ANNEX III

LABELLING AND PACKAGE LEAFLET

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE – COMBINED LABEL AND PACKAGE LEAFLET

Container
Case 1: As there is no outer packaging, all the information of the package leaflet is conveyed on the container. Consequently, no separate leaflet is provided in compliance with the current QRD Template

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Dopharma Research B.V.
Zalmweg 24
4941 VX Raamsdonksveer
The Netherlands

Manufacturer responsible for batch release:
Dopharma France S.A.S.
23 Rue du Prieuré – Saint Herblon
44150 Vair sur Loire
France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Distocur 34 mg/ml Oral suspension for cattle and sheep
oxyclozanide

3. STATEMENT OF THE ACTIVE SUBSTANCE (S) AND OTHER INGREDIENTS

Each ml contains:

Active substance:
Oxyclozanide …… 34.0 mg

Excipients:
Methyl parahydroxybenzoate (E218)……. 1.35 mg
Propyl parahydroxybenzoate ……. 0.15 mg

Whitish to beige suspension

4. PHARMACEUTICAL FORM

Oral Suspension

5. PACKAGE SIZE

1L
5L
10L

6. INDICATION(S)

For treatment of infections caused by the adult stage of *Fasciola hepatica*, sensitive to oxyclozanide.
For elimination of gravid tapeworm segments (*Monoezia* spp.).

7. CONTRAINDICATIONS

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

8. ADVERE REACTIONS

Slight softening of the faeces with animal showing increased frequency of defecation and transient inappetence may appear very rarely.

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).

If you notice any side effects, even those not already listed in this label or you think that the medicine has not worked, please inform your veterinary surgeon.

Alternatively you can report via your national reporting system {national system details}.

9. TARGET SPECIES

Cattle and sheep

10. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION PACKAGE SIZE

Oral use. Give as an oral drench. Shake the suspension at least 5 times before use.
To ensure administration of a correct dose, body weight should be determined as accurately as possible; accuracy of the dosing device should be checked. If animals are to be treated collectively rather than individually, they should be grouped according to their bodyweight and dosed accordingly, in order to avoid under – or overdosing.

Cattle:
Dose according to body weight at a rate of 10 mg oxyclozanide per kg body weight, corresponding to 3 ml of product per 10 kg body weight. For animal above 350 kg, dose is 3.5g oxyclozanide per animal, i.e. 103 ml of product.

Sheep:
Dose according to body weight at a rate of 15 mg oxyclozanide per kg body weight, corresponding to 4,4 ml of product per 10 kg body weight. For animal above 45 kg, dose is 0,68g oxyclozanide per animal, i.e. 20 ml of product.

11. ADVICE ON CORRECT ADMINISTRATION

Please see the section Dosage for each species, route(s) and method of administration.

12. WITHDRAWAL PERIOD(S)

Withdrawal periods:
Cattle:
Meat and offal: 13 days.
Milk: 4.5 days (108 hours).

Sheep:
Meat and offal: 14 days.
Milk: 7 days (168 hours).

13. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
After first opening, do not store above 25°C.
Do not use this veterinary medicinal product after the expiry date which is stated on the container after “EXP”. The expiry date refers to the last day of that month.

14. SPECIAL WARNING(S)

Special warning for each target species:

To date no resistance to oxyclozanide has been reported. Use of the product should be based on local (regional, farm) epidemiological information about susceptibility of *Fasciola hepatica* and recommendations on how to limit further selection for resistance to anthelmintics.
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 pharmaceutical class and having a different mode of action should be used.
At normal dose levels, oxyclozanide is not active against immature flukes present in liver tissue.
Milking cattle, particularly high yielders, may show a reduction in yield, occasionally of 5 % or more, for about 48 hours after handling. The effect of this small loss may be minimised by spreading herd dosing over a period of about one week.

Special precautions for use in animals:

To avoid injuriesof the pharyngeal region, care should be taken when administering the productby dosing gun.
Adverse effects (see section ADVERSE REACTIONS) are occasionally enhanced in animals suffering from severe impairment of liver function and/or dehydration at the time of dosing.
The physical condition of animals undergoing treatment should always be observed, particularly of those in advanced pregnancy and/or under stress from adverse weather conditions, poor nutrition, penning, handling, etc.

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

The veterinary medicinal product may cause irritation to skin, eyes and mucous membranes.
People with known hypersensitivity to oxyclozanide or any of the excipients should avoid contact with the veterinary medicinal product.
Wash hands after use.
Operators should wear impermeable rubber gloves when applying the product.
Do not smoke, eat or drink while handling the product.
In case of contact with the product, rinse the affected area immediately with plenty of water.
Contaminated clothing should be removed immediately.
In the event of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Other precautions:

Oxyclozanide is toxic to dung fauna. The risk can be reduced by avoiding too frequent and repeated use of oxyclozanide in cattle.

