

Public Assessment Report

Scientific discussion

Ketamin Abcur
(ketamine)

SE/H/1498/01-02/DC

This module reflects the scientific discussion for the approval of Ketamin Abcur. The procedure was finalised on 2015-12-22. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

The application for Ketamin Abcur, 10 mg/ml, 50 mg/ml, solution for injection, is a generic application made according to Article 10(1) of Directive 2001/83/EC. Abcur AB applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI and NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Ketalar, 10 mg/ml, solution for injection, authorised in SE since 1973, with Pfizer AB as marketing authorisation holder.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

Ketamine has a bioavailability of 90 % following intramuscular administration. Ketamine is rapidly absorbed following parenteral administration. Plasma protein binding is around 50%. Ketamine has a biphasic plasma profile with a distribution phase lasting about 45 minutes with a distribution half-life of 10-15 minutes. Ketamine is metabolised in the liver. The terminal half-life is around 80 minutes in adults and slightly shorter in children.

No bioequivalence study has been submitted. The applicant claims that a bioequivalence study is not necessary according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1) since the product is a parenteral solution.

The applied product can be administered intravenously or intramuscularly.

The applied product contains the same active substance in the same concentration as the currently authorised product, and none of the excipients are known to interact with the drug substance. Thus, the RMS concludes that regarding the intravenous use no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1).

Regarding the intramuscular use the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1) states that no bioequivalence studies are required for other parenteral routes, if the test product is of the same type of solution (aqueous or oily), contains the same concentration of the same active substance and the **same excipients in similar amounts** as the medicinal product currently approved. Moreover, a bioequivalence study is not required for an aqueous parenteral solution with **comparable excipients in similar amounts**, if it can be demonstrated that the excipients have no impact on the viscosity. In this case, the excipients differ between the test and reference product, since the reference product contains the preservative benzethonium chloride which is not included in the applied product. This difference is however not considered likely to affect the viscosity of the solution and thus the absence of bioequivalence studies is considered justified.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

IV.3 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Ketamin Abcur.

Table 1. Summary of safety concerns.

Summary of safety concerns	
Important identified risks	• Elevation of blood pressure • Hepatic impairment

Important potential risks	None
Missing information	• Use in pregnancy • Use in breastfeeding

Pharmacovigilance Plan

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

V. USER CONSULTATION

User consultation

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was Finnish.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of Ketamin Abcur is found adequate. There are no objections to approval of Ketamin Abcur 10 mg/ml, 50 mg/ml, solution for injection.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The Mutual recognition/Decentralised procedure for Ketamin Abcur, 10 mg/ml, 50 mg/ml, solution for injection, was positively finalised on 2015-12-22.

Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)