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GLUCOSE INTRAVENOUS INFUSION BP 50% W/V
PL 01502/0075

LAY SUMMARY

On 24\textsuperscript{th} February 2011, the MHRA granted Hameln Pharmaceuticals Limited a Marketing Authorisation (licence) for Glucose Intravenous Infusion BP 50\% w/v (PL 01502/0075).

Glucose Intravenous Infusion BP 50\% w/v 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 comas 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 taking Glucose Intravenous Infusion BP 50\% w/v outweigh the risks; hence a Marketing Authorisation has been granted.
GLUCOSE INTRAVENOUS INFUSION BP 50% W/V
PL 01502/0075

SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Marketing Authorisation for the product Glucose Intravenous Infusion BP 50% w/v to Hameln Pharmaceuticals Limited on 24th February 2011. This prescription only medicine (POM) is used to provide:

- A source of calories in a minimal volume of water. Glucose Intravenous Infusion BP 50% w/v is frequently used in both adults and children to restore blood glucose concentrations in the treatment of hypoglycaemia resulting from insulin excess or from other causes.

- 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 application for Glucose Intravenous Infusion BP 50% w/v is submitted according to Article 10c of Directive 2001/83/EC, cross-referring to Glucose Intravenous Infusion BP 50% w/v (PL 01502/0005R), which was licensed to Hameln Pharmaceuticals Limited on 4th December 1989.

It is considered that the pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring.

No new data were submitted nor were they necessary for this “simple” application, as the data are identical to that of the previously granted cross-reference product.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 01502/0075
PROPRIETARY NAME: Glucose Intravenous Infusion BP 50% w/v
ACTIVE(S): Glucose monohydrate
COMPANY NAME: Hameln Pharmaceuticals Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: POM

1. INTRODUCTION
This is a “simple” application for Glucose Intravenous Infusion BP 50% w/v (PL 01502/0075) submitted under Article 10c of Directive 2001/83/EC. The proposed MA holder is Hameln Pharmaceuticals Limited, Gloucester, United Kingdom.

This application cross-refers to Glucose Intravenous Infusion BP 50% w/v (PL 01502/0005R), which was licensed to Hameln Pharmaceuticals Limited on 4th December 1989.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 NAME(S)
The proposed name of the product is Glucose Intravenous Infusion BP 50% w/v. The product has been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The product contains glucose monohydrate. The finished product is packaged in:
   i) 20ml type I clear glass ampoules
   ii) 50ml type II clear glass vials
Both vials and ampoules are packed into cardboard cartons.

The product comes in pack sizes of:
20ml ampoules: 10 ampoules
50ml vials: 10 or 25 vials

The proposed shelf-life is 36 months with storage conditions ‘Store at less than 25°C’.

This is consistent with the details registered for the cross-reference product.

2.3 Legal status
Prescription only medicine (POM).

2.4 Marketing authorisation holder/Contact Persons/Company
Hameln Pharmaceuticals Limited, Gloucester, United Kingdom.

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers
The manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.
2.6 Qualitative and quantitative composition
The composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size for each product is stated.

2.8 Finished product/shelf-life specification
The finished product specification is in-line with the details registered for the cross-reference product.

2.9 Drug substance specification
The drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
None of the excipients used contain material of animal or human origin, which is supported by a statement from the Quality Expert. This information is consistent with the cross-reference product.

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts’ CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS
The summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product. No user testing results have been submitted for PIL for this product. This is because the PIL is identical to the PIL for the reference product, Glucose Intravenous Infusion BP 50% w/v (PL 01502/0005R). The PIL is satisfactory.

Labelling
The artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In-line with current legislation, the applicant has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

No new non-clinical data have been supplied with this application and none are required for applications of this type.
CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for applications of this type.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for this application are consistent with that previously approved for the cross-reference product and, as such, has been judged to be satisfactory.

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

EFFICACY
This application is identical to the previously granted application Glucose Intravenous Infusion BP 50% w/v (PL 01502/0005R), which was licensed to Hameln Pharmaceuticals Limited on 4th December 1989.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT
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 glucose monohydrate is considered to have demonstrated the therapeutic value of the compounds. The risk:benefit is, therefore, considered to be positive.
**STEPS TAKEN FOR ASSESSMENT**

1. The MHRA received the Marketing Authorisation Application on 17th August 2010.

2. Following standard checks and communication with the applicant the MHRA considered the application valid on 9th September 2010.

3. Following assessment of the application further information was requested regarding the quality section of the dossier on 18th January 2011.

4. The applicant responded to the MHRA’s requests, providing further information on 22nd January 2011 for the quality section.

