SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF VETERINARY MEDICAL PRODUCT

Combinex Cattle Oral Suspension

2. QUALITATIVE & QUANTITATIVE COMPOSITION

Active ingredients	% w/v
Triclabendazole	12.00
Levamisole hydrochloride	7.50
Other Ingredients	
Methyl Parahydroxybenzoate	0.08 antimicrobial preservative
Propyl Parahydroxybenzoate	0.03 antimicrobial preservative
Benzoic Acid	0.10 Antioxidant
Sodium metabisuphite	0.25 Antioxidant
Disodium edetate dihydrate	0.13 Antioxidant

For a full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension.

A cream coloured aqueous suspension for oral administration.

4. CLINICAL PARTICULARS

4.1 Target Species

Non-lactating cattle.

4.2 Indications for use, specifying target species

For the treatment and control of parasitic bronchitis, parasitic gastro-enteritis and fascioliasis in cattle. When used at the recommended dose rate, the product is effective against mature and developing immature stages of Levamisole susceptible *Haemonchus, Trichostrongylus, Cooperia, Nematodirus, Bunostromum* and *Oesophagostomum* species in the gastro-intestinal tract, and *Dictyocaulus spp* in the lungs. The product is effective against developing immature and adult *Ostertagia*, but is not active against inhibited larvae. It is also effective against all stages of Triclabendazole susceptible *Fasciola hepatica* from

two week old early immature to adult fluke, and so is indicated against both acute and chronic fascioliasis.

4.3 Contra-indications

None

4.4 Special warnings for each target species

Efficacy of this product against roundworms is reduced if levamisole resistant strains are present. Efficacy of this product against liver fluke is reduced if triclabendazole resistant strains are present.

Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:

- Too frequent and repeated use of anthelmintics from the same class, over an extended period of time
- Underdosing which may be due to underestimation of body weight, misadministration of the product or lack of calibration of the dosing device (if any).

Suspected clinical cases of resistance to anthelmintics should be further investigated using appropriate tests (e.g. Faecal Egg Count Reduction Test). Where the results of the test(s) strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to another pharmacological class and having a different mode of action should be used.

Resistance to levamisole has been reported in *Teladorsagia* species in cattle in developed countries such as New Zealand. Therefore the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of the nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

4.5 Special precautions for use

i. Special precautions for use in animals

Assess bodyweight as accurately as possible before calculating the dosage.

Clean drenching equipment before and after use.

Shake container thoroughly before use and use undiluted product from the original container.

Intensive use or misuse of anthelmintics can give rise to resistance. To reduce this risk, dosing programmes should be discussed with your Veterinary Adviser.

ii. Special precautions to be taken by the person administering the product

When administering, do not eat, drink or smoke.

Wash splashes from eyes and skin immediately.

Immediately remove any contaminated clothing.

Wash hands and exposed skin before meals and after work.

Levamisole can cause idiosyncratic reactions and serious blood disorders in a very small number of people. If symptoms such as dizziness, nausea, vomiting or abdominal discomfort are experienced when using the product, or sore mouth/throat or fever occurs shortly afterwards, then medical advice should be sought immediately

4.6 Adverse reactions (frequency and seriousness)

When the product is used at the recommended dose rate side effects are rare. At higher dosages, transient side effects due to levamisole may occur (i.e. salivation and slight muscle tremors).

4.7 Use during pregnancy, lactation or lay

The product can be administered safely to pregnant cattle. For dairy cattle, see section 4.11.

4.8 Interaction with other medicaments and other forms of interaction

Do not treat simultaneously with products containing organophosphorus compounds.

4.9 Amounts to be administered and administration route

Given as an oral drench. Suitable for use through most types of automatic drenching gun. It can be safely administered to young or pregnant cattle.

Recommended dose rate: 7.5mg levamisole hydrochloride/kg and 12mg triclabendazole/kg. This is equivalent to 1ml of the product per 10kg bodyweight.

To ensure administration of correct dose, body weight should be determined as accurately as possible; accuracy of the dosing device should be checked.

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

At higher doses transient side effects due to levamisole may occur (i.e. salivation and dose dependent muscle tremors).

4.11 Withdrawal period(s)

Animals must not be slaughtered for human consumption during treatment.

Cattle may be slaughtered for human consumption only after 56 days from the last treatment.
Not authorised for use in cattle producing milk for human consumption including during the dry period. Do not use during the last trimester of pregnancy in heifers which are intended to produce milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

ATC Vet Code: QP52AE51

Pharmacotherapeutic group: Anthelmintics, Imidazothiazoles

5.1 Pharmacodynamic properties

Levamisole is an anthelmintic acting by causing muscular paralysis and expulsion of the nematode. Triclabendazole is a flukicide, highly active against all life stages of *Fasciola* from 2 weeks.

5.2 Pharmacokinetic particulars

Majority of triclabendazole oral dose in rats, sheep, goats and rabbits is eliminated in faeces after 6-10 days, as unchanged drug or products of biliary excretion. Urinary excretion is minimal. Sulphone, sulphoxide, ketone and 4-hydroxy triclabendazole derivatives are the main metabolites identified in plasma. Levamisole is rapidly absorbed after oral administration, is extensively metabolised and by 8 days after application excretion is virtually complete.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Benzoic acid
Propyl Parahydroxybenzoate (E216)
Methyl Parahydroxybenzoate (E218)
Disodium edetate dihydrate
Sodium metabisulphite (E223)
Povidone K30 (E1201)
Macrogol 6000
Sodium chloride
Silica, colloidal anhydrous
Citric acid monohydrate
Simeticone
Sodium hydroxide (for pH adjustment)
Water, deionised

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf life of veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 1 year

6.4 Special precautions for storage

Do not store above 25^{o}C.

Protect from light. Protect from frost.

Following withdrawal of the dose, use the product within 1 year. Discard unused material.

6.5 Nature and composition of immediate packaging

1 and 2.5 litre natural HDPE flexipack. Heat sealed polyethylene closure. White HDPE screw cap.

0.8, 2.2 or 5 litre white HDPE flexipack, red polypropylene cap (screw fit)
12 or 21 litre white HDPE container, red HDPE closure.

1, 2.5, 12 and 21 litre presentations: most types of drenching gun may be used.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused medicinal product or waste materials, if any

DANGEROUS to fish and aquatic life.
Do not contaminate ponds, waterways or ditches with the product or empty container.
Any unused product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Elanco Europe Ltd
Form 2, Bartley Way
Bartley Wood Business Park
Hook
RG27 9XA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 00879/4083

9. DATE OF FIRST AUTHORISATION

13 August 1991

10. DATE OF REVISION OF THE TEXT

September 2020

Approved 25 September 2020