Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Azaporc 40 mg/ml

Solution for Injection for Pigs

Date: 09 February 2022

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0330/001/DC
Name, strength and pharmaceutical form	Azaporc 40 mg/ml Solution for Injection for Pigs
Applicant	Serumwerk Bernburg AG Hallesche Landstraße 105 b 06406 Bernburg Germany
Active substance(s)	Azaperone
ATC Vetcode	QN05AD90
Target species	Pig
Indication for use	A neuroleptic sedative: 1) For the use in animals with aggressive behaviour - following re-grouping - in sows (devouring of piglets) 2) For the use in animals with stress and prevention of stress - cardiovascular stress - transport-related stress 3) Obstetrics 4) Premedication for local or general anaesthesia 5) For palliative use in animals with nutritional muscular dystrophy.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	18 May 2020
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure CMS 1st Repeat Use CMS 2nd Repeat Use	AT BE, DK, ES, FR, IE, IT, NL, UK(NI) BG, CZ, HU, PL, PT, RO, SK

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.
The safety and efficacy aspects of this product are identical to Stresnil Injektionslösung für Schweine (authorisation number: 6762247.00.00, Lilly Deutschland GmbH). The initial application for Stresnil Injektionslösung für Schweine was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 40 mg /ml azaperone for veterinary use as active substance and the excipients sodium metabisulfite, methyl parahydroxybenzoate, propyl parahydroxybenzoate, tartaric acid, sodium hydroxide and water for injections.

The product is packaged in 100 ml clear glass vial (Ph.Eur. type II) closed with a siliconised bromobutyl rubber stopper (Ph. Eur. type I) and sealed with an aluminium-plastic cap.

The choice of the formulation and the presence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is azaperone for veterinary use, an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

D. <Control on intermediate products>

Not applicable.

E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

The claim of a 28 days stability after broaching is based on the demonstration of stability for a batch broached and stored 28 days at 25 °C.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13(1) of Directive 2001/82/EC, as amended, and bioequivalence with a reference product has been demonstrated, results of safety tests are not required.

Warnings and precautions as listed on the product literature are essentially the same as those of the reference product, some product-specific and further adjustments have been introduced to explicitly address pregnant and breastfeeding users and to be in line with current guidelines. The warnings and precautions are adequate to ensure safety of the product to users, the environment, and consumers.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the initial predicted environmental concentration in soil (PECsoil,

initial = 17.38 µg/kg) is less than 100 µg/kg. The medicinal product Azaporc 40mg/ml will not pose a risk for the environment when used in accordance with the SPC.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted as this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product is proven.

MRLs

Azaperone is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active Substance	**Marker residue**	**Animal Species**	**MRL**	**Target Tissues**	**Other Provisions**	**Therapeutic Classification**
Azaperone	Sum of azaperone and azaperol	Porcine	100 µg/kg 100 µg/kg 100 µg/kg 100 µg/kg	Muscle Skin and fat Liver Kidney	NO ENTRY	Agents acting on the nervous system/Agents acting on the central nervous system

All excipients are included either in Table 1 of the Annex of Commission Regulation (EU) No 37/2010 with a “No MRL required” status for all food producing species or in the “Out of scope list”.

Withdrawal Periods

Based on the outcome of referral procedure EMEA/V/A/138, a withdrawal period of 18 days for meat in pigs is justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13(1) of Directive 2001/82/EC, as amended, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product. The product literature has been updated as requested by the RMS and CMS.

IV.A Pre-Clinical Studies

This is a generic application according to Article 13(1) of Directive 2001/82/EC, as amended. The reference and the generic product are aqueous solutions for intramuscular injection. They are comparable in terms of the qualitative and quantitative composition of the active substance and excipients and the pharmaceutical form. Therefore, exemption from need to demonstrate bioequivalence *in vivo* according to section 7.1 b of the Guideline for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMEA/CVMP/016/00-Rev. 2) is justified and data on pharmacodynamics, pharmacokinetics or target animal tolerance are not required. The pharmacodynamics and pharmacokinetic properties of the product are properly reflected in the SPC in line with the reference product.

Tolerance in the Target Species of Animals

The product literature accurately reflects the adverse effects which might be expected.

IV.B Clinical Studies

Since this is a generic application according to Article 13(1) of Directive 2001/28/EC as amended, and bioequivalence is established, no data on clinical efficacy are required.

V. OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
DE/V/0330/II/003/G - Variation to harmonise the quality dossier and the product information texts between the original and new CMS following a repeat use procedure: • Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits • Change in the specification parameters and/or limits of the finished product - Tightening of specification limits • Change in test procedure for the finished product - Minor changes to an approved test procedure • Harmonization of the product information texts (Type II C.I.z)	II/A	14.07.2021

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated in Module 3**	**Approval date**
DE/V/0330/001/IA/002 – Variation to implement the outcome of the referral procedure EMEA/V/A/138	IIIB	13.11.2020