ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Intermectin 10 mg/ml solution for injection for cattle, sheep and pigs (EL)
Intermectin Injection 10 mg/ml solution for injection for cattle, sheep and pigs (NL, HR, CY, CZ, FR, HU, IT, LT, MT, PT, SK, SI, ES)
Ivocure 10 mg/ml solution for injection for cattle, sheep and pigs (AT, LV, DE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Ivermectin 10.0 mg

Excipients:

Qualitative composition of excipients and other constituents
Glycerol formal
Propylene glycol

Clear, colourless solution, free from visible suspended particles.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, sheep and pig.

3.2 Indications for use for each target species

For cattle, sheep and pigs with, or at risk from mixed infections by species of nematodes, warbles, mites and lice. The veterinary medicinal product is only indicated when treatment against the following parasites is indicated at the same time:

Cattle:

Gastrointestinal nematodes: *Ostertagia ostertagi* (adult, L3, L4, inhibited larvae), *Ostertagia lyrata* (adult, L4), *Haemonchus placei* (adult, L3, L4), *Trichostrongylus axei* (adult, L4), *T. colubriformis* (adult, L4), *Cooperia oncophora* (adult, L4), *C. punctata* (adult, L4), *C. pectinata* (adult, L4), *Cooperia* spp. (L3), *Oesophagostomum radiatum* (adult, L3, L4), *Nematodirus helvetianus* (adult), *N. spathiger* (adult), *Strongyloides papillosus* (adult), *Bunostomum phlebotomum* (adult, L3, L4), *Toxocara vitulorum* (adult).

Lungworms: *Dictyocaulus viviparus* (adult, L4, inhibited larvae).

Roundworms: *Parafilaria bovicola*, *Thelazia* spp. (adult).

Warbles: *Hypoderma bovis, H. lineatum, Dermatobia hominis.*

Lice: *Linognathus vituli, Haematopinus eurysternus, Solenopotes capillatus.*

Mites: *Psoroptes ovis, Sarcoptes scabiei* var. *bovis, Chorioptes bovis*

Persistent Activity:
Given at the recommended dosage of 0.2 mg ivermectin per kg bodyweight, the veterinary medicinal product controls re-infection with the following nematodes up to the duration shown:

Cooperia spp.	7 days
Ostertagia spp.	7 days
Dictyocaulus viviparus	14 days

Sheep:

Gastrointestinal nematodes: *Teladorsagia* (*Ostertagia*) *circumcincta* (adult, L3, L4, inhibited larvae), *Teladorsagia* (*Ostertagia*) *trifurcata* (adult, L4), *Haemonchus contortus* (adult, L3, L4), *Trichostrongylus axei* (adult), *T. colubriformis* (adult, L3, L4), *T. vitrinus* (adult), *Cooperia curticei* (adult, L4), *Oesophagostomum columbianum* (adult, L3, L4), *O. venulosum* (adult), *Chabertia ovina* (adult, L3, L4), *Trichuris ovis* (adult), *Nematodirus filicollis* (adult, L4), *N. spathiger* (L3, L4), *Strongyloides papillosus* (L3, L4).

Lungworms: *Dictyocaulus filaria* (adult, L3, L4), *Protostrongylus rufescens* (adult).

Warbles: *Oestrus ovis* (all larval stage).

Mites: *Psoroptes communis* var. *ovis, Sarcoptes scabiei, Psorergates ovis.*

Pig:

Gastrointestinal nematodes: *Ascaris suum* (adult, L4), *Hyostrongylus rubidus* (adult, L4), *Oesophagostomum* spp. (adult, L4), *Strongyloides ransomi* (adult).

Lungworms: *Metastrongylus* spp. (adult).

Kidneyworms: *Stephanurus dentatus* (adult, L4).

Lice: *Haematopinus suis.*

Mites: *Sarcoptes scabiei* var. *suis.*

3.3 Contraindications

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

3.4 Special warnings

Treatment scheme in areas where hypodermosis occurs:
Ivermectin is highly effective against all stages of cattle grubs. However, a proper timing of the treatment is very important. Adult *Hypoderma* flies are known to fly predominantly during the summer months. However, it is possible for a few flies to remain active during the late summer and fall. To achieve optimal results, animals should be treated as soon as possible once heel fly season has ended. As is the case with other veterinary medicinal products for treatment of hypodermosis, the destruction of *Hypoderma* larvae may cause adverse reactions in the host when these larvae are situated in the vital parts of the animal, which may particularly be the case in the period from December to March. The destruction of *Hypoderma lineatum* may cause bloating when the larvae are located at the height of the submucosa of the oesophagus. The destruction of *H. bovis* may cause staggering or paralysis. Therefore, cattle should be treated before or after the presence of these larvae in vital parts of the body.

