Public Assessment Report

UKPAR

Domperidone 10mg Tablets

(Domperidone maleate)

UK Licence No: PL 44041/0011

Noumed Life Sciences
LAY SUMMARY

Domperidone 10mg Tablets
(Domperidone maleate, tablet, 10 mg)

This is a summary of the Public Assessment Report (PAR) for Domperidone 10mg Tablets (PL 44041/0011). It explains how Domperidone 10mg Tablets were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Domperidone 10mg Tablets.

The product will be referred to as Domperidone Tablets throughout the remainder of this public assessment report (PAR).

For practical information about using Domperidone Tablets patients should read the package leaflet or contact their doctor or pharmacist.

What are Domperidone Tablets and what are they used for?
Domperidone Tablets are used in adults and children for the relief of the symptoms of nausea (feeling sick) and vomiting (being sick).

This medicine is the same as Domperidone 10mg Tablets (PL 21880/0110) which is already authorised. The company (Medreich Plc) that makes Domperidone 10mg Tablets (PL 21880/0110) has agreed that its scientific data can be used as a basis for the grant of an identical licence for Domperidone Tablets (informed consent).

How do Domperidone Tablets work?
This medicine contains the active ingredient called domperidone which belongs to a group of medicines called ‘dopamine antagonists’. Domperidone works by helping to move food faster through the patient’s food pipe (oesophagus), stomach and gut. This is so that it does not stay in the same place for too long. It also helps stop food flowing the wrong way back up the food pipe.

How are Domperidone Tablets used?
The pharmaceutical form of this medicine is a tablet and the route of administration is oral.

The patient must always take this medicine exactly as their doctor has told them. The patient should check with their doctor or pharmacist if they are not sure.

This medicine is for oral use only. The tablets must be swallowed with a glass of water.

The patient should take the tablets 15 to 30 minutes before meals and, if needed, before they go to bed. Do not crush or chew the tablets.

The patient must follow these instructions closely unless their doctor has advised them otherwise.

Domperidone Tablets can only be obtained with a prescription.

For further information on how Domperidone Tablets are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.
What benefits of Domperidone Tablets have been shown in studies?
Domperidone Tablets are considered identical to previously authorised Domperidone 10mg Tablets (PL 21880/0110), with the same benefits and risks. So no new studies have been provided for Domperidone Tablets but reference is made to the studies for Domperidone 10mg Tablets (PL 21880/0110).

What are the possible side effects from Domperidone Tablets?
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Domperidone Tablets are considered to be identical to the previously authorised application for Domperidone 10mg Tablets (PL 21880/0110) with the same benefits and risks.

For a full list of all the side effects reported with Domperidone Tablets see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

For the full list of restrictions, see the package leaflet.

Why are Domperidone Tablets approved?
The MHRA decided that the benefits of Domperidone Tablets are greater than their risks and recommended that they be approved for use.

What measures are being taken to ensure the safe and effective use of Domperidone Tablets?
A Risk Management Plan has been developed to ensure that Domperidone Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Domperidone Tablets including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Domperidone Tablets
A Marketing Authorisation was granted in the UK on 18 July 2016.

The full PAR for Domperidone Tablets follows this summary.

For more information about treatment with Domperidone Tablets read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in August 2016.
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I INTRODUCTION
The Medicines and Healthcare products Regulatory Agency (MHRA) granted Noumed Life Sciences a Marketing Authorisation for the medicinal product Domperidone Tablets (PL 44041/0011) on 18 July 2016. The product is a prescription only medicine (POM) and is indicated for the relief of the symptoms of nausea and vomiting.

This application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the reference product Domperidone 10mg Tablets (PL 21880/0110), which was authorised to Medreich Plc on 16 June 2011.

Domperidone is a dopamine antagonist with anti-emetic properties which does not readily cross the blood-brain barrier. In domperidone users, especially in adults, extrapyramidal side effects are very rare, but domperidone promotes the release of prolactin from the pituitary. Its anti-emetic effect may be due to a combination of peripheral (gastrokinetic) effects and antagonism of dopamine receptors in the chemoreceptor trigger zone, which lies outside the blood-brain barrier in the area postrema. Animal studies, together with the low concentrations found in the brain, indicate a predominantly peripheral effect of domperidone on dopamine receptors.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to that of the previously granted cross-referenced product.
II QUALITY ASPECTS

II.1 Introduction
This is an abridged application for Domperidone Tablets (PL 44041/0011) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to Domperidone 10mg Tablets (PL 21880/0110) which was first authorised to Medreich Plc on 16 June 2011. The application is considered valid.