5. The application was determined on 24th February 2011.
GLUCOSE INTRAVENOUS INFUSION BP 50% W/V
PL 01502/0075

STEPS TAKEN AFTER ASSESSMENT

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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Glucose Intravenous Infusion BP 50% w/v.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ml contains 50% w/v of Glucose EP

3 PHARMACEUTICAL FORM
Sterile Injection.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS
Glucose 50% is hypertonic and provides a source of calories in a minimal volume of water. Glucose 50% is frequently 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 50% 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.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
Glucose 50% must be administered by the intravenous route; it must not be administered by subcutaneous or intramuscular route. Except in the emergency treatment of severe hypoglycaemia, Glucose 50% should be administered via a central vein after appropriate dilution. When used for the emergency treatment of hypoglycaemia, Glucose 50% may be administered slowly into a peripheral vein at a rate not greater than 3mls per minute.

Dosage of Glucose depends on the age, weight, clinical condition, the fluid, electrolyte and acid base balance of the patient. For the treatment of hypoglycaemia resulting from insulin excess or other causes in adults (including the elderly) and children, the usual dose is as follows:

20-50ml of Glucose 50% administered slowly intravenously. This represents 3mls per minute.

Repeated doses and supportive therapy may be required in some cases.

4.3 CONTRAINDICATIONS
Glucose 50% is contraindicated in patients with the glucose – galactose malabsorption syndrome.
Hypertonic Glucose solutions are contraindicated in patients with anuria or intraspinal or intracranial haemorrhage, or ischaemic stroke and in patients with delirium tremens if such patients are already dehydrated. Hypertonic Glucose solutions are also contraindicated in patients with diabetic coma or known allergy to corn or corn products.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Hypertonic solutions of Glucose should be administered via a large central vein to minimise damage at the site of injection (see section 4.2 Posology).

Glucose solutions should be used with caution in patients with overt or known sub-clinical diabetes mellitus, carbohydrate intolerance for any reason, severe under-nutrition, thiamine deficiency, hypophosphataemia, haemodilution, sepsis, trauma, shock, metabolic acidosis or severe dehydration.

Rapid administration of hypertonic glucose solutions may produce substantial hyperglycaemia and hyperosmolar syndrome; patients should be observed for signs of mental confusion and loss of consciousness, especially those patients with chronic uraemia or carbohydrate intolerance.

Prolonged use in parenteral nutrition may affect insulin production; blood and urine glucose should be monitored.

Changed in fluid balance, electrolyte concentrations and acid-base balance should be evaluated during prolonged therapy. Intravenous administration of Glucose may result in hypokalaemia, hypophosphataemia and hypomagnesaemia.
4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
None known.

4.6 PREGNANCY AND LACTATION
Intravenous glucose may result in foetal insulin production, with an associated risk of rebound hypoglycaemia in the neonate. Infusions of glucose administered during Caesarean section and labour should not exceed 5-10g glucose/hour.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
None known.

4.8 UNDESIRABLE EFFECTS

Metabolic and nutrition disorders:
Hyperglycaemia, hypokalaemia, hypophosphataemia, hypomagnesaemia, fluid and electrolyte imbalance.

Hyperglycaemia (possibly indicated by mental confusion or loss of consciousness) and glycosuria may occur as a result of the rate of administration or metabolic insufficiency. If undetected and untreated hyperglycaemia can lead to dehydration, hyperosmolar coma and death.

The administration of glucose without adequate levels of thiamine may precipitate overt deficiency states e.g. Wernicke’s encephalopathy. Sodium retention, oedema, pulmonary oedema and congestive heart failure may be induced in patients with severe under-nutrition.

Nervous system:
See Metabolic and nutrition disorders.

General and administration site disorders:
Pain at the injection site, vein irritation, venous thrombosis, phlebitis.

4.9 OVERDOSE
Overdose of Glucose 50% may lead to hyperglycaemia and glycosuria leading to dehydration, hyperosmolar coma and death.

In the event of overdose of Glucose 50% it may be necessary to administer appropriate doses of insulin.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES
Not applicable.

5.2 PHARMACOKINETIC PROPERTIES
Not applicable.

5.3 PRECLINICAL SAFETY DATA
No further information other than that which is included in the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS
Hydrochloric Acid
Water for Injections Ph. Eur.

6.2 INCOMPATIBILITIES
Glucose solutions which do not contain electrolytes, should not be administered concomitantly with blood through the same infusion set, because of the possibilities of agglomeration.

6.3 SHELF LIFE
36 months.
6.4 SPECIAL PRECAUTIONS FOR STORAGE
Store at less than 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER
20ml type I clear glass ampoules, packed in cardboard cartons to contain 10 ampoules x 20ml.
50ml type II clear glass vials, packed in cardboard cartons to contain 10 or 25 vials x 50ml.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
Use as directed by the physician.