In sheep treatment of psoroptic mange (sheep scab) with one injection is not recommended because, although a clinical improvement may be seen, elimination of all mites may not occur.

Sheep scab (*Psoroptes ovis*) is an extremely contagious external parasite of sheep. To ensure complete control great care must be taken to avoid re–infestation, as mites may be viable for up to 15 days off the sheep. It is important that all sheep which have been in contact with infected sheep are treated. Contact between treated, infected and untreated flocks must be avoided until at least seven days after treatment. For an effective control of mite infestations, care must be taken to prevent reinfestation from exposure to untreated animals or contaminated facilities. Louse eggs are unaffected by ivermectin and may require up to three weeks to hatch. Louse infestations developing from hatching eggs may require retreatment.

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the veterinary medicinal product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each herd/flock.
Repeated use for an extended period, particularly when using the same class of substances, increases the risk of resistance development. Within a herd, maintenance of susceptible refugia is essential to reduce that risk. Systematically applied interval-based treatment and treatment of a whole herd should be avoided. Instead, if feasible, only selected individual animals or selected subgroups should be treated (targeted selective treatment). This should be combined with appropriate husbandry and pasture management measures. Guidance for each specific herd should be sought from the responsible veterinarian.
In the absence of risk of co-infection of nematodes, warbles, mites and lice, a narrow spectrum veterinary medicinal product should be used.

Resistance to ivermectin has been reported in *Cooperia spp.* and *Ostertagia ostertagi* in cattle within the EU, as well as in in *Haemonchus contortus*, *Rhipicephalus* (*Boophilus*) *annulatus*, and *Rhipicephalus microplus* in cattle outside the EU.

In sheep, resistance to ivermectin is widespread in *Teladorsagia circumcincta*, *Trichostrongylus* spp., *Haemonchus contortus* and in other gastro-intestinal parasite species.
Multiple resistance was reported in *Teladorsagia circumcincta* to benzimidazoles, macrocyclic lactones and levamisole and in *Haemonchus contortus* to ivermectin and benzimidazoles.
Multiple resistance to macrocyclic lactones has also been reported in *Psoroptes ovis* scab mites in sheep and in cattle.

The use of this veterinary medicinal product should take into account local information about susceptibility of the target parasites, where available. It is recommended to further investigate cases of suspected resistance, using an appropriate diagnostic method (e.g., Faecal Egg Count Reduction Test).

Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.

3.5 Special precautions for use

Special precautions for safe use in the target species:
This veterinary medicinal product is not to be used intramuscularly or intravenously.

Avermectins may not be well tolerated in all non-target species. Cases of intolerance are reported in dogs – especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product may cause neurologic effects and may be irritating to the eye. Accidental injection may cause local irritation and/or pain at the injection site. Avoid skin and eye contact. Do not eat or drink during use of this veterinary medicinal product. Avoid self-injection. In case of accidental contact, wash the contacted area with water. In the case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Wash hands after use.

This veterinary medicinal product may cause harm to the unborn foetus. The veterinary medicinal product should not be administered by pregnant women.

Special precautions for the protection of the environment:
The veterinary medicinal product is very toxic to aquatic organisms, soil organisms and dung insects.
The veterinary medicinal product should not be allowed to enter surface waters as it has harmful effects on aquatic and sediment organisms.
Treated cattle should not have direct access to surface water for 31 days and sheep for 16 days after treatment to avoid adverse effects on aquatic organisms.
Long-term effects of ivermectin on the population dynamics of dung organisms have not been investigated. Therefore, it is advisable not to treat animals on the same pasture every season.
In order to avoid accumulation of ivermectin in soil, it is advised not to spread manure containing the active substance on the same area of land in successive years.
Repeated treatments on a pasture within a season should only be given on the advice of a veterinarian.

3.6 Adverse events

Cattle, sheep and pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic and anaphylactic-type reactions[1]

[1] These reactions can be associated with signs like ataxia, convulsions and/or tremor.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

For subcutaneous use.

Cattle:
This veterinary medicinal product should be given only by subcutaneous injection at the recommended dosage level of 0.2 mg ivermectin per kg bodyweight (corresponding to 1 ml per 50 kg bodyweight), as a single dose.
Inject under the loose skin in front of or behind the shoulder.
As with any injection, aseptic precautions should be taken. Sterile equipment should be used.

