Public Assessment Report

Pharmacy to General Sales List Reclassification

Omeprazole 20mg Gastro-Resistant Tablets

Omeprazole (20mg)

PL 14017/0277 – 0022

DEXCEL PHARMA LIMITED

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The Medicines and Healthcare products Regulatory Agency (MHRA) is the UK Government agency responsible for regulating medicines and medical devices. We continually review the safety of medicines and vaccines in the UK, and inform healthcare professionals and the public of the latest updates through several means, including public reclassification reports. Suspected side effects to any drug or vaccine can be reported to MHRA by both healthcare professionals and members of the public via the Yellow Card Scheme (https://yellowcard.mhra.gov.uk/).

Alternative format versions of this report are available on request from reclassification@mhra.gov.uk

1. Background on deciding where medicines are available

The role of MHRA

MHRA regulates medicines and medical devices in the UK, on behalf of the UK Licensing Authority. This means that MHRA decides whether medicines are available:

- on prescription only - 'prescription only medicine' (POM)
- bought from pharmacies - 'pharmacy medicine' (P)
- bought from other shops - 'general sales list medicine' (GSL)

What is re-classification of a medicine?

Making a change on where a medicine is available is called 're-classification'. This is sometimes referred to as 'switching'. To decide on this change, MHRA may:

- take advice from the Commission on Human Medicines and its Expert Advisory Groups[1]
- take advice from a group ('stakeholder group') of health professionals and representatives of people affected by the classification change
- run a public consultation

To be reclassified from P to GSL, a medicine must be a medicine which can, with reasonable safety, be sold or supplied otherwise than by, or under the supervision of a pharmacist. "Reasonable safety" has been defined as: "where the hazard to health, the risk of misuse, or the need to take special precautions in handling is small, and where wider sale would be a convenience to the purchaser."

These conditions are set out in the Human Medicines Regulations 2012, regulation 62(5).

What evidence is needed?

A company or organisation can ask MHRA for a medicine to be available as a pharmacy medicine or a general sale medicine. To do this, they need to get together evidence to show that the medicine

a) is likely to be used appropriately, and

b) with relatively little danger to the public.

This evidence needs to focus on the risk to the public. This includes evidence on the possible abuse or misuse of the medicine. The evidence may include:

- clinical studies
- evidence showing acceptable level of side effects
- advice of experts
- views of relevant health professionals and their professional bodies
- views of relevant public associations and individuals with an interest in the medicine under consideration.

[1] The Commission on Human Medicines (CHM) is an advisory non-departmental public body, sponsored by the Department of Health. The CHM advises ministers on the safety, efficacy and quality of medicines. The CHM is supported in its work by Expert Advisory Groups (EAGs), covering various areas of medicine. The CHM's views are sought on reclassifications when more complex or new reclassifications of medicines are being proposed.

Who makes the final decision?

The final decision on whether to approve a change is made by the MHRA, on behalf of the UK Licensing Authority.

2. About Omeprazole 20mg Gastro-Resistant Tablets

Omeprazole 20mg Gastro-Resistant Tablets is a medicine to be taken by mouth for the short-term (up to 14 days) treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults.

The full name of the medicine is Omeprazole 20mg Gastro-Resistant Tablets. In this document, we will call it 'Omeprazole Tablets'.

The Medicines and Healthcare Products Regulatory Agency (MHRA) considers this product sufficiently safe to be sold on general sale. This report outlines the evidence that the MHRA reviewed and which led to the decision to approve the application.

What is in Omeprazole Tablets?

Each tablet of the product contains 20mg of omeprazole.

What are Omeprazole Tablets used for?

Omeprazole belongs to a group of medicines called proton pump inhibitors. They work by reducing the amount of acid that the stomach produces. Omeprazole Tablets are used for the short-term treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults. Reflux is the backflow of acid from the stomach into the gullet "foodpipe", which may become inflamed and painful. This may cause symptoms such as a painful burning sensation in the chest rising up to the throat (heartburn) and a sour taste in the mouth (acid regurgitation).

