SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cryptisel 0.5 mg/ml oral solution for calves [AT, CY, CZ, DE, EL, ES, HU, IE, IT, LT, LV, NL, PL, PT, RO, SK, UK]
Cryptisel, 0.5 mg/ml oral solution for calves [EE]
Cryptisel vet 0.5 mg/ml oral solution for calves [DK, NO, SE]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Halofuginone	0.50 mg
Equivalent to 0.6086 mg of Halofuginone lactate	

Excipients:

Benzoic acid (E 210)	1.00 mg
Tartrazine (E 102)	0.03 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Oral solution.
Clear yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (newborn calves).

4.2 Indications for use, specifying the target species

- Prevention of diarrhoea due to diagnosed *Cryptosporidium parvum*, in farms with history of cryptosporidiosis.
  Administration should start in the first 24 to 48 hours of age.
- Reduction of diarrhoea due to diagnosed *Cryptosporidium parvum*.
  Administration should start within 24 hours after the onset of diarrhoea.

In both cases, the reduction of oocysts excretion has been demonstrated.

4.3 Contraindications

Do not use on an empty stomach.
Do not use in cases of diarrhoea established for more than 24 hours and in weak animals.
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

Administer after colostrum feeding, or after milk or milk replacer feeding only, using an appropriate device for oral administration. For treatment of anorexic calves, the veterinary medicinal product should be administered in half a litre of an electrolyte solution. The animals should receive enough colostrum according to good breeding practice.

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

- People with known hypersensitivity to the active substance or any of the excipients should administer the veterinary medicinal product with caution.
- Repetitive contact with the product may lead to skin allergies.
- Avoid skin, eye or mucosal contact with the product. Wear protective gloves while handling the product.
- In case of skin, eye and mucosa contact wash the exposed area thoroughly with clean water. If eye irritation persists, seek medical advice.
- Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, an increase in the level of diarrhoea has been observed in treated animals.

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

None known.

4.9 Amounts to be administered and administration route

For oral use in calves after feeding

The dosage is: 100 µg of halofuginone / kg bw / once a day for 7 consecutive days, i.e. 2 ml of the veterinary medicinal product / 10 kg bw / once a day for 7 consecutive days.

The consecutive treatment should be done at the same time each day.

Once the first calf has been treated, all the forthcoming newborn calves must be systematically treated as long as the risk for diarrhoea due to *C. parvum* persists.

Bottle without a pump: To ensure a correct dosage, the use of an appropriate device for oral administration (e.g. a syringe) is necessary.

Bottle with a pump: To ensure a correct dosage, an appropriate metering pump is included.

1) Insert the suction pipe into the free hole located in the base of the pump cap.
2) Remove the cap of the bottle and screw the pump on.
3) Remove the protector cap from the tip of the nozzle of the pump.
4) If the metering pump is used for the first time (or has not been used for a few days), carefully pump until a drop of solution is formed on top of the nozzle.
5) Restrain the calf and insert the nozzle of the metering pump into its mouth.
6) Pull the trigger of the metering pump completely for release of a dose that equals 4 ml of solution.
   - For animals weighing from more than 35 kg but less than or equal to 45 kg, pull two times (equivalent to 8 ml)
   - For animals weighing from more than 45 kg but less than or equal to 60 kg, pull three times (equivalent to 12 ml)
7) Unscrew the metering pump on the bottle.
8) Close the bottle with the screw cap.
9) Pull twice or three times in order to empty the remaining product in the metering pump.
10) Put the protector cap back on the nozzle.

The metering pump should not be used upside down.

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

As clinical signs of toxicity may occur at twice the therapeutic dose, it is necessary to apply the recommended dosage strictly. Clinical signs of toxicity include diarrhoea, visible blood in faeces, decline in milk consumption, dehydration, apathy and prostration. Should clinical signs of overdosing occur, the treatment must be stopped immediately and the animal fed unmedicated milk or milk replacer. Rehydration may be necessary.

4.11 Withdrawal period(s)

Meat and offal: 13 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiprotozoals, Agents against protozoal disease.
ATCvet code: QP51AX08

5.1 Pharmacodynamic properties

The active substance, halofuginone, is an antiprotozoal agent of the quinazolinone derivatives group (nitrogenous polyheterocycles). Halofuginone lactate is a salt whose antiprotozoal properties and activity against *Cryptosporidium parvum* have been demonstrated both in *in vitro* conditions and in artificial and natural infections. The compound has a cryptosporidiostatic effect on *Cryptosporidium parvum*. It is mainly active on the free stages of the parasite (sporozoïte, merozoïte). The concentrations to inhibit 50 % and 90 % of the parasites, in an *in vitro* test system, are $IC_{50} < 0.1$ µg/ml and IC_{90} of 4.5 µg/ml, respectively.

5.2 Pharmacokinetic particulars

The bioavailability of the drug in the calf, following single oral administration, is about 80 %. The time necessary to obtain the maximum concentration T_{max} is 11 hours. The maximum concentration in plasma C_{max} is 4 ng/ml. The apparent volume of distribution is 10 l/kg. The plasmatic concentrations of halofuginone after repeated oral administrations are comparable to the pharmacokinetic pattern after single oral treatment. Unchanged halofuginone is the major component in the tissues. Highest values have been found in the liver and the kidney. Halofuginone is mainly excreted in the urine. The terminal elimination half-life is 11.7 hours after IV administration and 30.84 hours after single oral administration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzoic acid (E 210)
Lactic acid (E 270)
Tartrazine (E 102)
Water, Purified

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: 30 months.
Shelf-life after first opening the immediate packaging: 6 months.

6.4 Special precautions for storage

Keep the bottle in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Bottle of 300 ml: High-density polyethylene (HDPE) bottle sealed with a polyethylene terephthalate (PET) foil and closed with a polypropylene screw cap.

Bottles of 500 ml and 1000 ml: High-density polyethylene (HDPE) bottles sealed with a polyethylene (PE) foil and closed with a HDPE screw cap.

The medicinal product can be supplied with or without a 4 ml metering pump, made of low and linear low-density polyethylene, polypropylene, stainless steel and silicone with a low-density polyethylene (LDPE) suction pipe.

Package sizes:
Cardboard box with 1 bottle of 300 ml (containing 290 ml of solution) with a 4 ml metering pump
Cardboard box with 1 bottle of 300 ml (containing 290 ml of solution)
Cardboard box with 1 bottle of 500 ml (containing 490 ml of solution) with a 4 ml metering pump
Cardboard box with 1 bottle of 500 ml (containing 490 ml of solution)
Cardboard box with 1 bottle of 1000 ml (containing 980 ml of solution) with a 4 ml metering pump
Cardboard box with 1 bottle of 1000 ml (containing 980 ml of solution)

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.
The product should not enter watercourses as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

LIVISTO Int'l, S.L.
Av. Universitat Autònoma, 29
08290 Cerdanyola del Vallès (Barcelona)
Spain

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: DD/MM/YYYY
Date of last renewal: DD/MM/YYYY

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.