Sheep:
This veterinary medicinal product should be given only by subcutaneous injection at the recommended dosage level of 0.2 mg ivermectin per kg bodyweight (corresponding to 0.5 ml per 25 kg bodyweight), as a single dose.
Inject under the loose skin behind the shoulder.
In sheep with much wool you must ensure that the needle has penetrated the wool and skin before giving the dose. Use sterile equipment.

Pig:
This veterinary medicinal product should be given only by subcutaneous injection in the neck at the recommended dosage level of 0.3 mg ivermectin per kg bodyweight (corresponding to 1 ml per 33 kg bodyweight), as a single dose.
The injection may be administered with a single-dose syringe or automatic syringe equipment.
Work aseptically.

Underdosing could result in ineffective use and may favour resistance development.
To ensure a correct dosage, body weight should be determined as accurately as possible. If animals are to be treated collectively, reasonably homogeneous groups should be set up, and all animals of a group should be dosed at the rate corresponding to the heaviest one.
Accuracy of the dosing device should be thoroughly checked.

When treating groups of animals use only an automatic dosing device. The use of 21G × 1 ½″ needle is suggested. When treating groups of animals in one run, use a draw-off needle that has been placed in the bottle stopper to avoid excess broaching of the stopper. The draw-off needle should be removed after treatment. Bottle stoppers must not be broached more than 20 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

The toxicity of ivermectin is low; even if the recommended dose is exceeded, the occurrence of intoxication is unlikely. No antidote has been identified.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Cattle
Meat and offal: 49 days.
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 60 days of expected parturition.

Sheep
Meat and offal: 63 days.
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 60 days of expected parturition.

Pigs
Meat and offal: 28 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP54AA01.

4.2 Pharmacodynamics

Ivermectin is a member of the macrocyclic lactone class of endectocides, which have a unique mode of action. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels, which occur in invertebrate nerve and muscle cells. This leads to an increase in the

permeability of the cell membrane to chloride ions with hyperpolarisation of the nerve or muscle cell, resulting in paralysis and death of the parasite. Compounds of this class may also interact with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).

The margin of safety for compounds of this class is attributable to the fact that mammals do not have glutamate-gated chloride channels, the macrocyclic lactones have a low affinity for other mammalian ligand-gated chloride channels and they do not readily cross the blood-brain barrier.

Due to advances in molecular technology, mechanisms of resistance in worms are becoming increasingly understood. As per the published literature, resistance in worms can be the result of a variety of mechanisms and can be roughly categorised as genetic changes in the drug target, changes in the drug transport (e.g. ATP-binding Cassette (ABC) transporters), or changes in the metabolism of the drug within the parasite.
Mutations in the extracellular domain of the glutamate-gated chloride channel of *Haemonchus contortus* and of a closely related nematode, *Cooperia oncophora*, are associated with ivermectin resistance. Ivermectin due to its ability to increase P-glycoprotein expression levels can cause increasing of resistance to triclabendazole in *Fasciola hepatica*. The ovine *Teladorsagia circumcincta* P-glycoprotein-9 (*Tci-pgp-9*) gene has been implicated in multiple-anthelmintic resistance in this parasite. The P-glycoprotein, a cell membrane transport protein able to transport many different drugs (including ivermectin, benzimidazoles and imidazothiazole derivatives), may lead to multidrug resistance by increasing the active transport of drugs. Studies have shown that UDP-glycosyltransferases (*UGT*), glutathione S-transferase (*GST*), cytochrome P450 (*CYP*), and p-glycoprotein (*Pgp*) genes play important roles in *H. contortus* drug resistance isolated from sheep.

4.3 Pharmacokinetics

Cattle
At a dose level of 0.2 mg ivermectin/kg a maximum plasma concentration of 35-50 ng/ml is reached in about 2 days and the half-life in plasma is 2.8 days. It is also established that ivermectin is transported mainly in the plasma (80%). This distribution between plasma and blood cells remains relatively constant.

Sheep
At a dose level of 0.3 mg ivermectin/kg an average peak of 16 ng/ml is reached one day after injection.

Pig
During trials carried out at a dose rate of 0.2 mg/kg ivermectin, a plasma concentration of 10-20 ng/ml was reached in about 2 days; half-life in plasma was 0.5 days.