7 MARKETING AUTHORISATION HOLDER
Hameln pharmaceuticals Ltd
Gloucester
UK

8 MARKETING AUTHORISATION NUMBER(S)
PL 1502/0075

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
24/02/2011

10 DATE OF REVISION OF THE TEXT
24/02/2011
Glucose Intravenous Infusion 50% w/v

Important information about your medicine

- Your doctor or nurse will give you the injection.
- If this injection causes you any problems talk to your doctor, nurse or pharmacist.
- Please tell your doctor or pharmacist, if you have any other medical conditions or have an allergy to any of the ingredients of this medicine.
- Please tell your doctor or pharmacist, if you are taking any other medicines.

Read all of this leaflet carefully before you start using this medicine. In some circumstances this may not be possible and this leaflet will be kept in a safe place should you wish to read it.

Keep this leaflet. You may need to read it again.

If you have any further questions, please ask your doctor or your pharmacist.

This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

Where to find information in this leaflet

1. What Glucose Intravenous Infusion 50% w/v is and what it is used for
2. Before you are given Glucose Intravenous Infusion 50% w/v
3. How to use Glucose Intravenous Infusion 50% w/v
4. Possible side effects
5. Storing Glucose Intravenous Infusion 50% w/v
6. Further information

1. What Glucose Intravenous Infusion 50% w/v is and what it is used for

Glucose Intravenous Infusion 50% w/v 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 comas due to low blood sugar.
- correct high blood potassium levels and some forms of low sodium blood levels.

2. Before you are given Glucose Intravenous Infusion 50% w/v

You should NOT be given Glucose Intravenous Infusion 50% w/v if you:

- Are sensitive or allergic to Glucose Intravenous Infusion 50% w/v or any of the other ingredients in this injection.
- You are allergic to corn or corn products.
- You have glucose-galactose malabsorption syndrome.
- You have been bleeding in the spine or brain.
- You cannot pass urine.

- You have had a stroke.
- You have a condition known as Delerium Tremens - uncontrolled bouts of shaking after stopping drinking alcohol.

Please tell your doctor or nurse before being given the injection if you:

- are a diabetic
- are under-nourished
- have low levels of phosphates (a mineral) or thiamine (vitamin B1) in your blood
- have an infection
- have had a recent injury
- are dehydrated

Using other medicines:

Please tell your doctor or nurse if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy or breast feeding:

Please tell your doctor or nurse before being given this injection if you are pregnant or breast feeding. The doctor will then decide if the injection is suitable for you.
Driving and using machines:
You should not drive or use machinery if you are affected by the administration of Glucose Intravenous Infusion 50% w/v.

3. How to use Glucose Intravenous Infusion 50% w/v

Your nurse or doctor will give you the injection.
Your doctor will decide the correct dosage for you and how and when the injection will be given.
Since the injection will be given to you by a doctor or nurse, it is unlikely that you will be given too much. If you think you have been given too much, you must tell the person giving you the injection.

4. Possible side effects
Like all medicines, Glucose Intravenous Infusion 50% w/v can cause side effects, although not everybody gets them.
- You may suffer from vein clots, inflammation of the veins, local pain at the injection site.
- You may develop hyperglycaemia (a higher than normal level of sugar in your blood and there may also be sugar in your urine). If this happens you may feel tired and confused or lose consciousness. You may also feel thirsty and pass urine more frequently.
- You may develop an imbalance in the level of fluid and of certain minerals in your body. You may develop low potassium, phosphate and magnesium blood levels.
- If you are administered glucose and you have low levels of thiamine (vitamin B1) in your blood you may develop Wernicke’s encephalopathy a condition where you may feel confused and unsteady on your feet.
- If you are administered glucose and you are severely under-nourished your body may retain water and salt. Your skin may swell and you may have difficulty in breathing.

If you think this injection is causing you any problems, or you are at all worried, talk to your doctor, nurse or pharmacist.

5. Storing Glucose Intravenous Infusion 50% w/v

Your injection will be stored at less than 25°C and protected from light. The nurse or doctor will check that the injection is not past its expiry date before giving you the injection.

6. Further information

What Glucose Intravenous Infusion 50% w/v contains:
This injection contains the active ingredient glucose (50% w/v or 500 g/l) in a sterile solution. This injection contains the following inactive ingredients: Sterile water for injections.

What Glucose Intravenous Infusion 50% w/v looks like and contents of the pack:
Glucose Intravenous Infusion 50% w/v is supplied in 20 ml clear glass ampoules (10 ampoules per carton) and in a 50 ml clear glass vial packed in cartons to contain either 10 vials or 25 vials.
Not all pack sizes may be marketed.
The marketing authorisation number of this medicine is: PL 01502 0075

Marketing Authorisation Holder:
hameln pharmaceuticals ltd
Gloucester
United Kingdom

Manufacturer:
hameln pharmaceuticals gmbh
Langes Feld 13
31789 Hameln
Germany

For any information about this medicine, please contact the Marketing Authorisation Holder

This leaflet was last approved

43871/43850/28/09