Pharmacy (P) medicines can be supplied without prescription only from pharmacies, by or under the supervision of a pharmacist. General Sales List (GSL) medicines can be sold or supplied in retail outlets other than pharmacies (such as shops and supermarkets).

Omeprazole Tablets (product licence[2] [PL] 14017/0277) have been available as a P medicine in the UK market since January 2015 for the treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults in pack sizes of 7 and 14.

The treatment of reflux symptoms such as heartburn and acid reflux in the GSL setting is very common with antacids, alginates and H_2-receptor antagonists all available as GSL medicines. These all work in a different way to Omeprazole Tablets.

However, a product that is very similar to Omeprazole Tablets, which is called esomeprazole 20mg tablets has been available as a GSL medicine for the short-term treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults since 2015. Esomeprazole is also a proton pump inhibitor which is chemically similar to omeprazole and so they both work in the body in the same sort of way.

[2] By law, before a medicine can be placed on the market, it must be given a marketing authorisation (product licence) by the MHRA.

Who has made the proposal?
The licence holder[3], Dexcel Pharma Limited, applied to make Omeprazole Tablets available as a General Sales List medicine for sale through general retail outlets.

3. Proposed Terms of Reclassification

What are the details of this change?

Omeprazole Tablets will be made available through general retail outlets with the following terms of reclassification:

a) For oral use in the form of tablets
b) For the short-term treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults
c) Maximum strength: 20mg
d) Maximum dose: 20 mg
e) Maximum daily dose: 20mg
f) Maximum duration of treatment: 14 days
g) Maximum pack size: 14 tablets

4. How the application was assessed

Under the provisions of The Human Medicines Regulations 2012, regulation 62(5), General Sales List is appropriate for medicines that can, with reasonable safety, be sold or supplied by someone other than a pharmacist. The term “with reasonable safety” has been defined as: “where the hazard to health, the risk of misuse, or the need to take special precautions in handling is small and where wider sale would be a convenience to the purchaser."

Assessment of suitability for General Sales List availability

The MHRA assessed the application against the General Sales List criterion, as stated in the paragraph above.

Hazard to health

Safety Profile

The safety and efficacy[4] of omeprazole for the treatment of reflux symptoms is well established.

Based on the post-marketing experience[5] between October 2000 to April 2017, there has been approximately 196,258,216 patient-days use of Omeprazole Tablets available as both a POM and a P product in the UK. There has been approximately 8,833,726,542 patient-days use worldwide which includes all strengths of Omeprazole Tablets (10, 20 and 40mg).

[3] A licence holder or marketing authorisation holder is the company with legal authorisation to make the medicine available to patients
[4] How well a medicine works
[5] Post-marketing experience estimates how many people have taken a medicine and how many side effects have been reported after it has been released onto the market.

Adverse events

During the same period, a total of 3564 adverse events were reported with the use of Omeprazole Tablets over the counter worldwide: 3461 (97.1%) were non-serious and 103 (2.9%) cases were serious. This includes the different strengths of Omeprazole Tablets as the availability of medicines over the counter vary across the world.

The number of adverse events reported compared to the patient exposure data is relatively low. The most common adverse events associated with omeprazole are headache, abdominal (stomach) pain, constipation, diarrhoea, flatulence (wind) and nausea (feeling sick)/vomiting (being sick). The majority of these events are mild, non-serious and self-limiting in nature.

As esomeprazole works in the body in the same sort of way as omeprazole, it has a similar safety profile. There have been no additional safety concerns for esomeprazole since its' availability as a GSL medicine.

Overall, the safety profile of omeprazole is considered acceptable for GSL availability.

Drug Interactions

The summary of product characteristics[6] includes the interaction of Omeprazole Tablets with several medicines, none of which are commonly used with Omeprazole Tablets. If a patient is on any of the medicines that does interact with Omeprazole Tablets, patients are alerted to the interaction on the label and patient information leaflet (PIL)[7].