Ivermectin is very toxic to aquatic organisms and dung fauna and can accumulate in soil and sediment. Like other macrocyclic lactones, ivermectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of ivermectin may take place over a period of several weeks. Faeces containing ivermectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Keep the glass bottle in the outer carton in order to protect from light.
Keep the bottle in an upright position.

5.4 Nature and composition of immediate packaging

Clear glass bottles (type II) closed with a bromobutyl rubber stopper and sealed with an aluminium cap or an aluminium flip-off cap with polypropylene cover packed into an outer cardboard box.

Pack sizes:
Cardboard box with one vial with 50 ml solution for injection.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
The veterinary medicinal product should not enter water courses as ivermectin is very toxic for fish and other aquatic organisms as well as for dung insects.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Interchemie werken “De Adelaar” B.V

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX II

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Intermectin Injection 10 mg/ml solution for injection for cattle, sheep and pigs

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Active substance:
Ivermectin 10.0 mg

3. PACKAGE SIZE

50 ml

4. TARGET SPECIES

Cattle, sheep and pig.

5. INDICATION(S)

Read the package leaflet before use.

6. ROUTES OF ADMINISTRATION

For subcutaneous use.

Read the package leaflet before use.

7. WITHDRAWAL PERIODS

Withdrawal period:

Cattle
Meat and offal: 49 days.
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals that are intended to produce milk for human consumption within 60 days of expected parturition.

Sheep
Meat and offal: 63 days.
Not authorised for use in animals producing milk for human consumption.

Do not use in pregnant animals that are intended to produce milk for human consumption within 60 days of expected parturition.

Pigs
Meat and offal: 28 days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use within 28 days.
Once broached use by _____.

9. SPECIAL STORAGE PRECAUTIONS

Keep the glass bottle in the outer carton in order to protect from light.
Keep the bottle in an upright position.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Interchemie werken "De Adelaar" B.V.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Glass injection bottles of 50 ml closed with a rubber stopper and an aluminium cap

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Intermectin Injection 10 mg/ml solution for injection for cattle, sheep and pigs

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Active substance:
Ivermectin 10.0 mg

3. TARGET SPECIES

Cattle, sheep and pig.

4. ROUTES OF ADMINISTRATION

For subcutaneous use.

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:

Cattle
Meat and offal: 49 days.
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals that are intended to produce milk for human consumption within 60 days of expected parturition.

Sheep
Meat and offal: 63 days.
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals that are intended to produce milk for human consumption within 60 days of expected parturition.

Pigs
Meat and offal: 28 days.

6. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use within 28 days.
Once broached use by _____.

7. SPECIAL STORAGE PRECAUTIONS

Keep the glass bottle in the outer carton in order to protect from light.
Keep the bottle in an upright position.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Interchemie werken “De Adelaar” B.V.

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Intermectin Injection 10 mg/ml solution for injection for cattle, sheep and pigs

2. Composition

Each ml contains:
Active substance:
Ivermectin 10.0 mg

Excipients:
Glycerol formal
Propylene glycol

Clear, colourless solution, free from visible suspended particles.

3. Target species

Cattle, sheep and pig.

4. Indications for use

For cattle, sheep and pigs with, or at risk from mixed infections by species of nematodes, warbles, mites and lice. The veterinary medicinal product is only indicated when use against the following parasites is indicated at the same time:

Cattle:

Gastrointestinal nematodes: *Ostertagia ostertagi* (adult, L3, L4, inhibited larvae), *Ostertagia lyrata* (adult, L4), *Haemonchus placei* (adult, L3, L4), *Trichostrongylus axei* (adult, L4), *T. colubriformis* (adult, L4), *Cooperia oncophora* (adult, L4), *C. punctata* (adult, L4), *C. pectinata* (adult, L4), *Cooperia* spp. (L3), *Oesophagostomum radiatum* (adult, L3, L4), *Nematodirus helvetianus* (adult), *N. spathiger* (adult), *Strongyloides papillosus* (adult), *Bunostomum phlebotomum* (adult, L3, L4), *Toxocara vitulorum* (adult).

Lungworms: *Dictyocaulus viviparus* (adult, L4, inhibited larvae).

Roundworms: *Parafilaria bovicola*, *Thelazia* spp. (adult).

