IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

CONTINENCE 40 mg/ml syrup for dogs

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

PRODUCT SUMMARY

EU Procedure number	IE/V/0446/001/DC
Name, strength and pharmaceutical form	Continence 40 mg/ml syrup
Active substance(s)	Phenylpropanolamine hydrochloride
Applicant	SUPPORT PHARMA, S.L., General Álvarez de Castro 39 - 28010 Madrid Spain
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation/ completion of procedure	09/07/2019
Target species	Dogs
Indication for use	For the management of urinary incontinence associated with urethral sphincter incompetence in the bitch, particularly that associated with ovariohysterectomy.
ATCvet code	QG04BX91
Concerned Member States	UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.
The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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.
It has been shown that the product can be safely used in the target species; the slight reactions observed are indicated in the SPC.
The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains 40.28 mg/ml of the active moiety phenylpropanolamine, as phenylpropanolamine hydrochloride, and the excipient liquid sorbitol (non-crystallising).
The container/closure system is 50 ml high-density polyethylene (HDPE) bottles with a low-density polyethylene (LDPE) dosing syringe adaptor and a child-proof screw-cap in polypropylene and polyethylene, and a 1.5 ml LDPE/polystyrene dosing syringe.

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 for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is phenylpropanolamine hydrochloride, an established 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 has been provided.

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

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

F. Stability

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

G. Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This application has been submitted in accordance with paragraph 1 of Article 13 of Directive 2001/82/EC, as amended, (a generic application). The reference product cited in this application is Propalin syrup 40 mg/ml, containing phenylpropanolamine.

The safety aspects of this product are considered to be identical to that of the reference product. Warnings and precautions as listed on the product literature are in line with those approved for the reference product.

III.A Safety Testing

Pharmacological Studies

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application and therefore data on pharmacodynamics are not required.
The applicant claims exemption from the requirement to conduct bioequivalence studies in accordance with paragraph 7.1(d) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016/00-Rev.2). Paragraph 7.1(d) of the guideline permits exemption from the requirement for bioequivalence studies where;

"*the formulations are identical (identical active substances and excipients as well as physicochemical properties [e.g. identical concentration, dissolution profile, crystalline form, pharmaceutical form and particle size distribution with identical manufacturing process]).*"

Based on the argumentation and quality data provided by the applicant, the claimed exemption is accepted. Studies have been conducted to determine the composition of this product compared with that of the reference product and it was accepted that the results confirm that the products are comparable in terms of composition and physicochemical properties. Consequently, systemic availability of the active substance following administration of 'Continence 40 mg/ml' is assumed to be equivalent to that achieved following administration of the reference product "Propalin 40 mg/ml', with the result that it was accepted that 'Continence 40 mg/ml' and the reference product will have a similar safety and efficacy profile.
Hence bioequivalence can be assumed and *in vivo* bioequivalence studies are not required. Given that bioequivalence with the authorised reference product can be accepted and that the test product is intended to be administered to the same target species, using the same routes of administration at the same dose rates as already approved for the reference product, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials.

Toxicological Studies

As this application was submitted in accordance with paragraph 1 of Article 13 of Directive 2001/82/EC (as amended), i.e. a generic application. As bioequivalence with a reference product is accepted, results of toxicological tests are not required.
The safety aspects of this product are expected to be identical to those of the reference product.
Warnings and precautions as listed on the product literature are broadly in line with those of the reference product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that that the product does not present any greater risk to the user than that presented by the reference product. The proposed user safety statements are broadly in line with those of the reference product and are acceptable.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:

Phenylpropanolamine hydrochloride is toxic when overdoses are ingested. Adverse effects may include dizziness, headache, nausea, insomnia or restlessness, and increased blood pressure. Accidental ingestion by a child may be fatal.
To avoid accidental ingestion, the product must be used and kept out of sight and reach of children. Always replace the cap securely after use and store the syringe and bottle inside the cardboard box at all times.
In case of accidental ingestion, seek medical attention immediately and show the package leaflet or the label to the physician.
In the event of accidental skin contact, wash the contaminated area with soap and water. Wash hands after use of the product.
In the event of accidental eye contact, rinse the eye with clean water for about 15 minutes and seek medical advice.

Environmental Risk Assessment

Phase I

The environmental risk assessment can end at Phase I and no Phase II assessment is required because the product will only be administered to non-food producing animals (dogs). **Conclusion**
Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT

As this is a generic application submitted in accordance with paragraph 1 of Article 13 of Directive 2001/82/EC, as amended, and exemption from the requirement to demonstrate bioequivalence with the reference product has been satisfactorily justified, safety and efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product. In addition, it is considered that the risk to the target species will be similar for both the test and the reference products. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

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.

VI. 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 HPRA website.
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.

Changes:
None.