriate consumers who currently access medication from supermarkets without requiring them to change their normal behaviours towards the problem. Thus, the proposed reclassification offers the opportunity to promote a high standard of self-care by making available first-line medication to people suffering symptoms more than once a week (but not every day) that only or mainly purchase their medications from a supermarket.

### *6. Consumer Convenience/Accessability*

The efficacy and safety of omeprazole in the treatment of reflux symptoms (heartburn and acid regurgitation) is well established. The 10 mg tablets offer the flexibility to take either two tablets (2 x 10 mg) or one tablet (10 mg), in order to maintain the treatment at the lowest possible effective dose. The 10 mg strength is the most appropriate presentation of omeprazole for reclassification to General Sales Medicine because:-

* It is the lowest strength of omeprazole available and so intuitively represents the safest option to offer to the consumer
* It is the only strength that allows maintenance of treatment at the lowest possible dose i.e. offers the possibility of dosing at 10 mg per day.

In New Zealand omeprazole 10 mg has been available over-the-counter as a Pharmacist Only Medicine since 2009. However, in other countries it has been available, effectively as a Pharmacy Medicine, for much longer - in the UK, the 10 mg tablet form has been licensed Pharmacy (‘P’) at a dose of 10 – 20 mg since 2004. Wider availability in New Zealand, through reclassification to General Sales Medicine, would be convenient to the purchaser with respect to offering greater choice and improved efficacy in the treatment of common upper gastrointestinal symptoms.

The current package carton and leaflet clearly directs the purchaser to determine whether the product is suitable for their condition and to seek medical advice if symptoms persist, recur or change. These warnings would remain unchanged for Losec 10 mg as a General Sales Medicine.

Consumers have demonstrated themselves well able to use omeprazole safely and effectively. A German pharmacy-based observational study investigating the use of an antacid for self‑medication in more than 4,000 patients demonstrated that the symptoms “heartburn and acid regurgitation” were responsibly managed. The patients used the study product correctly, i.e. in accordance with the indications and dosage instructions22. In a study by Fendrick et al.9, patients with heartburn distinguished reliably between sporadic and frequent heartburn in selecting appropriate medication. Accordingly, patients’ ability to identify their symptoms as heartburn and acid regurgitation is generally rated as excellent.

After the introduction of omeprazole as an over-the-counter product in the USA, an observational trial performed there demonstrated that 97% of patients taking omeprazole for heartburn followed the recommendations of the package insert and that 86% of patients not free from symptoms after 14 days consulted a physician for further diagnosis and therapy9. Only 5% of subjects continued to take omeprazole for more than two weeks, whereby 85% of them consulted a doctor. Self-medication beyond the prescribed period of two weeks without any medical supervision was observed in only 1% of patients. In the choice of omeprazole for treating dyspepsia, 81% of patients fulfilled all criteria for a correct selection of the substance; every single criteria was met by 90% to 100% of subjects. Only 9.5% of patients did not pay heed to contraindications (in the sense of primary symptoms requiring clarification) initially, and none of these patients continued the dosage for more than two weeks. On the other hand, around 65% of patients went to see a doctor before, during or after taking the test medication. In the case of 10%, this was their first visit in connection with dyspepsia.

This “actual use” study demonstrates that the majority of patients who fail to respond to treatment consult a physician, who can then institute further diagnostic and therapeutic measures. The possible delay of at most 14 days is not clinically relevant for the subsequent course, with regard to either progression of the underlying condition or a delay in diagnosis caused by the patient’s own perception of the “triviality” of symptoms. The information given in the package leaflet, as shown by Fendrick et al., can also raise patients’ awareness of warning symptoms and thus prompt patients who might not otherwise have sought medical attention for their symptoms to consult a physician.

Clearly, especially when taking into account that in the USA little medical consultation and advice is available from drug store personnel, consumers can responsibly use omeprazole for self-medication without the direct involvement of a pharmacy. Furthermore, it appears that less restrictive availability of omeprazole has some potential to send patients that have not already done so to their doctors for advice.

Over-the-counter experience with omeprazole in the United Kingdom appears to have been similar. McCaig et al.10 investigated early experiences with over the counter omeprazole, surveying pharmacists approximately 6 months after the product became available without prescription (essentially a Pharmacy Medicine). They found that only 3.5% of pharmacists had refused sales on the basis that omeprazole was inappropriate for the presenting condition or due to a potential drug interaction. Given the early switch in the United Kingdom (from an international perspective), and the short time between switch and the survey, this low rate of sales refusal appears likely to be a worst case scenario and suggests that inappropriate consumer selection of omeprazole is likely to be very low.

Cost is a further barrier to consumers, as margins within pharmacies tend to be higher than those at the retail outlets that can be accessed by General Sales Medicines.

Overall the risk of misuse of omeprazole is low6, and the product has a well-established safety profile in terms of patient exposure5. The significant post marketing experience available for omeprazole as a non-prescription medicine strongly suggests that it can be safely used by consumers. World-wide clinical and post-marketing experience indicates that no significant additional safety concerns resulting from reclassification from Pharmacy Medicine to General Sales Medicine are to be expected. Taking all of these considerations into account, the current barriers to access for Losec 10 mg appear not to be warranted, and the product should be classified equivalent to other comparable treatments such as ranitidine 150 mg.

**APPENDICES**

***Appendix One***

Current labelling for Losec 10 mg (7 tablet pack) as a Pharmacy Medicine.

***Appendix Two***

Proposed Consumer Medicine Information for Losec 10 mg as a General Sales Medicine.

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