SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tri-Solfen cutaneous solution for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Lidocaine	40.6 mg (as 50 mg lidocaine hydrochloride monohydrate)
Bupivacaine	4.2 mg (as 5 mg bupivacaine hydrochloride monohydrate)
Adrenaline/Epinephrine	0.025 mg (as 0.045 mg adrenaline acid tartrate/epinephrine acid tartrate)
Cetrimide	5.0 mg

Excipients:

Sodium metabisulfite	0.045 mg
Brilliant blue FCF (E133)	0.05 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cutaneous solution.
Clear, blue, semi-viscous liquid with no visible particles.

4. CLINICAL PARTICULARS

4.1 Target species

Pig.

4.2 Indications for use, specifying the target species

Local anaesthesia during and following castration of piglets, and provision of castration wound antisepsis.

4.3 Contraindications

Do not administer in cases of hypersensitivity to any of the active substances or to any of the excipients.

4.4 Special warnings for each target species

For use in piglets up to 7 days of age.

The veterinary medicinal product will provide local anaesthesia within 30 seconds of application, with a duration of effect of approximately 1 hour. Additional analgesia or

anaesthesia should be considered, according to recognised veterinary practice. No data are available on concurrent use with other products (see also Section 4.8).

4.5 Special precautions for use

Special precautions for use in animals

In the clinical field trial, the product was not tested on piglets less than 3 days of age or weighing less than 1 kg. Use only according to the benefit-risk assessment by the responsible veterinarian.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Contact with skin or eyes can cause irritation and repetitive exposure can lead to allergic reactions. Pharmacological effects (i.e. local anaesthesia) are likely to occur in case of contact with the product.
Lidocaine and bupivacaine can form a metabolite (2,6-xylidine) in humans, which can induce carcinogenic effects at high doses in long-term toxicology studies in rats.
Avoid skin, eye or oral contact with the product. Wear disposable impermeable gloves when handling the product and treating animals.
In case of accidental spillage onto skin, wash off immediately with soap and water.
Avoid ingestion of and do not smoke or eat while handling the veterinary medicinal product.
In case of accidental ingestion, seek medical advice and show the package insert to the physician.
People with known hypersensitivity to any of the active substances or to any of the excipients (e.g., sodium metabisulfite) should administer the product with caution.
Exposure to this product whilst using another medicinal product which also contains a locally acting amide anaesthetic may cause cross sensitivity.
Wash hands thoroughly after use.

4.6 Adverse reactions (frequency and seriousness)

Mild, transient (5-11 days duration) application site inflammation was the most commonly reported adverse reaction in the clinical field trial. There was an isolated report of anaphylaxis in one piglet.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Not applicable

4.8 Interaction with other medicinal products and other forms of interaction

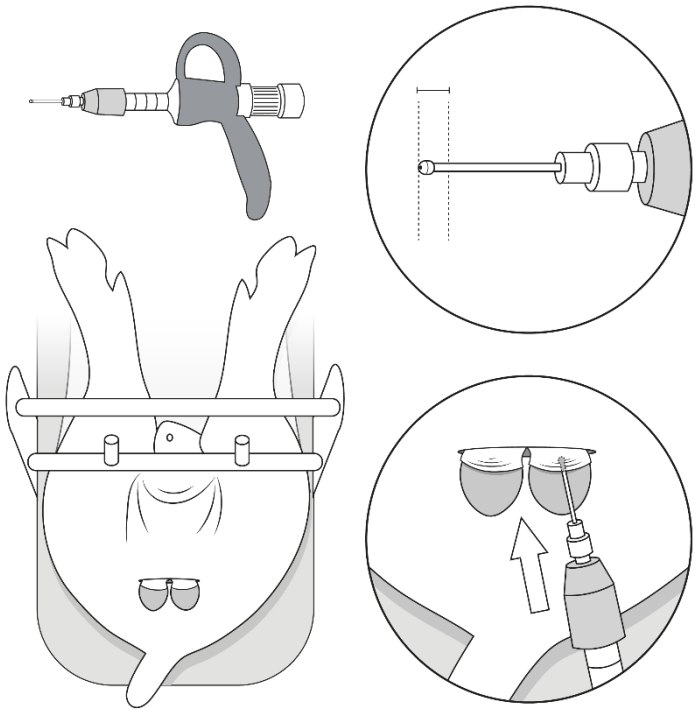
As no data are available on interactions, it is recommended not to apply other products to the castration site when using this product.

4.9 Amounts to be administered and administration route

For cutaneous use only.

<2 kg bw = 1 ml per piglet
2-4 kg bw = 2 ml per piglet

Assemble the applicator as directed below. Set the dose at 0.5 ml. Incise the scrotum and exteriorise the testis, exposing the spermatic cord. Instil 1 or 2 doses (depending on the bodyweight) of 0.5 ml to the opened scrotal sac, to fully coat the spermatic cord and the cut skin edge, then repeat for the other testicle. Wait 30 seconds before severing the spermatic cords.



