Glucose 20% w/v Solution for Infusion

(Glucose monohydrate)

PL 01502/0083

UKPAR

TABLE OF CONTENTS

Lay Summary ........................................ Page 2
Scientific discussion ............................... Page 3
Steps taken for assessment ......................... Page 10
Summary of Product Characteristics ............... Page 11
Patient Information Leaflet ....................... Page 12
Labelling ............................................. Page 13
Glucose 20% w/v Solution for Infusion

PL 01502/0083

LAY SUMMARY

On 6\textsuperscript{th} June 2013, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Hameln Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Glucose 20% w/v Solution for Infusion (PL 01502/0083). This medicine is only available on prescription from your doctor.

Glucose 20% w/v Solution for Infusion is a sterile solution of glucose in water and is used to:

• Restore blood glucose levels
• Provide temporary relief from the symptoms of a swollen brain and coma due to low blood sugar.
• Correct high blood potassium levels and some forms of low sodium blood levels.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of treatment with Glucose 20% w/v Solution for Infusion outweigh the risks. Hence, a Marketing Authorisation has been granted.
Glucose 20% w/v Solution for Infusion

PL 01502/0083

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction
Pharmaceutical assessment
Non-clinical assessment
Clinical assessment
Overall conclusions and benefit-risk assessment

Page 4
Page 5
Page 7
Page 8
Page 9
INTRODUCTION

The MHRA granted a Marketing Authorisation for the medicinal product Glucose 20% w/v Solution for Infusion (PL 01502/0083) on 6th June 2013. This is a prescription only medicine (POM) used in both adults and children to restore blood glucose concentrations in the treatment of hypoglycaemia resulting from insulin excess or from other causes.

Glucose 20% may be used to provide temporary relief from the symptoms of cerebral oedema and from hypoglycaemic coma. Hyperosmotic Glucose with or without insulin may correct hyperkalaemia in renal failure and also some forms of hyponatraemia.

This was a generic application submitted according to Article 10(1) of Directive 2001/83/EC, as amended. The reference product is Glucose Intravenous Infusion BP 200 g/Litre (PL 01883/6129R) authorised to Macarthys Laboratories Ltd., since 19th October 1989.

No new non-clinical or clinical studies were necessary for this application, which is acceptable given that this is a generic application, which refers to an originator product that has been licensed over 10 years. Bioequivalence studies are not necessary to support this application for a parenteral product.

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

The MHRA considers that the pharmacovigilance system as described by the Marketing Authorisation Holder (MAH) fulfils the requirements and provides adequate evidence that the MAH has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Satisfactory justification has been provided for the non-submission of the Risk Management Plan (RMP).
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Nomenclature
rINN: Glucose monohydrate

Chemical Names: (+)-D-Glucopyranose monohydrate

Structure:

\[
\begin{align*}
\text{HO} & \text{OH} \\
\text{HO} & \text{OH} \\
\text{HO} & \text{OH} \\
\end{align*}
\]

\[\text{Molecular Formula: } C_6H_{12}O_6, H_2O\]

Molecular Weight: 198.2 g/mol

Appearance: A white or almost white, crystalline powder.
Solubility: It is soluble in water, sparingly soluble in ethanol (96%).

Glucose monohydrate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance glucose monohydrate are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

DRUG PRODUCT

Other ingredients
Other ingredients consist of the pharmaceutical excipients hydrochloric acid and water for injections.

The excipients used comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for both excipients.

The applicant has confirmed that neither of the excipients are of animal or human origin.

Pharmaceutical development
Suitable pharmaceutical development data have been provided for this application.

Manufacture
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated on two production scale batches and has shown
satisfactory results. The applicant has committed to perform process validation on a third commercial-scale batch.

**Finished product specification**
The finished product specification is satisfactory. Test methods have been described and adequately validated. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for any working standards used.

**Container Closure System**
The product is supplied in a type I clear colourless glass infusion bottle with rubber stopper and cap, packed in cardboard cartons. The pack sizes are 1, 10 or 25 vials x 100 ml.

Specifications and Certificates of Analysis for all packaging materials have been provided. These are satisfactory. All primary packaging complies with EU legislation regarding contact with food.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 30 months with storage conditions “Do not store above 25°C” and “Keep the bottle in the outer carton in order to protect from light” have been set. These statements are satisfactory.

**Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling**
The SmPC, PIL and labelling are pharmaceutically satisfactory.

User testing of the package leaflet has been accepted, based on a bridging report provided by the applicant making reference to the user-testing of the PIL for Glucose 50% w/v Intravenous Infusion (PL 01502/0005R). The products are from the same therapeutic class and have similar indications. A critical analysis demonstrated that the key messages for safe and effective use for both leaflets were similar. The justification of the rationale for bridging is accepted.

