VELACTIS®

Product information

CONTENTS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Velactis 1.12 mg/ml solution for injection for cattle.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Cabergoline ..... 1.12 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear pale yellow solution.

4. CLINICAL PARTICULARS

4.1 | Target species

Cattle (dairy cows)

4.2 | Indications for use, specifying the target species

For use in the herd management programme of dairy cows as an aid in the abrupt drying-off by reducing milk production to:

- reduce milk leakage at drying off.
- reduce the risk of new intramammary infections during the dry period.
- reduce discomfort.

4.3 | Contraindications

Do not use in case of hypersensitivity to cabergoline or to any of the excipients.

4.4 | Special warnings for each target species

Velactis should be used as part of a comprehensive mastitis and milk quality control program under veterinarian advice, which might include the need to use intramammary treatment.

For cows considered likely to be free of subclinical mastitis at drying off, in which antibiotic use is not justified/permitted, Velactis can be used as a dry cow treatment. The cows should be diagnosed to be free of subclinical mastitis by using suitable criteria such as bacterial examination of milk, somatic cell count or other recognized tests.

In a multicentric randomized clinical trial where dairy cows with no intramammary infections at the time of drying-off were administered either Velactis or placebo at the time of drying-off, the incidence of new intramammary infections within 7 days after subsequent calving was significantly lower among udder quarters of cows treated with Velactis (20.5%) as compared to placebo (26.0%). The difference in percentage of new intramammary infections during the dry period between Velactis treated animals and the placebo group was 5.5% (95% confidence interval 0.5-10.4%). The efficacy of Velactis in reducing the risk of new intramammary infections during the dry period when administered concomitantly with antimicrobial treatment to cows with intramammary infections has not been investigated compared to antimicrobial treatment alone.

In the same study, incidence of milk leakage was significantly lower among Velactis treated animals (2.0%) as compared to placebo treated animals (10.7%). The difference between groups was 8.7% (95% confidence interval 4.9-12.6%). This was confirmed in another multicentric randomized clinical trial where incidence of milk leakage was significantly lower among Velactis treated animals (3.9%) as compared to placebo treated animals (17.6%). The difference between groups was 13.7% (95% confidence interval 6.4-21%).

In a randomized and placebo controlled clinical study Velactis treated cows presented less signs of udder pain in comparison with controls on the first two days after drying-off. The difference in occurrence of pain was 9.9% (95% confidence interval 4.0-15.8%) between the Velactis treated cows compared to placebo treated animals. In a randomized and placebo controlled clinical study, reduced discomfort was demonstrated during the first day after drying-off by increasing daily lying time by 143 +/- 17 minutes in Velactis treated animals in comparison with untreated controls.

4.5 | Special precautions for use

i Special precautions for use in animals

Normal aseptic procedures for administration of an intramuscular injection should be followed. Only use a dry sterile needle and avoid the introduction of humidity/water during use.

The product should only be used in dairy cows at the time of drying-off.

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

The veterinary medicinal product may cause skin sensitization. Persons with a known hypersensitivity to cabergoline or any of the excipients should avoid contact with the veterinary medicinal product. Administer the veterinary medicinal product with caution to avoid self-injection.

In case of accidental self-injection, seek medical advice, and show the package leaflet or the label to the physician. Wash hands after use.

Studies in laboratory animals have shown a risk for embryonic death following repeat oral exposure to cabergoline. In the absence of data on pregnancy outcome in humans following injection of cabergoline, pregnant women and women attempting to conceive should avoid contact with the product. Due to its pharmacological effect (inhibition of lactation) breastfeeding women should avoid contact with the product.

iii Other precautions

Cabergoline should not enter surface waters as it has harmful effects on aquatic species. Therefore, Velactis-treated cows should not be allowed to have access to open water, and should not contaminate watercourses with faeces until at least 5 days after administration.

4.6 | Adverse reactions (frequency and seriousness)

Slight injection site reactions (mostly swellings) were commonly observed after injection of the product and may persist for at least 7 days.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 | Use during pregnancy, lactation or lay

Can be used during pregnancy.

Velactis reduces milk production. Therefore, the product should only be administered to dairy cows at the time of drying-off.

4.8 | Interaction with other medicinal products and other forms of interaction

In vitro, some macrolide antibiotics, like erythromycin, inhibited the activity of bovine Cytochrom P 450-enzymes (CYP3A4-subclass). This could theoretically decrease the metabolisation of cabergoline, and prolong its persistence in plasma from cows treated concomitantly with Velactis and such products. However, administration of tylosin concomitantly with Velactis in cows did not show any changes of cabergoline pharmacokinetic properties.

4.9 | Amounts to be administered and administration route

Intramuscular use.

The recommended dose is 5.6 mg of cabergoline (corresponding to 5 ml of solution for injection) per animal in one single injection at the day of drying-off after the last milking. The product should be administered within 4 hours after the last milking.

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

Overdoses resulted in some cases in slight and transient decrease of appetite. This was observed following 1.5-2 times of the recommended dose and was more pronounced at higher doses. The administration of three or five times the recommended dose for 3 consecutive days (i.e. corresponding to 9 and 15 times the recommended dose, respectively) resulted in addition in some cases in transient and reversible digestive signs such as diarrhoea. At 9 times the recommended dose a decrease in ruminal activity may be observed. Fatal meteorism has been observed in a single cow following a second administration of 5 times the recommended dose. Three consecutive administrations of 1, 3 or 5 times the recommended dose may result in transient and reversible slight elevation of plasma glucose levels.

4.11 | Withdrawal period(s)

Meat and offal: 23 days

Milk:

- Zero hours after calving when the dry period length is 32 days or more.
- 4 days (8 milkings) after calving when the dry period length is less than 32 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Other gynaecologicals, prolactin inhibitors, cabergoline.
ATCvet code: QG02CB03.

5.1 | Pharmacodynamic properties

Cabergoline is a synthetic ergot derivative, which is a potent dopamine receptor agonist on D2 receptors. It acts on dopamine receptors of prolactin producing cells in the pituitary gland suppressing the prolactin production and leading to the inhibition of prolactin secretion dependent process. Consequently, cabergoline administration induces a reduction of milk production leading to a reduction in udder engorgement and intramammary pressure. Subsequently udder pain and discomfort are reduced at one and two days after drying off, respectively.

5.2 | Pharmacokinetic particulars

After intramuscular administration in cattle, the systemic absorption of cabergoline is rapid and important (bioavailability over 90%), with a peak concentration observed around 3 h after administration and followed by a high tissue distribution.
More than 74% of cabergoline is bound to plasma protein.
Cabergoline is rapidly metabolized principally by liver and is eliminated with a mean half-life of about 20h.
Approximately 66% of the administered dose is eliminated by faeces. Urine is the second pathway of elimination.

6. PHARMACEUTICAL PARTICULARS

6.1 | List of excipients

Dimethyl sulfoxide
Triglycerides, medium-chain

6.2 | Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

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: 28 days.

6.4 | Special precautions for storage

This veterinary medicinal product does not require any special storage condition.

6.5 | Nature and composition of immediate packaging

Brown glass vials closed by bromobutyl stoppers and crimped with aluminium and plastic flip capsules.

Pack sizes:
Cardboard box with 1 vial of 5 ml, 25 ml or 50 ml, or 5 vials of 5 ml.
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.
Velactis should not enter water courses as this may be dangerous for fish and other aquatic organisms.