Warbles: *Hypoderma bovis, H. lineatum, Dermatobia hominis.*

Lice: *Linognathus vituli, Haematopinus eurysternus, Solenopotes capillatus.*

Mites: *Psoroptes ovis, Sarcoptes scabiei* var. *bovis, Chorioptes bovis*

Persistent Activity:
Given at the recommended dosage of 0.2 mg ivermectin per kg bodyweight, the veterinary medicinal product controls re-infection with the following nematodes up to the duration shown:

Cooperia spp.	7 days
Ostertagia spp.	7 days

Dictyocaulus viviparus 14 days

Sheep:

Gastrointestinal nematodes: *Teladorsagia* (*Ostertagia*) *circumcincta* (adult, L3, L4, inhibited larvae), *Teladorsagia* (*Ostertagia*) *trifurcata* (adult, L4), *Haemonchus contortus* (adult, L3, L4), *Trichostrongylus axei* (adult), *T. colubriformis* (adult, L3, L4), *T. vitrinus* (adult), *Cooperia curticei* (adult, L4), *Oesophagostomum columbianum* (adult, L3, L4), *O. venulosum* (adult), *Chabertia ovina* (adult, L3, L4), *Trichuris ovis* (adult), *Nematodirus filicollis* (adult, L4), *N. spathiger* (L3, L4), *Strongyloides papillosus* (L3, L4).

Lungworms: *Dictyocaulus filaria* (adult, L3, L4), *Protostrongylus rufescens* (adult).

Warbles: *Oestrus ovis* (all larval stage).

Mites: *Psoroptes communis* var. *ovis, Sarcoptes scabiei, Psorergates ovis.*

Pig:

Gastrointestinal nematodes: *Ascaris suum* (adult, L4), *Hyostrongylus rubidus* (adult, L4), *Oesophagostomum* spp. (adult, L4), *Strongyloides ransomi* (adult).

Lungworms: *Metastrongylus* spp. (adult).

Kidneyworms: *Stephanurus dentatus* (adult, L4).

Lice: *Haematopinus suis.*

Mites: *Sarcoptes scabiei* var. *suis.*

5. Contraindications

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

6. Special warnings

Special warnings for safe use in the target species:
Treatment scheme in areas where hypodermosis occurs:
Ivermectin is highly effective against all stages of cattle grubs. However, a proper timing of the treatment is very important. Adult *Hypoderma* flies are known to fly predominantly during the summer months. However, it is possible for a few flies to remain active during the late summer and fall. To achieve optimal results, animals should be treated as soon as possible once heel fly season has ended. As is the case with other veterinary medicinal products for treatment of hypodermosis, the destruction of *Hypoderma* larvae may cause adverse reactions in the host when these larvae are situated in the vital parts of the animal, which may particularly be the case in the period from December to March. The destruction of *Hypoderma lineatum* may cause bloating when the larvae are located at the height of the submucosa of the oesophagus. The destruction of *H. bovis* may cause staggering or paralysis. Therefore, cattle should be treated before or after the presence of these larvae in vital parts of the body.

In sheep treatment of psoroptic mange (sheep scab) with one injection is not recommended because, although a clinical improvement may be seen, elimination of all mites may not occur.
Sheep scab (*Psoroptes ovis*) is an extremely contagious external parasite of sheep. To ensure complete control great care must be taken to avoid re–infestation, as mites may be viable for up to 15 days off the

sheep. It is important that all sheep which have been in contact with infected sheep are treated. Contact between treated, infected and untreated flocks must be avoided until at least seven days after treatment. For an effective control of mite infestations, care must be taken to prevent reinfestation from exposure to untreated animals or contaminated facilities. Louse eggs are unaffected by ivermectin and may require up to three weeks to hatch. Louse infestations developing from hatching eggs may require retreatment.

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In sheep, resistance to ivermectin is widespread in *Teladorsagia circumcincta*, *Trichostrongylus* spp., *Haemonchus contortus* and in other gastro-intestinal parasite species.
Multiple resistance was reported in *Teladorsagia circumcincta* to benzimidazoles, macrocyclic lactones and levamisole and in *Haemonchus contortus* to ivermectin and benzimidazoles.
Multiple resistance to macrocyclic lactones has also been reported in *Psoroptes ovis* scab mites in sheep and in cattle.

The use of this veterinary medicinal product should take into account local information about susceptibility of the target parasites, where available. It is recommended to further investigate cases of suspected resistance, using an appropriate diagnostic method (e.g., Faecal Egg Count Reduction Test). Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.

Special precautions for use in the target species:
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Avermectins may not be well tolerated in all non-target species. Cases of intolerance are reported in dogs – especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises.

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This veterinary medicinal product may cause neurologic effects and may be irritating to the eye. Accidental injection may cause local irritation and/or pain at the injection site. Avoid skin and eye contact. Do not eat or drink during use of this veterinary medicinal product. Avoid self-injection. In case of accidental contact, wash the contacted area with water. In the case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Wash hands after use.