Use of Applicator:
Connect the long nozzle to the dosing applicator. Connect the dosing applicator and draw-off tubing to the container as follows: Attach the tubing to the dosing applicator. Attach draw-off tubing to the spigot cap. Remove the screw cap and seal, replace with the spigot cap and draw-off tubing and check that they are firmly attached. Follow the dosing applicator manufacturer's directions for priming the application and for proper use and maintenance of the dosing applicator and draw-off tubing. The dosing applicator should be removed at the end of each day’s use of the product. Remove the spigot cap

and replace with screw cap, checking it is firmly attached. When the dosing gun is removed, expel any remaining product in it and clean according to the manufacturer's directions, before storage.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In a laboratory safety study in piglets, transient application site inflammation was seen following 3-fold and 5-fold overdose, but this was similar to that seen at the normal dose (see section 4.6). No other clinically relevant findings were seen after a five-fold overdose of Tri-Solfen was applied to the castration site.

4.11 Withdrawal period(s)

Zero days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anaesthetics for topical use; lidocaine, combinations
ATC vet code: QD04AB51

5.1 Pharmacodynamic properties

Lidocaine is an amide local anaesthetic agent which works by blocking the sodium channels in the neuronal cell membrane and other excitable cells. Lidocaine is characterized as having a fast onset of action, within 30 seconds of application to mucosal tissues.

Bupivacaine is also an amide agent that, like lidocaine, works by blocking ion channels to prevent nerve conduction. Bupivacaine has a slower onset of action when compared to lidocaine, but a longer duration of action (1 hour). Lidocaine in combination with bupivacaine results in an additive effect of both, with the rapid onset of action of lidocaine and the prolonged effect of bupivacaine.

Adrenaline (also known as epinephrine) is an endogenous catecholamine produced naturally by the medulla of the adrenal glands. It is a neurotransmitter with a sympathomimetic effect and is an agonist of alpha and beta-adrenergic receptors. The alpha-adrenergic stimulation leads to vasoconstriction. Topical adrenaline produces vasoconstriction at the treated site, counteracting the vasodilatory properties of the local anaesthetics. By reducing the rate of systemic absorption of the active substances, this results in prolonging the anaesthetic effect, minimising the risk of systemic toxicity, and helping produce haemostasis.

Cetrimide is an antiseptic (quaternary ammonium) and has the typical actions and uses of a cationic surfactant, binding strongly to skin and mucous membranes, but with weak percutaneous absorption. Cetrimide delivers its antiseptic effect by its surfactant effect on bacterial cytoplasmic membranes causing cellular lysis and leakage of cytoplasmatic contents.

5.2 Pharmacokinetic particulars

Lidocaine and bupivacaine distribution is extensive with the ability to cross the blood-brain and placental barriers, and can be found in milk. There is initial widespread distribution, particularly to highly perfused tissues including kidney, liver, lung and heart, followed by slower redistribution to muscle and fat. These local anaesthetics are eliminated more slowly from fat. Metabolism, through hydroxylation and alkylation via the P450 pathway, and (for lidocaine), amide hydrolysis via hepatic carboxylesterase enzymes, occurs rapidly in the liver with elimination via urine.
Adrenaline is poorly absorbed following topical administration. It is very rapidly metabolised by the liver with a plasma half-life of 2.5 minutes. It is metabolised by catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO) to inactive metabolites which are then excreted in the urine after conjugation with glucuronic acid or sulfates.
Cetrimide is poorly absorbed due to its cationic nature and binds strongly to the skin surface, mucosae and tissues. It is rapidly excreted in bile and faeces, mostly unmetabolised.
After application to piglet castration wounds, the following concentration (C_{max}) and time (T_{max}) of maximum levels in plasma of the active substances have been measured:

Parameter	Lidocaine	Bupivacaine	Cetrimide
C_{max} (µg/ml)	5.1	2.8	0.03
T_{max} (hours)	1.5	12	0.083

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulfite
Sodium hydroxide (for pH adjustment)
Sulfuric acid (for pH adjustment)
Sorbitol, liquid (crystallising)
Hydroxyethylcellulose
Citric acid (anhydrous)
Disodium edetate
Brilliant Blue FCF (E133)
Purified water

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 3 months

6.4 Special precautions for storage

Store below 25°C. Keep the container tightly closed in order to protect from light.

6.5 Nature and composition of immediate packaging

Induction-sealed high-density polyethylene containers with polypropylene caps, in a cardboard carton. Each bottle is supplied with a polypropylene spigot cap and (1 l or 5 l bottles only) low density polyethylene draw off tube.

Pack sizes of 250 ml, 500 ml 1 l or 5 l per container.
The product is supplied with a polypropylene/polyoxymethylene 1 ml applicator.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Dechra Limited
Snaygill Industrial Estate
Keighley Road
Skipton
North Yorkshire
BD23 2RW
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 10434/4100

9. DATE OF FIRST AUTHORISATION

25 January 2022

10. DATE OF REVISION OF THE TEXT

May 2024

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription.

Approved 18 May 2024
Gavin Hall