infarmed
Autoridade Nacional do Medicamento
e Produtos de Saúde I.P.

Public Assessment Report

Scientific discussion

Cloreto de Potássio 0,15% + Cloreto de Sódio 0,9% Kabi

1.5 mg/ml potassium chloride + 9 mg/ml sodium chloride *Solution for Infusion*
3 mg/ml potassium chloride + 9 mg/ml sodium chloride *Solution for Infusion*
(potassium chloride + sodium chloride)

PT/H/1153/001-002/DC

This module reflects the scientific discussion for the approval of Cloreto de potássio 0,15% + Cloreto de sódio 0,9% Kabi . The procedure was finalised at 25-06-2014. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Fresenius Kabi Deutschland GmbH.has applied for a marketing authorisation for Cloreto de potássio 0,15% + Cloreto de sódio 0,9% Kabi and Cloreto de potássio 0,3% + Cloreto de sódio 0,9% Kabi containing Potassium Chloride & Sodium Chloride as active substances in PT and BE, EE, ES, FR, IE, IT (just for strenght 02), LT, LV, NL, PL, SI and UK.

Cloreto de potássio 0,15% + Cloreto de sódio 0,9% Kabi and Cloreto de potássio 0,3% + Cloreto de sódio 0,9% Kabi are indicated for the prevention and treatment of potassium depletion and/or hypokalaemia, in sodium chloride and water-losing conditions.

This application concerns a generic application claiming essential similarity with the reference product is "Potassium Chloride 0.15 % w/v & Sodium Chloride 0.9 % Solution for Infusion BP" and "Potassium Chloride 0.3 % w/v & Sodium Chloride 0.9 % Solution for Infusion BP" (Baxter)). , registered 2004-04-19 by Baxter Healthcare Ltd.

The marketing authorization was granted nationally on 08-08-2014 based on Directive 2001/83/EC article 10.1 (a) (iii) first paragraph.

This type of application refers to information that is contained in the pharmacological-toxicological and clinical part of the dossier of the authorisation of the reference product. A reference product is a medicinal product authorised and marketed on the basis of a full dossier, i.e. including chemical, biological, pharmaceutical, pharmacological-toxicological and clinical data. This information is not fully available in the public domain. Authorisations for generic products are therefore linked to the 'original' authorized medicinal product, which is legally allowed once the data protection time of the dossier of the reference product has expired. For this kind of application, it has to be demonstrated that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the reference product. This generic product can be used instead of its reference product.

II. QUALITY ASPECTS

II.1 Introduction

Cloreto de potássio 0,15% + Cloreto de sódio 0,9% Kabi and Cloreto de potássio 0,3% + Cloreto de sódio 0,9% Kabi are clear and colourless solutions, free from visible particles, with osmolarity of 348 (strength 01) or 388 (strength 02) mOsm/l (approx.) and pH between 4.5 and 7.0.

The solution is available in 500 ml and 1000 ml low-density polyethylene bottles as primary packaging closed with a polyolefin cap containing a polyisoprene rubber stopper. It is supplied in packs of 10 bottles.

The excipients are:
Water for injections, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment)

II.2 Drug Substances

KCl and NaCl

The active substances KCl and NaCl are in line with requirements of current edition of European Pharmacopoeia.

II.3 Medicinal Product

The documentation provided complies with relevant EU guidelines and directives. Manufacture is performed in accordance with cGMP and consistency in quality and homogeneity is demonstrated.

The finished product specification is based on relevant development and stability studies. The development of the product has been described, the choice of excipients is justified and their functions explained.

Appropriate validation data have been provided for the analytical methods. Batch analyses data support the proposed finished product specification.

Stability studies were performed in line with the ICH guidance.

The proposed shelf-life of 30 months, without any special storage conditions for the drug product is considered acceptable. After the first opening, the solution should be used immediately.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of KCl and NaCl are well known. As KCl and NaCl arewidely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. An overview based on literature review is, thus, appropriate.

IV. CLINICAL ASPECTS

No bioequivalence study has been performed. According to the Appendix II of the "Guideline on The Investigation of Bioequivalence", the bioequivalence studies are generally not required if the test product is to be administered as an aqueous intravenous solution containing the same active substance as the currently approved product. The applicant proposed to waive the bioequivalence study and it was accepted.

Pharmacovigilance System

Fresenius Kabi runs a Global Pharmacovigilance System according to European and US-American standards. The vigilance system is run by the co-operation of local and corporate safety officers and Pharmacovigilance Competence Centers. The applicant has provided a Summary of the Pharmacovigilance System that includes a set of documents, namely: a signed statement appointing an European Union Qualified Person Responsible for Pharmacovigilance (EU-QPPV) signed by the applicant and the qualified person for pharmacovigilance – Marcus Metternich (MSc) and contact details of the EU-QPPV: Oberursel Germany; a signed statement appointing a Deputy QPPV– Dr. Hans.-Joachim Gamperl (DVM) and Dr. Elvira Madel (MD); reference where the Pharmacovigilance System Master File (PSMF) for the medicinal product is kept (Fresenius Kabi Global Vigilance Department, Oberursel, Germany.) and its access commitment by the MAH to EU QPPV; a signed statement confirming the acceptance of the obligations of the QPPV and obligations of the Marketing Authorisation Holder outlined in EU Directive 2001/83/EC as amended; a signed statement confirming that the necessary means for the collection and notification of any adverse reaction occurring either in the Community or in a third country are in place.

Risk Management Plan

Risk Management Plan - Version and Date: Version 1 -27 Jun 2013
No additional risk minimization measures are planned. The Marketing Authorisation Holder considers that the proposed routine risk minimization activities are sufficient to address all safety concerns. The applicant has provided a description of the risk management system in line with current template requirements (November 2012). RMS agrees with the identified safety concerns and with the proposed pharmacovigilance and risk minimization activities.
.

User testing
The readability of the package leaflet was successfully demonstrated.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The application for Cloreto de potássio 0,15% + Cloreto de sódio 0,9% Kabi and Cloreto de potássio 0,3% + Cloreto de sódio 0,9% Kabi contain adequate quality, non clinical and clinical data and the bioequivalence has been shown. A benefit/risk ratio comparable to the reference product can therefore be concluded.