IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Somulose Solution for Injection

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Somulose solution for injection
Active substance(s)	Secobarbital sodium
Applicant	Dechra Regulatory B.V., Handelsweg 25, 5531 AE Bladel, Netherlands
Legal basis of application	Bibliographical application in accordance with Article 13 (a) of Directive 2001/82/EC as amended.
Date of Authorisation	6th October 2006
Target species	Dogs, Cats, Horses and Cattle
Indication for use	Euthanasia
ATCvet code	QN05CB02

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

This section reflects the initial scientific discussion on the approval of Somulose. Please refer to section V for significant post-approval changes which are important for the quality, safety and efficacy of the product.

II. QUALITY ASPECTS

A.Qualitative and Quantitative Particulars

Composition of the Veterinary Medicinal Product

Active substances
Secobarbital Sodium 400 mg/ml
Cinchocaine Hydrochloride 25 mg/ml

Excipients
Propylene glycol
Boric acid
Potassium chloride
Isopropyl alcohol
Water for injection

Container/Closure System

30 ml and 50 ml amber type I Ph. Eur. glass vials with red chlorobutyl rubber bung and aluminium overseal.Fill volume for the 30 ml vial is 25 ml.The 50 ml vial is supplied with a 50 ml syringe, a 14 gauge cannula and a mini-spike dispensing adaptor.

The product is a solution for injection 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.

The product is manufactured using conventional manufacturing techniques.Satisfactory process validation has been provided.

C.Control of Starting Materials

Active Substance

The active substances are secobarbital sodium and cinchocaine hydrochloride, established substances. Secobarbital sodium is monographed in the USP and cinchocaine hydrochloride is monographed in the Ph. Eur.
The active substance specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with the specifications have been provided.

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

There are no substances of ruminant animal origin present or used in the manufacture of this product.

D.Control Tests During Production

Not applicable

E.Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the solution for injection. 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 Studies on the Active Substance

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

Stability Tests on the Finished Product

Stability data on the 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.

G.Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

Precise Identification of the Product concerned by the Application

The product is a solution for injection containing 400mg/ml of Secobarbital (Quinalbarbitone) sodium, and 25 mg/ml of Cinchocaine hydrochloride.

Pharmacological Studies

Secobarbital is a hypnotic derivative of barbituric acid which suppresses the central nervous system leading to rapid loss of consciousness and inhibiting the centres controlling respiration. Cinchocaine, an amide local anaesthetic, has a specific action on sodium channels and is directly cardiotoxic, rapidly leading to hypotension and cardiac arrest.

Pharmacodynamics

Secobarbital has a rapid onset of action, which profoundly depresses the central nervous system, including the respiratory centres. Barbiturates also affect the peripheral nervous system. Cinchocaine has marked cardiotoxic effects at high doses.When given in combination the barbiturate produces rapid loss of consciousness and cessation of respiration while the cinchocaine depresses cardiac conduction resulting in early cardiac arrest.

Pharmacokinetics

Secobarbital reaches effective drug concentrations in the brain following intravenous administration within a matter of seconds in dogs, cats and horses.

Toxicological Studies

The product is toxic in laboratory species in high doses as expected.

Single Dose Toxicity

LD50 for secobarbital in mice following intravenous administration is 100mg/kg.

Repeated Dose Toxicity

No data available.

Reproductive Toxicity, including Teratogenicity:

No information is available on the reproductive toxicity of quinalbarbitione and cinchocaine.

Mutagenicity

No data available.

Carcinogenicity

No data available.

Studies of other effects

Special Studies

Cinchocaine, like other local anaesthetics, may cause a skin sensitizing effect.

Data are provided which demonstrate that if carcasses are consumed following euthanasia of an animal with Somulose, marked effects, including death, can be seen in the animals consuming the carcass. These data validate the SPC, productlabel and carton warning: 'It is strongly recommended that carcasses of animals euthanized

with Somulose are incinerated'. It is also noted that barbiturates may survive the effects of rendering carcasses.
Somulose is an euthanasia product and is not indicated for use in food-producing animal species.

Observations in Humans

50-250 mg secobarbital will induce sleep in adults. The minimum human lethal dose of Secobarbital is estimated at about 2g (approx 5 ml of Somulose). Human fatalities have been reported following intravenous injection.
Concerning cinchocaine, oral ingestion of doses of 15 mg/kg have been fatal in humans.

Microbiological Studies (studies on human gut flora and organisms used in food processing)

Not relevant.

Studies on Metabolites, Impurities, Other Substances and Formulation.

Not relevant.

User Safety

A user safety assessment of the product shows that the principle route of human exposure is that of accidental self-injection, although splashing and contamination of skin or eyes and inhalation of aerosol droplets could also occur during filling of a syringe or administration to an animal. Somulose is restricted for use by Veterinary Practitioners only which limits the use of the product to trained operatives.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

A Phase 1 environmental risk assessment concludes that no further assessment is required.
Warnings and precaution as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV. CLINICAL ASSESSMENT

IV.APre-Clinical Studies

Pharmacology

Data have been provided which show that Somulose is an effective euthanasia agent, resulting in smooth collapse and rapid death.

Tolerance in the Target Species of Animals

Somulose is an euthanasia product, therefore target species tolerance studies are not relevant to the application.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance
Not applicable.

IV.B Clinical Studies

Laboratory Trials
Not relevant.

Field Trials

Field studies and provided bibliographical data show that the product is effective for the indication claimed. In a study doses of 1 ml/4 kg intravenously in dogs caused death within 33 seconds (loss of consciousness within 17 seconds) and 12 seconds in cats (loss of consciousness within 6 seconds). In horses, 1ml/10kg caused death within 70 seconds (loss of consciousness within 20 seconds). Only a small proportion of animals appeared to suffer pain with the majority suffering no pain (84%) or only slight pain (97%), no side effects or only slight side effects (91%).The product was judged either satisfactory or excellent in 98% of cases by the presiding veterinary surgeons.
A further field study concludes that the optimal dosage is 1 ml/10kg in horses and the administration of the product should be administered over a period of 10-15 seconds.
In a report on field use of the product in nine dairy cows, it was reported that *'following Somulose injection there was a lag period of about eight seconds before the animal rapidly lost consciousness and became flaccid… In all cases slaughter appeared humane, without suffering or discomfort'.* In a further study on 43 cattle administered a dose rate of 1ml/20kg, euthanasia was rapid and without complications in most cases.

V. OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

Somulose contains secobarbital sodium and cinchocaine hydrochloride in a non-sterile liquid comprising standard pharmaceutical constituents. As the indication is for euthanasia, the non-provision of standard pharmacological and toxicity studies is justified. The applicant has shown the product is efficacious for the target species. The main risk is for the human operator using the product but this is adequately addressed by label warnings and by the restriction on use of the product to veterinary surgeons. There are additional risks relating to relay consumption of carcasses of animals treated with Somulose.However, if followed, the label warnings are adequate to prevent this. The environmental impact for use of the product is positive, it being understood that animals which receive the product are incinerated and not buried.

VI. POST-AUTHORISATION ASSESSMENTS

Not applicable.