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)

MUTUAL RECOGNITION PROCEDURE

Draft

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Compagel gel for horses

Date: 14 October 2008

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0121/001/MR
Name, strength and pharmaceutical form	Compagel Gel for Horses
Applicant	Boehringer Ingelheim Vetmedica GmbH Binger Str. 173 55218 Ingelheim Germany
Active substance(s)	Heparin sodium Levomenthol Hydroxyethyl salicylate
ATC Vetcode	QM02AC99
Target species	Horses
Indication for use	For the treatment of local inflammatory swellings and bruising, including tendonitis, tenosynovitis, bursitis and other acute inflammatory conditions of the musculo-skeletal system in the horse. Compagel also promotes the early reabsorption of haematoma and oedematous swelling resulting from such conditions.

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MODULE 2

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

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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 Mutual recognition procedure	26 October 2007
Date product first authorised in the Reference Member State (MRP only)	31 May 2003
Concerned Member States for original procedure	Denmark, France, The Netherlands, Sweden, United Kingdom

I. SCIENTIFIC OVERVIEW

The safety and efficacy aspects of this product are identical to Tensolvet 50000 (BVL authorisation number 15923.00.00). The initial application for Tensolvet 50000 was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

II. QUALITY ASPECTS

A. Composition

The product contains heparin sodium, hydroxyethyl salicylate and levomenthol as active ingredients and the excipients macrogolglycerol cocoate, propylene glycol, carbomer 980, copper complexes of chlorophylls and chlorophyllins (E 141), trolamine, isopropyl alcohol, and purified water.

The container/closure system is a polyethylene tube with screw closure with tilting cover. The particulars of the containers and controls performed are provided and conform to the regulation.

The product is an established pharmaceutical form and the choice of the formulation is justified.

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B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from 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 substances, heparin sodium, hydroxyethyl salicylate and levomenthol, are established active substances described in the European Pharmacopoeia. They are manufactured in accordance with the principles of good manufacturing practice.

The specifications of the active substances are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with the specifications have been provided.

Both for heparin sodium and levomenthol reference is made to the certificates of suitability issued by the EDQM[1].

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

There are no substances within the scope of the TSE[2] Guideline present or used in the manufacture of this product.

E. Control on intermediate products

There are no intermediate products.

F. 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.

[1] European Directorate for the Quality of Medicines & HealthCare
[2] Transmissible Spongiform Encephalopathy

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G. Stability

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 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 3 months stability after broaching is based on the demonstration of stability for a batch broached and stored for up to 6 months at +25°C.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

As this is a generic application according to Article 13 of Directive 2001/82/EC based on the essential similarity of Compagel and the reference product Tensolvet 50000, results of pharmacological and toxicological tests are not required.

The applicant has made full reference to the SPC of the reference product Tensolvet 50000 granted in Germany. However, as this was not completely identical to the SPCs authorised for this product in other concerned member states, efforts have been made during the mutual recognition procedure to produce a harmonised overall accepted product literature for Compagel. Warnings and precautions as listed in the product literature are adequate to ensure safety of Compagel to the user and the environment.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. No warnings are therefore required.

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III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because this is a generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended based on the essential similarity of the reference product Tensolvet 50000.

MRLs

The pharmacologically active constituents of Compagel (heparin, hydroxyethyl salicylate, levomenthol) are listed in Annex II of Council Regulation (EEC) No 2377/90 for all food producing species.

Active Substances	**Annex CR2377/90**	**Species**	**Remarks**	**Date of publication[1]**
Heparin and its salts	II	All food producing species		*O.J. L290, 05/12/95*
Hydroxyethyl salicylate	II	All food producing species except fish	For topical use only	*O.J. L264, 01/10/02*
Levomenthol	II	All food producing species		*O.J. L170, 08/07/96*

[1]Official Journal of the European Union

Withdrawal Periods

Based on the essentially similar composition and the same topical use between the generic and the reference product a withdrawal period of 0 days for meat and offal of horse was set.
Compagel do not use in pregnant and lactating animals which are intended to produce milk for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with the reference product Tensolvet 50000 can be assumed, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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IV. A Pre-Clinical Studies

Tolerance in the Target Species of Animals

As bioequivalence with the reference product Tensolvet 50000 can be assumed no new target species tolerance data have been presented.
The applicant provided a translation of the study of Feldmann (1989)[3]. In this study horses received under bandage treatment with a gel comparable to the reference product for 8 days on the shorn metacarpus of one leg. No significant changes in blood clotting times or plasma heparin levels have been detected.
The applicant presented periodic safety update reports, no SADR[4]s were reported, and it was concluded that the use of Compagel is well tolerated under field conditions.

IV.B Clinical Studies

As bioequivalence with the reference product, Tensolvet 50000, can be assumed and Compagel should be used for the treatment of the same indications in horses and under the same conditions as Tensolvet, the applicant is exempted from providing efficacy data. The reference product has been authorized at a time when no public assessment report has been required. Therefore no such information can be provided by the German authority.

CONCLUSION AND BENEFIT-RISK ASSESSMENT

The product literature is deemed acceptable and is in line with that authorized for the reference product, Tensolvet 50000. This is a generic application. The reference product and its generic Compagel have been authorized in Germany for several years. Comparable products have been authorized in other European member states. No adverse drug reactions were reported for a reflected period of 3 years where considerable quantity of packages of Compagel (assumed treatments) had been sold. In conclusion the risk-benefit profile for the horse is considered favourable.

[3] Blutgrinnungsanalytische Untersuchungen nach kutaner Heparinapplikation beim Pferd, Inaugural-Dissertation zu Erlangung des Grades eines Doctor Medicinae Veterinariae durch die Tierärztliche Hochschule Hannover, Bibliothek Tierärztliche Hochschule Hannover, 1989
[4] Serious adverse drug reactions

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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.

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated in Module 3**	**Approval date**
Change of indications (DE/V/0121/001/II/001)	IV Module 1	24/07/2008

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