II.2 Drug Substance
Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

II.3 Medicinal Product
Name
The proposed product name for this application is Domperidone 10mg Tablets. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each tablet contains domperidone maleate equivalent to 10 mg domperidone base. The finished product is packaged into polyvinyl chloride (PVC) and aluminium foil blisters and is available in pack sizes of 30 and 100 tablets.

The proposed shelf life of the unopened product is 24 months with the storage conditions ‘Do not store above 25°C. Store in the original package.’

The proposed packaging, shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status
On approval, the product will be available as a prescription only medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company
Noumed Life Sciences, 1st Floor Cattle Market, Hexham, Northumberland, NE46 1NJ, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

Manufacturing process
The proposed manufacturing processes are consistent with the details registered for the cross-reference product and the maximum batch size is stated.
Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference product.

TSE Compliance
With the exception of lactose monohydrate, none of the excipients contain materials of animal or human origin. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula utilising the same processes as the cross-reference product, Domperidone 10mg Tablets (PL 21880/0110).

Expert Report
The applicant cross-refers to the data for Domperidone 10mg Tablets (PL 21880/0110) to which this application is claimed to be identical. This is acceptable.

Product Name and Appearance
See Section II.3 ‘Medicinal Product; Name’ for details of the proposed product name. The appearance of each product is identical to that of the cross-reference product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The data submitted with the application is acceptable. The grant of a Marketing Authorisation is recommended.
III NON-CLINICAL ASPECTS
Introduction
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Ecotoxicity/environmental risk assessment (ERA)
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

Discussion on the non-clinical aspects
The grant of a Marketing Authorisation is recommended.

IV CLINICAL ASPECTS
Introduction
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Risk Management Plan (RMP)
The marketing authorisation holder (MAH) has submitted a risk management plan (RMP), in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Domperidone Tablets.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, are listed below:

Summary table of safety concerns:

| Important identified risks | • Cardiac events (QTc prolongation, Torsades de Pointes, serious ventricular arrhythmia and sudden cardiac death) |
|                           | • Hypersensitivity (including anaphylaxis) |
|                           | • Off-label use (e.g. stimulation of lactation in breast feeding women, gastroesophageal reflux disease, diabetic and non-diabetic gastroparesis and symptoms of postural hypotension in patients with Parkinson's disease) |
| Important potential risks | • None |
| Missing information       | • Use during pregnancy and lactation |
|                           | • Use in patients with hepatic impairment |
Summary table of risk minimisation measures:

<table>
<thead>
<tr>
<th>Safety Concern</th>
<th>Routine Measures</th>
<th>Risk Minimization Measures</th>
<th>Additional Risk Minimization Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Important Identified Risks</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac events (QTc prolongation, Torsades de Pointes, serious ventricular arrhythmia and sudden cardiac death)</td>
<td>The risk of Cardiac events (QTc prolongation, Torsades de Pointes, serious ventricular arrhythmia and sudden cardiac death) associated with the use of the drug product is described in the SmPC Sections 4.3, 4.4, 4.6 and 4.8 and PL Sections 2 and 4 and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
<td></td>
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<tr>
<td>Hypersensitivity (including anaphylaxis)</td>
<td>The risk of Hypersensitivity (including anaphylaxis) associated with use of the drug product is described in the SmPC Sections 4.3 and 4.8 and PL Sections 2 and 4, and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
<td></td>
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<tr>
<td>Off-label use (e.g. stimulation of lactation in breast feeding women, gastroesophageal reflux disease, diabetic and non-diabetic gastroparesis and symptoms of postural hypotension in patients with Parkinson’s disease)</td>
<td>The risk of Off label use is monitored through routine pharmacovigilance activities, including review of incoming case reports, aggregate safety data and review of the medical literature.</td>
<td>None</td>
<td></td>
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<tr>
<td><strong>Important Potential Risks</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>None</td>
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<tr>
<td><strong>Missing Information</strong></td>
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<tr>
<td>use during pregnancy and lactation</td>
<td>The SmPC section 4.6 and PL section 2 states that there are limited post-marketing data on the use of domperidone in pregnant women. A study in rats has shown reproductive toxicity at a high, maternally toxic dose. The potential risk for humans is unknown. Therefore, domperidone</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>
Discussion on the clinical aspects
The grant of a Marketing Authorisation is recommended.

V User consultation
A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to the product for Domperidone 10mg Tablets (PL 21880/0110). The bridging report submitted by the applicant is acceptable.

VI Overall conclusion, benefit/risk assessment and recommendation
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with domperidone maleate is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels

The Summary of Product Characteristics and Patient Information Leaflet (PIL) are consistent with the details registered for the cross-reference products.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for this medicine is presented below:

**Braille Reads:**

Domperidone

#10 mg Tablets