**Marketing Authorisation Application (MAA) Form**
The MAA form is pharmaceutically satisfactory.

**Expert Report/Quality Overall Summary**
The quality overall summary is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**
There are no objections to the approval of this product from a pharmaceutical point of view.
NON-CLINICAL ASSESSMENT

The pharmacodynamic, pharmacokinetic and toxicological properties of glucose monohydrate are well-known. Thus, the applicant has not provided additional studies and further studies are not required.

A non-clinical overview has been provided, written by an appropriately qualified person. This is satisfactory.

Suitable justification has been provided for non-submission of an environmental risk assessment.

There are no objections to the approval of this product from a non-clinical point of view.
**CLINICAL ASSESSMENT**

**Clinical Pharmacology**
The clinical pharmacology of glucose monohydrate is well known.

Bioequivalence studies may be submitted to support the pharmacokinetic profile for a generic application. However, as per guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr**), a bioequivalence study is not requested if the test product is an aqueous solution at the time of administration and contains an active substance in the same concentration as an approved solution. Bioequivalence studies may be waived if the excipients contained in the product do not affect gastrointestinal transit, absorption, solubility or *in-vivo* stability of the active substance. These criteria are fulfilled. Therefore, no biostudies are provided by the applicant and none are required.

**Clinical efficacy**
No new efficacy data have been submitted and none are required for applications of this type. The clinical efficacy of glucose monohydrate is well known.

**Clinical safety**
No new safety data were supplied or required for this generic application. No new safety issues have been raised with this application.

**Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling**
The SmPC, PIL and labelling are medically satisfactory.

**Clinical Expert Report (Clinical Overall Summary)**
The clinical overview summary, written by an appropriately qualified physician, has been provided. This is satisfactory.

**Marketing Authorisation Application (MAA) Form**
The MAA form is medically satisfactory.

**Clinical Conclusion**
There are no objections to the approval of this product from a clinical point of view.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Glucose 20% w/v Solution for Infusion are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

CLINICAL
This application is identical to the previously granted application for Glucose Intravenous Infusion BP 200 g/Litre (PL 01883/6129R), which was licensed to Macarthys Laboratories Ltd. on 19th October 1989.

No new safety or unexpected concerns arose from this application.

PRODUCT LITERATURE
The SmPC, PIL and labelling are satisfactory.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Glucose monohydrate is a well known active substance. Extensive clinical experience with glucose monohydrate is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is therefore considered to be positive.
## STEPS TAKEN FOR ASSESSMENT

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the Marketing Authorisation application on 16(^{\text{th}}) December 2011</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 23(^{\text{rd}}) February 2012.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the quality dossier on 31(^{\text{st}}) May 2012 and 21(^{\text{st}}) December 2012 and on the non-clinical 19(^{\text{th}}) April 2013</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information to the quality section on 31(^{\text{st}}) October 2012 and 20(^{\text{th}}) March 2013 and on the non-clinical section on 17(^{\text{th}}) May 2013</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 6(^{\text{th}}) June 2013</td>
</tr>
</tbody>
</table>

---

**Glucose 20% w/v Solution for Infusion**

**PL 01502/0083**
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) for products that are granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU the Patient Information Leaflets (PIL) for products that are granted Marketing Authorisations at a national level are available on the MHRA website.
UKPAR Glucose 20% w/v Solution for Infusion   PL 01502/0083

LABELLING

20 g in 100 ml
1 x 100 ml vial
For intravenous use.

1 ml solution for injection contains:
Glucose, anhydrous, 200 mg
Excipients: sorbitol, saccharose, citric acid and water for injection.

Do not store above 25°C.

Keep the bottle in the outer carton in order to protect from light.
Keep out of the reach and sight of children.

Use as directed by a physician. Read the package leaflet before use. If only part used discard the remaining solution.

Glucose 20% w/v Solution for Infusion

hameln

Batch:
EXP:
UKPAR Glucose 20% w/v Solution for Infusion

20 g in 100 ml

Glucose 20% w/v Solution for Infusion

20 g in 100 ml
10 x 100 ml vials. For intravenous use.
1 ml solution for injection contains: Glucose, anhydrous 200 mg
Excipients: Hydrochloric acid and water for injections.

Do not store above 25°C.
Keep the bottle in the outer carton in order to protect from light.
Keep out of the reach and sight of children.
Use as directed by a physician. Read the package leaflet before use. If only part used discard the remaining solution.

hameln
Glucose 20% w/v Solution for Infusion

20 g in 100 ml
For intravenous use.

hameln pharmaceuticals ltd

PL 01502/0083
Batch: EXP.