Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion BP

Glucose monohydrate and potassium chloride

PL 00116/0656

UKPAR

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LAY SUMMARY

On 2nd July 2013, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Baxter Healthcare Limited a Marketing Authorisation (licence) for the medicinal product Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion BP (PL 00116/0656). This medicine is only available on prescription from your doctor.

Potassium Chloride 0.15 % w/v and Glucose 10 % w/v Solution for Infusion is a solution of potassium chloride and glucose in water.

Potassium chloride is a chemical substance (often called a "salt") found in the blood. Glucose is one of the body's sources of energy. This solution for infusion provides 400 kilocalories per litre.

Potassium Chloride 0.15% w/v/Glucose 10% w/v Solution for Infusion BP is used to:

- provide a source of carbohydrate (sugar) for parenteral nutrition. Parenteral nutrition is used to feed patients who are unable to eat. It is given as an Infusion (slow Injection) into a vein.
- prevent or treat a low level of sugar in the blood (hypoglycaemia, that is causing symptoms, but is not life-threatening)
- give you extra fluid if your body does not have enough water (dehydration), and you need extra carbohydrate (sugar).
- prevent or treat a loss of potassium from the body (potassium depletion, e.g. after treatment with certain diuretics [water tablets])
- prevent or treat a low level of potassium in the blood (hypokalaemia) in situations that may cause potassium chloride and water loss including:

- when you cannot eat or drink, due to illness or after surgery
- pronounced sweating due to high fever
- extensive skin loss, as can occur in severe burns

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of treatment with Potassium Chloride 0.15% w/v and Glucose 10 % w/v Solution for Infusion BP outweigh the risks. Hence, a Marketing Authorisation has been granted.

Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion BP

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Marketing Authorisation for the medicinal product Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion BP (PL 00116/0656) on 2nd July 2013.

Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion is used in adults, the elderly, adolescents, children and infants (aged 28 days to 23 months) for:

- Prevention and treatment of potassium depletion and/or hypokalemia in cases where supply of water, potassium chloride and carbohydrates is required due to restriction of the intake of fluids and electrolytes by normal routes.
- Supply of carbohydrate and potassium during parenteral nutrition.
- Prevention and treatment of hypoglycaemia.

Rehydration in case of water loss and dehydration states in patients with high carbohydrate need.

This application was submitted as an abridged, bibliographic application according to Article 10a (well-established use) of Directive 2001/83/EC, as amended.

No new non-clinical or clinical studies were necessary for this application, which is acceptable given that this is a bibliographic application for a product containing active ingredients of well-established use.

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).

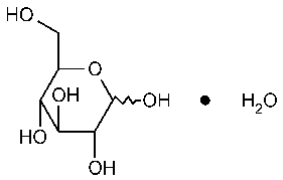
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Nomenclature
rINN: Glucose monohydrate

Chemical Names: (+)-D-Glucopyranose monohydrate

Structure:



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.

rINN: Potassium Chloride

Chemical Names: potassium chloride

Structure:

Molecular Formula: KCl

Molecular Weight: 74.5 g/mol

Appearance: A white or almost white, crystalline powder.
Solubility: It is soluble in glycerol, slightly soluble in alcohol and insoluble in ether.

Potassium chloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance potassium chloride 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 this product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Process validation data on commercial batches have been provided. The results are satisfactory.

Finished product specification

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

Container Closure System

The product is supplied in bags known as Viaflo which are composed of polyolefin/polyamide co-extruded plastic. The bags are overwrapped with a protective plastic pouch composed of polyamide/polypropylene.

The bag size is 500 ml. Outer carton contents are 20 bags or 24 bags of 500 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 24 months with no special storage conditions has been set. This is satisfactory.

In-use shelf life (Additives):
Chemical and physical stability of any additive medication at the pH of the Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion in the Viaflo container should be established prior to use.

From a microbiological point of view, the diluted product must be used immediately, unless dilution has taken place under controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions are the responsibility of the user.

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 Sodium Lactate and Glucose 5% w/v Solution for Infusion (UK/H/0482/001/DC). 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 and potassium chloride 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 and Efficacy

This application was submitted as an abridged application according to Article 10a of Directive 2001/83/EC, as amended, a well-established use application.

No new clinical studies were conducted, which is acceptable given that this is a well-established use application containing an active substance that has been in clinical use for many years.

Safety

No new safety concerns have been raised by this application.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling

The SmPC, PIL and labelling are medically satisfactory.

Clinical Expert Report

The clinical expert report is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

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 Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion BP 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

No new efficacy data were submitted and none are required for applications of this type. As the safety profile of glucose monohydrate and potassium chloride is well-known, no additional data were required. No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE

The SmPC, PIL and labelling are satisfactory and consistent with those for similar marketed products.

BENEFIT-RISK ASSESSMENT

The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with glucose monohydrate and potassium chloride is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is therefore considered to be positive.

Potassium Chloride 0.15% w/v and Glucose 10% w/v Solution for Infusion BP

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STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the Marketing Authorisation application on 2nd February 2012
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 23rd April 2012.
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 31st July 2012
4	The applicant responded to the MHRA's requests, providing further information to the quality section on 20th December 2012
5	The application was determined on 2nd July 2013.

