SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Exflow 10 mg/g powder for use in drinking water for cattle (calves), pigs, chickens, turkeys and ducks

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:
Active substance:
Bromhexine..... 9.11 mg
(as bromhexine hydrochloride 10.00 mg)

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for use in drinking water
White to slightly beige powder

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (Calves), pigs, chickens, turkeys and ducks.

4.2 Indications for use, specifying the target species

Mucolytic treatment of congested respiratory tract.

4.3 Contraindications

Do not use in cases of pulmonary oedema.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
In case of serious lungworm infection, the drug should only be used 3 days after the commencement of the anthelmintic treatment.
In case of primary and/or secondary infection, the combination with antibiotics should be considered. When administered concomitantly with the product, antimicrobial agents should not be underdosed.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
This product may cause hypersensitivity reactions (allergy). People with known hypersensitivity to bromhexine or any of the excipients should avoid contact with the product.
This product may cause irritation to the skin, eyes and mucous membranes.
During preparation and administration, inhalation of dust particles should be avoided. Wear an appropriate dust mask (either a disposable half-mask respirator conforming to European Standard EN149) or a non-disposable respirator to European Standard EN 140 with a filter to EN 143), when handling the product. If respiratory symptoms develop following exposure, seek medical advice and show this warning to the physician.
Avoid direct contact with the product. Wear gloves and protective glasses during the use of the product. Wash hands and any exposed skin after use. If accidental contact occurs, rinse the affected area with large amounts of clean water.
Do not eat, drink or smoke while handling this product.

4.6 Adverse reactions (frequency and seriousness)

None known

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals have not produced evidence of foetotoxic effects or effects on fertility at the recommended dose. However this has not been specifically studied in the target species. Use only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

The product may be used in conjunction with antibiotics and/or sulphonamides and bronchodilators. Bromhexine modifies the distribution of antibiotics in the organism and increases their concentration in the serum especially in the respiratory tract (in bronchial and nasal secretions). Such effect has been observed especially for oxytetracycline, spiramycin, tylosin, erythromycin, ampicillin, doxycycline, amoxicillin and cefuroxime.

4.9 Amounts to be administered and administration route

For oral use in drinking water
0.45 mg of bromhexine per kg bodyweight daily, equivalent to 5 g of product per 100 kg bodyweight per day administered for 3 to 10 consecutive days, in drinking water.

In order to obtain the correct dosage the concentration of bromhexine has to be adjusted accordingly.

The following formula may be used to calculate the required concentration of product (in milligrams of product per litre drinking water):

$$\frac{\text{50.mg of the product per kg body weight and per day} \times \text{Average body weight (kg) of animals to be treated}}{\text{Average daily water intake (l/animal)}} = \text{... mg of the product per litre of drinking water}$$

The required amount of product should be weighed as accurately as possible using suitably calibrated weighing equipment.

Recommendation for dilution:

- Prepare a relevant quantity of water in a container.
- Add the product to the water while stirring the solution.
- Prepare the solution with fresh water immediately before use.

When using a water proportionner, adjust the pump between 1% to 5% and adapt the volume of preparation accordingly. Do not set up the dosing pump below 1%.

When using a water tank, it is recommended to prepare a stock solution of at least 1g of product/L and to dilute it to the target final concentration.
The solubility of the product has been tested at the maximum concentration of 100 g/L at 20°C.
Turn off the water supply to the tank until all the medicated solution is consumed.
For example :
Prepare a stock solution at 1 g of product/L, dilute 1/3 to obtain a medicated solution at 0.33g of powder/L eq to 1g of powder/3L.

For pigs, when administered during the meal, first dissolve the product in water and then add feed. Administration during the meal should be restricted to individual treatment or for treatment of a small group of animals. The preparation must be used immediately. Care should be taken that the intended dose will be completely ingested.

The intake of medicated water depends on the clinical condition of the animals.

Any unused medicated water should be discarded after 24 hours.

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

None known.

4.11 Withdrawal period(s)

Cattle (calves)
Meat and offal: 2 days
Not permitted for use in cows producing milk for human consumption.

Pigs
Meat and offal: Zero days.

Chickens, turkeys and ducks
Meat and offal: Zero days

Do not use in birds producing eggs for consumption, during and 4 weeks before the laying phase.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Expectorants, excl. combinations with cough suppressants, mucolytics.
ATCvet code: QR05CB02.

5.1 Pharmacodynamic properties

Bromhexine is a mucoregulator. By activating the secretion of the seromucous glands, bromhexine helps to re-establish the viscosity and elasticity of bronchial secretions in the tracheobronchial tree. In addition, its expectorant action encourages mobilisation of mucus and enables effective bronchial drainage, thereby improving the functioning and defence capability of the lung.
These two simultaneous actions lead to an abundant discharge and facilitate a productive cough.
It breaks down the network of acid glycoprotein fibres found in mucoid sputum, which are mainly responsible for the characteristic viscosity.

5.2 Pharmacokinetic particulars

Absorption
In pigs, bromhexine is rapidly absorbed following oral administration with a peak plasma concentrations obtained in one to three hours. The concentration plateau is reached 12 hours after the second or third administration.
In cattle, plasma concentrations increase progressively over several hours following administration.
In turkeys or broilers, peak plasma concentrations are reached within 2 to 4 hours of oral administration.

Distribution
Due to the lipophilic character of bromhexine, it has a strong affinity for lipid tissues and a slow depletion profile from these tissues.

Metabolism
Bromhexine is largely metabolised into more polar compounds.

Elimination
The apparent total radioactivity plasma half-life elimination after the last administration is 20 to 30 hours in a pig, 40 to 50 hours in cattle and 40 to 50 hours in chickens and turkeys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid
Lactose monohydrate

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: 3 months
Shelf life after dilution in drinking water according to directions: 24 hours

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Polyethylene/ polyamide/ aluminium/ polyethylene terephthalate bags closed by a zip: 500 g, 1 kg, 2.5kg, 5kg

White HDPE jars with a yellow polypropylene screw stopper: 500 g,1 kg

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Ceva Animal Health Ltd
Explorer House
Mercury Park
Wycombe Lane
Wooburn Green
High Wycombe
Buckinghamshire
HP10 0HH
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8. MARKETING AUTHORISATION NUMBER

Vm 15052/4073

9. DATE OF FIRST AUTHORISATION

07 October 2015

10. DATE OF REVISION OF THE TEXT

September 2022

Approved 28 September 2022