Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Isosorbide Mononitrate 20 mg Tablets
Isosorbide Mononitrate 40 mg Tablets

Isosorbide mononitrate

PL 28444/0269-70

Activase Pharmaceuticals Limited

LAY SUMMARY

Isosorbide Mononitrate 20 mg and 40 mg Tablets
Isosorbide mononitrate

This is a summary of the Public Assessment Report (PAR) for Isosorbide Mononitrate 20 mg and 40 mg Tablets. It explains how these products 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 these products.

For practical information about using Isosorbide Mononitrate 20 mg and 40 mg Tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What are Isosorbide Mononitrate 20 mg and 40 mg Tablets and what are they used for?
These applications are the same as Isosorbide Mononitrate 20 mg and 40 mg Tablets (PL 21880/0117-0118) which are already authorised.

The Company responsible for Isosorbide Mononitrate 20 mg and 40 mg Tablets (PL 21880/0117-0118) has agreed that its scientific data can be used as the basis for the grant of identical licences for Isosorbide Mononitrate 20 mg and 40 mg Tablets.

Isosorbide Mononitrate 20 mg and 40 mg Tablets are used to relieve the symptoms of angina pectoris. Angina pectoris is a painful tightness in the chest, which occurs when the muscles of the heart are not receiving enough oxygen. Pain may also be felt in the neck and arms.

The tablets are also used to treat heart failure.

How do Isosorbide Mononitrate 20 mg and 40 mg Tablets work?
These medicines contain the active ingredient isosorbide mononitrate, which belongs to a group of medicines called nitrates. Isosorbide mononitrate works by relaxing the blood vessels to the heart, so the blood and oxygen supply to the heart is increased.

How are Isosorbide Mononitrate 20 mg and 40 mg Tablets used?
The pharmaceutical form of these medicines is a tablet and the route of administration is oral (by mouth).

The usual dose in adults and the elderly is one tablet, taken two to three times a day. The dose may be increased to 120 mg per day. The patient should always follow their doctor’s advice.

These medicines are not recommended for use in children.

For further information on how Isosorbide Mononitrate 20 mg and 40 mg Tablets are used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

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

What benefits of Isosorbide Mononitrate 20 mg and 40 mg Tablets have been shown in studies?
Isosorbide Mononitrate 20 mg and 40 mg Tablets are considered identical to the previously authorised products with the same benefits and risks. No new studies have been provided for Isosorbide Mononitrate 20 mg and 40 mg Tablets, however, reference is made to the studies for Isosorbide Mononitrate 20 mg and 40 mg Tablets (PL 21880/0117-0118).

What are the possible side effects of Isosorbide Mononitrate 20 mg and 40 mg Tablets?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Isosorbide Mononitrate 20 mg and 40 mg Tablets are considered to be identical to the previously authorised products with the same benefits and risks.

Why were Isosorbide Mononitrate 20 mg and 40 mg Tablets approved?
The MHRA decided that the benefits of Isosorbide Mononitrate 20 mg and 40 mg Tablets are greater than the risks and recommended that these medicines are approved for use.

What measures are being taken to ensure the safe and effective use of Isosorbide Mononitrate 20 mg and 40 mg Tablets?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Isosorbide Mononitrate 20 mg and 40 mg Tablets. The RMP details the important risks of Isosorbide Mononitrate 20 mg and 40 mg Tablets, how these risks can be minimised, any uncertainties about Isosorbide Mononitrate 20 mg and 40 mg Tablets (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Isosorbide Mononitrate 20 mg and 40 mg Tablets.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Isosorbide Mononitrate 20 mg and 40 mg Tablets are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Isosorbide Mononitrate 20 mg and 40 mg Tablets
Marketing Authorisations were granted in the UK on 03 May 2024.
The full PAR for Isosorbide Mononitrate 20 mg and 40 mg Tablets follows this summary.
This summary was last updated in June 2024.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Isosorbide Mononitrate 20 mg and 40 mg Tablets (PL 28444/0269-0270) could be approved.

The products are approved for the following indications:

- For the prophylaxis of angina pectoris
- As adjunctive therapy in congestive heart failure not responding to cardiac glycosides or diuretics.

Isosorbide mononitrate is an organic nitrate, which, in common with other cardioactive nitrates, is a vasodilator. It produces decreased left and right ventricular end-diastolic pressures to a greater extent than the decrease in systemic arterial pressure, thereby reducing afterload and especially the preload of the heart.

Isosorbide mononitrate influences the oxygen supply to ischaemic myocardium by causing the redistribution of blood flow along collateral channels and from epicardial to endocardial regions by selective dilation of large epicardial vessels.

It reduces the requirements of the myocardium for oxygen by increasing venous capacitance, causing a pooling of blood in peripheral veins, thereby reducing ventricular volume and heart wall distension.

These are national abridged applications approved under Regulation 56 of The Human Medicines Regulation 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as informed consent applications. The applications cross-refer to the reference products Isosorbide Mononitrate 20 mg and 40 mg Tablets (PL 21880/0117-0118).

No new non-clinical or clinical data have been supplied and none are required for these informed consent applications.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the applications are for identical versions of already authorised products, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

National marketing authorisations were granted in the UK on 03 May 2024.

II. EXPERT REPORT

The applicant cross-refers to the data for Isosorbide Mononitrate 20 mg and 40 mg Tablets (Medreich PLC), to which these applications are claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

Summaries of Product Characteristics (SmPCs)

The SmPCs are in line with those for Isosorbide Mononitrate 20mg and 40 mg Tablets (PL 21880/0117 - 0118) dated 05/02/2014.

PATIENT INFORMATION LEAFLET
A leaflet mock-up has been provided which has been aligned with that for those for Isosorbide Mononitrate 20 mg and 40 mg Tablets (PL 21880/0117 - 0118), dated July 2013.

LABEL
Label mock-ups have been provided.

IV. QUALITY ASPECTS

IV.1 Drug Substance

Drug substance specification
The source of the active substance is in line with the cross-reference products. The proposed drug substance specification is consistent with the details registered for the cross-reference products.

IV.2. Drug Product

The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Isosorbide Mononitrate 20 mg and 40 mg Tablets are available in PVC/Aluminium foil blisters in a cardboard carton, in a pack size of 56 or 60 tablets.

The appearance of the products is identical to that of the cross-reference products.

The proposed shelf life of the product is 3 years with the recommended storage condition ‘Do not store above 25°C’.

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

Legal status
Prescription only medicine (POM).

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

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

Manufacturing process & control of critical steps
The proposed manufacturing processes and process controls are consistent with the details registered for the reference products and the maximum batch size is stated.

Finished product release/shelf life specifications
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference products.

TSE Compliance
With the exception of lactose monohydrate, no excipients of animal or human origin are used in the final products.

The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

These products do not contain or consist of genetically modified organisms (GMO).

V. NON-CLINICAL ASPECTS
As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new non-clinical data have been supplied and none are required.

VI. CLINICAL ASPECTS
As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new clinical data have been supplied and none are required.

VII. RISK MANAGEMENT PLAN (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VIII. USER CONSULTATION
A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference products and positive.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**