COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Betadine alcohol 200 mg/2.88 ml, impregnated dressing

(povidone iodine/ethanol 96%)

NL Licence RVG 125091

Date: 22 January 2021

This module reflects the scientific discussion for the approval of Betadine alcohol 200 mg/2.88 ml, impregnated dressing. The marketing authorisation was granted on 1 July 2020. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Medicines Evaluation Board (MEB) of the Netherlands has granted a marketing authorisation for Betadine alcohol 200 mg/2.88 ml, impregnated dressing from Mylan Healthcare B.V.

The product is indicated for preoperative disinfection of skin and hands. Disinfection of intact skin prior to injections, incisions and infusions.

A comprehensive description of the indications and posology is given in the SmPC.

This national procedure concerns a change to an existing marketing authorisation. It is a line extension to Betadine alcohol solution for cutaneous use 50 mg/ml / 0.72 ml/ml (NL Licence RVG 22302) which was authorised in the Netherlands on 13 September 1999. The marketing authorisation holder is Mylan Healthcare B.V.

The MAH confirmed that no changes to the manufacturing process and/or control of the manufacturing process of the solution have been made in this dossier. The MAH indicated that there is no difference between the Betadine alcohol solution for cutaneous use and the alcoholic betadine solution used to prepare the final drug product Betadine alcohol impregnated dressing.

In line with the MAH's formulation Betadine alcohol solution for cutaneous use 50 mg/ml / 0.72 ml/ml, the marketing authorisation has been granted pursuant to Article 8(3) of Directive 2001/83/EC.

II. QUALITY ASPECTS

II.1 Introduction

Betadine alcohol 200 mg/2.88 ml is a non-woven dressing (13 cm x 13 cm), folded several times, impregnated with a brown solution with alcoholic odour. Each impregnated dressing contains 200 mg povidone iodine and 2.88 ml ethanol 96%.

The impregnated dressing is packed in a multi-layer laminate (polyinert-aluminum-polyamide-paper) sachet.

The excipients are:
impregnating solution - macrogol lauric ether, glycerol 85% (E422), purified water.

The non-woven gauze is made of viscose and polyester (0.8 g).

II.2 Drug Substances

The active substances povidone iodine and ethanol 96% were already assessed and approved upon authorisation of Betadine alcohol solution for cutaneous use 50 mg/ml / 0.72 ml/ml. Both drug substances are described in the European Pharmacopoeia (Ph.Eur.).

II.3 Medicinal Product

Pharmaceutical development

The development of the product has been described, the choice of excipients is justified and their functions explained. The product is a dermatological antiseptic and disinfectant. The choices of the packaging and manufacturing process are justified. The solution as such was already approved. No changes to the manufacturing process and/or control of the manufacturing process of the solution have been made in this dossier.

The impregnating volume of the dressings allowing impregnation of the support sufficient and without excess of solution: the quantity of 4 ml of solution impregnating the support was determined in order to obtain a sufficient impregnation of the dressing and without excess. This volume of solution corresponds to 200 mg of povidone iodine.

The dressing is a neutral support for the impregnating solution. There is no interaction between the impregnation solution and the support, as shown in a conducted interaction study. The physical chemical and biological properties of the Betadine alcohol 200 mg, impregnated dressing have not changed in comparison with the Betadine alcohol solution.

Manufacturing process

The impregnated dressing are manufactured by preparing the alcoholic betadine solution and transferring the solution by automated machine to the non-woven material. The manufacturing process has been adequately validated according to relevant European guidelines. Process validation data on the product has been presented for 2 pilot-scale batches. Process validation for full-scale batches will be performed post authorisation.

Control of excipients

The excipients comply with Ph. Eur. requirements where applicable, or with other relevant compendial requirements. These specifications are acceptable. The specification of the gauze is based on the Ph.Eur. monograph n° 0034 “viscose wadding, absorbent”. The specifications are acceptable.

Quality control of drug product

The product specification includes tests appearance, identity, assay, average mass and microbiological quality. The analytical methods have been adequately described and validated. Batch analytical data from the proposed production site have been provided on 2 pilot-scale batches, demonstrating compliance with the release specification.

Stability of drug product

Stability data on the product has been provided 2 pilot-scale batches packaged in the proposed container closure system and 3 pilot-scale batch produced with a slightly different

gauze and sachet composition. The batches were stored at 25°C/60% RH (18 and 24 months respectively) and 30°/65% RH (12 months) and 40°C/75% RH (6 months). The conditions used in the stability studies are according to the ICH stability guideline. Under long-term, intermediate and accelerated conditions all batches remain within specification for 24 months. A shelf-life of 2 years, if stored below 25°C in polyinert-aluminum-polyamide-paper sachet, is acceptable in view of the available stability data.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the MEB considers that Betadine alcohol 200 mg/2.88 ml, impregnated dressing has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.
No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Betadine alcohol 200 mg/2.88 ml, impregnated dressing is expected to replace existing products containing the same active substances, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

This product is a line extension to Betadine alcohol solution for cutaneous use 50 mg/ml / 0.72 ml/ml which is authorised in the Netherlands. Reference is made to the preclinical data obtained with this formulation.
A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the MEB agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Risk Management Plan

The MAH submitted a statement on the absence of a Risk Management Plan. This application concerns a line extension of an active ingredient with a well-known safety profile that has been in use for many years. No change to the list of safety concerns or no new additional pharmacovigilance activity or risk minimisation activity is needed. The MEB agrees that, in line with Good Pharmacovigilance Practices (GVP), no RMP is required in the context of this line extension application and that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for Betadine alcohol 200 mg/2.88 ml, impregnated dressing.

IV.2 Discussion on the clinical aspects

For this line extension authorisation, reference is made to the clinical dossier of Betadine alcohol solution for cutaneous use. Povidone iodine and ethanol are well-known active substances with established efficacy and tolerability. The MEB agreed that no new clinical studies were conducted. Risk management is sufficiently addressed.

V. USER CONSULTATION

A user consultation with target patient groups on the package leaflet (PL) has been performed on the basis of a bridging report making reference to the approved PL for Betadine 5 % alcoholic solution. The route of administration for both products is identical and the safety information is the same. The class of medicinal product is identical. Betadine 5 % alcoholic solution is not subject to medical prescription and Betadine impregnated dressing is also intended for sale without medical prescription. The bridging report submitted by the MAH has been found acceptable; bridging is justified for both content and layout of the leaflet.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Betadine alcohol 200 mg/2.88 ml, impregnated dressing has a proven chemical-pharmaceutical quality and is a legitimate line extension to Betadine alcohol solution for cutaneous use. Betadine alcohol solution is a well-known medicinal product with an established favourable efficacy and safety profile. No new preclinical or clinical studies were required.

The Board followed the advice of the assessors. The MEB, on the basis of the data submitted, has granted a marketing authorisation. Betadine alcohol 200 mg/2.88 ml, impregnated dressing was authorised in the Netherlands on 1 July 2020.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Scope	Type of modification	Product Information affected	Date of end of the procedure	Approval/ non approval	Summary/ Justification for refuse