Pregnancy and lactation:

Laboratory studies with oxyclozanide during different phases of reproduction have not produced any evidence of teratogenic or foetotoxic effects, or negative effects on fertility.
Can be used during, pregnancy and lactation.
However care should be taken when treating heavily pregnant animals and animals under stress from adverse weather conditions, poor nutrition, penning, handling etc.

Interaction with other medicinal products and other forms of interaction:

No information is available on the safety and efficacy of this veterinary medicinal product when used with any other veterinary medicinal product.
A decision to use this veterinary medicinal product before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Overdose (symptoms, emergency procedures, antidotes):

The adverse reactions observed at normal doses are more pronounced at increased doses. At doses of 50mg/kg there is a risk of death.
The effects of oxyclozanide overdosage are dullness and some loosening of faeces in sheep and possible diarrhoea, inappetance and loss of weight in cattle. These effects are occasionally very rarely enhanced in animals suffering from severe impairment of liver function and/or dehydration at the time of dosing.

Incompatibilities:

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

15. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

16. DATE ON WHICH THE LABEL WAS LAST APPROVED

May 2021

17. OTHER INFORMATION

Opaque high density polyethylene container (1L, 5L and 10L) closed by opaque high density polyethylene screw cap.

Not all pack sizes may be marketed.

Environmental properties:
Faeces containing oxyclozanide excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on dung degradation.
Oxyclozanide is persistent in soils.

18. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.
For OTC products:

19. THE WORDS "KEEPS OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

20. EXPIRY DATE

EXP << >>
Shelf life after first opening the container: 1 year
Once opened, use by_____.

21. MARKETING AUTHORISATION NUMBER(S)

Vm 28365/4014

22. MANUFACTURER'S BATCH NUMBER

Lot << >>

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Container
Case 2: When all the information of the package leaflet cannot be conveyed on the container. Consequently, a separate leaflet is provided in compliance with the current QRD Template

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Distocur 34 mg/ml Oral suspension for cattle and sheep
oxyclozanide

2. STATEMENT OF THE ACTIVE SUBSTANCES

Each ml contains:
Oxyclozanide …… 34.0 mg

3. PHARMACEUTICAL FORM

Oral Suspension

4. PACKAGE SIZE

1L
5L
10L

5. TARGET SPECIES

Cattle and sheep

6. INDICATION(S)

For OTC products
For treatment of infections caused by the adult stage of *Fasciola hepatica*, sensitive to oxyclozanide.
For elimination of gravid tapeworm segments (*Monoezia* spp.).

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use. Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal periods:

Cattle:
Meat and offal: 13 days.
Milk: 4.5 days (108 hours).

Sheep:
Meat and offal: 14 days.
Milk: 7 days (168 hours).

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP << >>Shelf life after first opening the container: 1 year
Once opened, use by_____.

11. SPECIAL STORAGE CONDITIONS

After first opening, do not store above 25°C.

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

For OTC products:

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Dopharma Research B.V.
Zalmweg 24
4941 VX Raamsdonksveer
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

Vm 28365/4014

17. MANUFACTURER'S BATCH NUMBER

Lot << >>

PACKAGE LEAFLET

Case 2: If all the information of the package leaflet cannot be conveyed on the container.

Distocur 34 mg/ml Oral suspension for cattle and sheep

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Dopharma Research B.V.
Zalmweg 24
4941 VX Raamsdonksveer
The Netherlands.

Manufacturer responsible for batch release:
Dopharma France S.A.S.
23 Rue du Prieuré – Saint Herblon
44150 Vair sur Loire
France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Distocur 34 mg/ml Oral suspension for cattle and sheep
Oxyclozanide

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains:

Active substance:
Oxyclozanide 34.0 mg

Excipients:
Methyl parahydroxybenzoate (E218) 1.35 mg
Propyl parahydroxybenzoate 0.15 mg

Whitish to beige suspension.

4. INDICATION(S)

For treatment of infections caused by the adult stage of *Fasciola hepatica,* sensitive to oxyclozanide.
For elimination of gravid tapeworm segments (*Monoezia* spp.).

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Slight softening of the faeces with animal showing increased frequency of defecation and transient inappetence may appear very rarely.

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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

Alternatively you can report via your national reporting system {national system details}.

