SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Combinex Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient(s)	% w/v
Triclabendazole	5.00
Levamisole hydrochloride	3.75
Excipient(s)	
Methyl hydroxybenzoate	0.095 antimicrobial preservative
Propyl hydroxybenzoate	0.035 antimicrobial preservative
Benzoic Acid	0.10 Antioxidant
Sodium metabisulphite	0.25 Antioxidant
Disodium edetate	0.13 Antioxidant

In an aqueous suspension

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

Sheep.

4.2 Indications for use, specifying the target species

For the treatment and control of parasitic bronchitis, parasitic gastro-enteritis and fascioliasis in sheep. When used at the recommended dose rate, the product is effective against mature and developing immature stages of levamisole-susceptible *Haemonchus, Ostertagia, Trichostrongylus, Cooperia, Nematodirus, Bunostomum, Chabertia* and *Oesophagostomum* species in the gastro-intestinal tract, and *Dictyocaulus spp* in the lungs. It is also effective against all stages of Triclabendazole susceptible *Fasciola hepatica* from two day old early immature to adult fluke, and so is indicated against both acute and chronic fascioliasis.

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4.3 Contraindications

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.

4.5 Special precautions for use

i. Special precautions for use in animals

Assess bodyweight as accurately as possible before calculating the dosage.

Animals must not be treated within a period of 14 days before or after treatment with organophosphorus compounds.

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.

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*, *Cooperia* and *Trichostrongylus* species in sheep in a number of countries, including ones in the EU. There are reports of resistance in *Haemonchus* in sheep outside the EU. Resistance to triclabendazole has been reported in *Fasciola* species in small ruminants in a number of countries including ones in the EU. Therefore

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the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and trematodes and recommendations on how to limit further selection for resistance to anthelmintics.

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

When using, do not eat, drink or smoke.
Wash splashes from eyes and skin immediately.
Take off immediately 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 and animals are not overly stressed, 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 or lactating sheep. For dairy sheep, see section 4.11.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Do not mix with other products.

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

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

Recommended dose rate: 7.5 mg levamisole hydrochloride/kg and 10 mg triclabendazole/kg. This is equivalent to 1 ml of the product per 5 kg bodyweight.

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).

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4.11 Withdrawal period(s)

Animals must not be slaughtered for human consumption during treatment.
Sheep may be slaughtered for human consumption only after 56 days from the last treatment.
Not authorised for use in ewes producing milk for human consumption including during the dry period. Do not use within 1 year prior to the first lambing in ewes intended to produce milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anthelmintic

ATCvet code: QP52AE51

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 days.

5.2 Pharmacokinetic particular

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

Methyl hydroxybenzoate
Propyl hydroxybenzoate
Benzoic acid
Sodium metabisulphite
Disodium edetate
Macrogol
Sodium chloride
Silica, Colloidal anhydrous
Citric acid monohydrate
Simeticone (based on dimethypolysiloxane, water and silica)
Sodium hydroxide (for pH adjustment)
Water, deionised

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6.2 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: 1 year.

6.4 Special precautions for storage

Do not store above 25°C.
Protect from light.
Protect from freezing.
Following withdrawal of the first dose, use the product within 1 year.

6.5 Nature and composition of immediate packaging

1, 2.5 or 5 litre natural HDPE bottles. Heat sealed polyethylene closure. White HDPE screw cap.

0.8, 2.2 or 5 litre white HDPE bottles with blue polyethylene screw cap.

12 or 21 litre white HDPE bottles with blue HDPE closure.

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

DANGEROUS to fish and aquatic life. Do not contaminate ponds, waterways or ditches with the product or empty container.

Any unused veterinary medicinal 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

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8. MARKETING AUTHORISATION NUMBER

Vm 00879/4084

9. DATE OF FIRST AUTHORISATION

13 August 1991

10. DATE OF REVISION OF THE TEXT

September 2020

Approved 25 September 2020

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