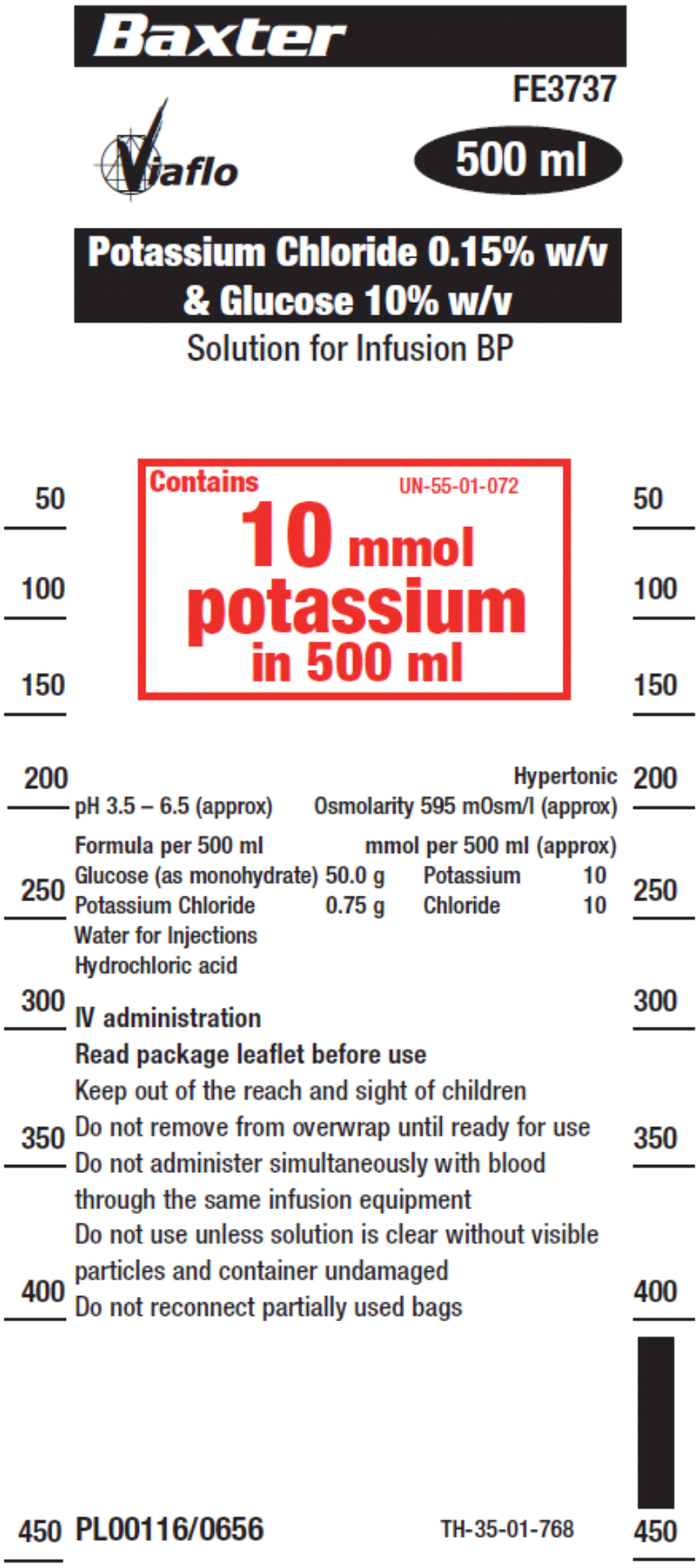
SUMMARY OF PRODUCT CHARACTERISTICS

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.

LABELLING


Baxter
FE3737
Viaflo
500 ml
Potassium Chloride 0.15% w/v
& Glucose 10% w/v
Solution for Infusion BP
50
100
150
200
250
300
350
400
450
Contains
UN-55-01-072
10 mmol
potassium
in 500 ml
Hypertonic
pH 3.5 – 6.5 (approx)
Osmolarity 595 mOsm/l (approx)
Formula per 500 ml
mmol per 500 ml (approx)
Glucose (as monohydrate) 50.0 g
Potassium 10
Potassium Chloride 0.75 g
Chloride 10
Water for Injections
Hydrochloric acid
IV administration
Read package leaflet before use
Keep out of the reach and sight of children
Do not remove from overwrap until ready for use
Do not administer simultaneously with blood through the same infusion equipment
Do not use unless solution is clear without visible particles and container undamaged
Do not reconnect partially used bags
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TH-35-01-768

20 or 24 x 500 ml (≈12.0 kg)

Potassium Chloride 0.15% w/v & Glucose 10% w/v

Solution for Infusion BP

Formula per 500 ml		mmol per 500 ml (approx)	
Glucose (as monohydrate)	50.0 g	Potassium	10
Potassium Chloride	0.75 g	Chloride	10

Contains 10 mmol potassium in 500 ml

Water for Injections
Hydrochloric acid
Osmolarity 595 mOsm/l (approx)

pH: 3.5 – 6.5 (approx)

IV administration.
Read package leaflet before use.
Keep out of the reach and sight of children.
Do not administer simultaneously with blood through the same infusion equipment.
Do not reconnect partially used bags.

PLXXXX/XXXX
PAXXX/XX/XX