This veterinary medicinal product may cause harm to the unborn foetus. The veterinary medicinal product should not be administered by pregnant women.

Special precautions for the protection of the environment:
The veterinary medicinal product is very toxic to aquatic organisms, soil organisms and dung insects.

The veterinary medicinal product should not be allowed to enter surface waters as it has harmful effects on aquatic and sediment organisms.
Treated cattle should not have direct access to surface water for 31 days and sheep for 16 days after treatment to avoid adverse effects on aquatic organisms.
Long-term effects of ivermectin on the population dynamics of dung organisms have not been investigated. Therefore, it is advisable not to treat animals on the same pasture every season.
In order to avoid accumulation of ivermectin in soil, it is advised not to spread manure containing the active substance on the same area of land in successive years.
Repeated treatments on a pasture within a season should only be given on the advice of a veterinarian.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose:
The toxicity of ivermectin is low; even if the recommended dose is exceeded, the occurrence of intoxication is unlikely. No antidote has been identified.

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

7. Adverse events

Cattle, sheep and pig.

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic and anaphylactic-type reactions[1]

[1] These reactions can be associated with signs like ataxia, convulsions and/or tremor.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

For subcutaneous use.

Cattle:
This veterinary medicinal product should be given only by subcutaneous injection at the recommended dosage level of 0.2 mg ivermectin per kg bodyweight (corresponding to 1 ml per 50 kg bodyweight), as a single dose.

Sheep:
This veterinary medicinal product should be given only by subcutaneous injection at the recommended dosage level of 0.2 mg ivermectin per kg bodyweight (corresponding to 0.5 ml per 25 kg bodyweight), as a single dose.

Pig:

This veterinary medicinal product should be given only by subcutaneous injection in the neck at the recommended dosage level of 0.3 mg ivermectin per kg bodyweight (corresponding to 1 ml per 33 kg bodyweight), as a single dose.

9. Advice on correct administration

Cattle:
Inject under the loose skin in front of or behind the shoulder.
As with any injection, aseptic precautions should be taken. Sterile equipment should be used.

Sheep:
Inject under the loose skin behind the shoulder. In sheep with much wool you must ensure that the needle has penetrated the wool and skin before giving the dose. Use sterile equipment.

Pig:
The injection may be administered with a single-dose syringe or automatic syringe equipment.
Work aseptically.

Underdosing could result in ineffective use and may favour resistance development.
To ensure a correct dosage, body weight should be determined as accurately as possible. If animals are to be treated collectively, reasonably homogeneous groups should be set up, and all animals of a group should be dosed at the rate corresponding to the heaviest one.

When treating groups of animals use only an automatic dosing device. The use of 21G × 1 ½″ needle is suggested. Syringes must be filled from the bottle through a dry sterile draw-off needle that has been placed in the bottle stopper. Bottle stoppers must not be broached more than 20 times.

10. Withdrawal periods

Cattle
Meat and offal: 49 days.
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals that are intended to produce milk for human consumption within 60 days of expected parturition.

Sheep
Meat and offal: 63 days.
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals that are intended to produce milk for human consumption within 60 days of expected parturition.

Pigs
Meat and offal: 28 days.

11. Special storage precautions

Keep out of the sight and reach of children.

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

Keep the bottle in an upright position.

Do not use this veterinary medicinal product after the expiry date which is stated on carton and bottle after Exp. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

The veterinary medicinal product should not enter water courses as ivermectin is very toxic for fish and other aquatic organisms as well as for dung insects.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Clear glass bottles (type II) closed with a bromobutyl rubber stopper and sealed with an aluminium cap or an aluminium flip-off cap with polypropylene cover packed into an outer cardboard box.

Pack sizes:
Cardboard box with one vial with 50 ml solution for injection.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Interchemie werken “De Adelaar” B.V.
Metaalweg 8
5804 CG Venray
The Netherlands
Tel: +31 (0)88 5252233
heetika@interchemie.com

Manufacturer responsible for batch release:
Interchemie Werken De Adelaar Eesti AS
Vanapere tee 14, Püünsi village, Viimsi municipality
Harju county 74013
Estonia

17. Other information

Ivermectin is very toxic to aquatic organisms and dung fauna and can accumulate in soil and sediment. Like other macrocyclic lactones, ivermectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of ivermectin may take place over a period of several weeks. Faeces containing ivermectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.