It is considered that the interaction profile is acceptable for GSL availability of the product which is intended for a short duration of use and supplied in a small pack.

Risk of Misuse

The MHRA considers that there is no reason to believe that there is a higher risk of misuse for Omeprazole Tablets compared to esomeprazole that has already been available in the UK as a GSL medicine since 2015. There is no evidence to suggest that omeprazole is misused to obtain an effect other than treatment of acid reflux. No reports have been received regarding intentional misuse of esomeprazole since its availability as a GSL medicine. The same would be expected for omeprazole so therefore, the risk of intentional misuse is considered to be low.

Self-diagnosis

Esomeprazole for the treatment of the exact same indication has been available as a GSL medicine since 2015. Antacids, alginates and H2-receptor antagonists have all been available as GSL medicines for the treatment of acid reflux symptoms for even longer. Therefore, a patient's ability to self-diagnose acid reflux has already been established.

Risk of misdiagnosis or delayed diagnosis of a more serious condition

Instructions about who should not use the product and warnings and precautions for when using it, including the symptoms which could indicate an underlying serious condition, are on the label and PIL. The maximum duration of use has been limited to 14 days, which has been emphasised clearly on the product information. This maximum duration of treatment is

[6] SmPC stands for Summary of Product Characteristics. The SmPC is a legal document describing a medicine's properties and how it can be used. SmPCs are available online via the MHRA.

[7] The label and leaflet (patient information leaflet) provide information to patients about the medicine, including information about how to use it.

considered safe enough for users to self-treat their condition without masking any underlying serious conditions or delaying the amount of time it takes for them to seek further advice from a healthcare professional. This is consistent with the supply of esomeprazole as a GSL medicine.

Pack Size

The 7 and 14 pack sizes are consistent with the dosage and duration of use for the GSL conditions of supply. The maximum pack size minimises the amount of time before a patient with a more serious condition would seek help.

Special Precautions in Handling

There are no special precautions required in handling.

Wider sale would be a convenience

The treatment of acid reflux is a well-established GSL indication within the UK environment. Consumers are used to buying indigestion remedies on self-selection in a general retail outlet. The MHRA accepts that the wider availability of omeprazole would be beneficial to patients as it would allow access to another proton pump inhibitor in the GSL setting.

5. Further details on the application

Risk Management Plan

The application contained a risk management plan (RMP). RMPs contain information on a medicine's safety profile and one or more of the following:

- How any risks identified in the safety profile will be prevented or minimised in patients
- Plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine
- Risk factors for side effects
- Measuring the effectiveness of measures taken to prevent or minimise risks.

The RMP for this product considered the main risks associated with the product and proposed additional warnings on the labelling and PIL about the symptoms which a patient should seek further advice from a doctor or pharmacist. The MHRA considers that apart from this, no further risk minimisation measures are need for this application.

6. Reasons for not seeking advice from the Commission on Human Medicines

No major issues have been identified in the assessment of this application for Omeprazole Tablets as a GSL medicine based on the following reasons:

- The treatment of heartburn is very common with other GSL medicines such as antacids, alginates, H2-receptor antagonists and another proton pump inhibitor (esomeprazole) all available to treat this condition.
- In 2015, CHM advised in favour of GSL classification for esomeprazole. Both active ingredients work in a similar way and have a similar safety profile.

- The changes to the product information recommended by CHM as risk minimisation measures for the supply of esomeprazole in the GSL setting have all been incorporated into the product information of this product.
- The proposed indication, dose, route of administration, strength, duration of treatment and maximum pack size are as per the currently approved GSL product esomeprazole.
- Since the reclassification of esomeprazole, no additional safety concern has been raised as a result of its availability as a GSL product

7. Conclusion

The MHRA has taken the decision to approve General Sales List legal status for Omeprazole Tablets with the following terms of reclassification:

a) For oral use in the form of tablets
b) For the short-term treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults
c) Maximum strength: 20mg
d) Maximum dose: 20 mg
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