7. TARGET SPECIES

Cattle and sheep.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Give as an oral drench (oral use). Shake the suspension at least 5 times before use.
To ensure administration of a correct dose, body weight should be determined as accurately as possible; accuracy of the dosing device should be checked. If animals are to be treated collectively rather than individually, they should be grouped according to their bodyweight and dosed accordingly, in order to avoid under – or overdosing.
Cattle:
Dose according to body weight at a rate of 10 mg oxyclozanide per kg body weight, corresponding to 3 ml of product per 10 kg body weight. For animal above 350 kg, the dose is 3.5g oxyclozanide per animal, i.e. 103 ml of product.
Sheep:
Dose according to body weight at a rate of 15 mg oxyclozanide per kg body weight, corresponding to 4,4 ml of product per 10 kg body weight. For animal above 45 kg, dose is 0,68g oxyclozanide per animal, i.e. 20 ml of product.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD(S)

Cattle:
Meat and offal: 13 days.
Milk: 4.5 days (108 hours).

Sheep:
Meat and offal: 14 days.
Milk: 7 days (168 hours).

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
After first opening, do not store above 25°C.
Do not use this veterinary medicinal product after the expiry date which is stated on the container after "EXP". The expiry date refers to the last day of that month.
Shelf life after first opening the container: 1 year.

12. SPECIAL WARNING(S)

Special warnings for each target species:

To date no resistance to oxyclozanide has been reported. Use of the product should be based on local (regional, farm) epidemiological information about susceptibility of *Fasciola hepatica* and recommendations on how to limit further selection for resistance to anthelmintics.
Care should be taken to avoid the following practices as 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 pharmaceutical class and having a different mode of action should be used.
At normal dose levels, oxyclozanide is not active against immature flukes present in liver tissue.
Milking cattle, particularly high yielders, may show a reduction in yield, occasionally of 5 % or more, for about 48 hours after handling. The effect of this small loss may be minimised by spreading herd dosing over a period of about one week.

Special precautions for use in animals:

To avoid injuries of the pharyngeal region, care should be taken when administering the product by dosing gun.
Adverse effects (see section ADVERSE REACTIONS) are occasionally enhanced in animals suffering from severe impairment of liver function and/or dehydration at the time of dosing.

The physical condition of animals undergoing treatment should always be observed, particularly of those in advanced pregnancy and/or under stress from adverse weather conditions, poor nutrition, penning, handling, etc.

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

The veterinary medicinal product may cause irritation to skin, eyes and mucous membranes.
People with known hypersensitivity to oxyclozanide or any of the excipients should avoid contact with the veterinary medicinal product.
Wash hands after use.
Operators should wear impermeable rubber gloves when applying the product.
Do not smoke, eat or drink while handling the product.
In case of contact with the product, rinse the affected area immediately with plenty of water.
Contaminated clothing should be removed immediately.
In the event of accidental ingestion, seek medical advice immediately and show the package leaflet or label to the physician.

Other precautions

Oxyclozanide is toxic to dung fauna. The risk can be reduced by avoiding too frequent and repeated use of oxyclozanide in cattle.

Pregnancy and lactation:

Laboratory studies with oxyclozanide during different phases of reproduction have not produced any evidence of teratogenic or foetotoxic effects, or negative effects on fertility.
Can be used during pregnancy and lactation.
However care should be taken when treating heavily pregnant animals, and animals under stress from adverse weather conditions, poor nutrition, penning, handling etc.

Interaction with other medicinal products and other forms of interaction:

No information is available on the safety and efficacy of this veterinary medicinal product when used with any other veterinary medicinal product.
A decision to use this veterinary medicinal product before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

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

The adverse reactions (see section ADVERSE REACTIONS) observed at normal doses are more pronounced at increased doses. At doses of 50mg/kg there is a risk of death.
The effects of oxyclozanide overdosage are dullness and some loosening of faeces in sheep and possible diarrhoea, inappetance and loss of weight in cattle. These effects are occasionally enhanced in animals suffering from severe impairment of liver function and/or dehydration at the time of dosing.

Incompatibilities:

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

Environmental properties:

Faeces containing oxyclozanide excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on dung degradation.
Oxyclozanide is persistent in soils.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

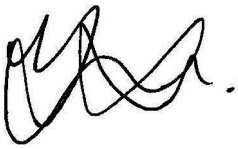
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

May 2021

15. OTHER INFORMATION

Opaque high density polyethylene container of 1L, 5L and 10L.
Not all pack sizes may be marketed.
Oxyclozanide is persistent in the soil.



Approved: 12 August 2021