SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zermex 100 mg/ml LA Solution for Injection for Cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains
Active substance:
Moxidectin 100 mg

Excipient(s):
Benzyl Alcohol (1519) 70 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear yellow liquid**.**

4. CLINICAL PARTICULARS

4.1 Target species

Cattle

4.2 Indications for use, specifying the target species

In cattle weighing from 100 to 500 kg bodyweight

Treatment and prevention of mixed infestations by the following gastro-intestinal nematodes, respiratory nematodes and certain arthropod parasites:

- Adult and immature gastro-intestinal nematodes:

. Haemonchus placei
. Haemonchus contortus
. Ostertagia ostertagi (including inhibited larvae)
. Trichostrongylus axei
. Trichostrongylus colubriformis
. Nematodirus helvetianus (adults only)
. Nematodirus spathiger
. Cooperia surnabada
. Cooperia oncophora
. Cooperia pectinata
. Cooperia punctata

. Oesophagostomum radiatum
. Bunostomum phlebotomum (adults only)
. Chabertia ovina (adults only)
. Trichuris spp. (adults only)

– Adult and immature respiratory tract nematode
. Dictyocaulus viviparus

– Warble grubs (migrating larvae)
. Hypoderma bovis
. Hypoderma lineatum

– Lice
. Linognathus vituli
. Haematopinus eurysternus
. Solenopotes capillatus
. Bovicola bovis (aid in control)

– Mange mites
. Sarcoptes scabiei
. Psoroptes ovis
. Chorioptes bovis (aid in control)

The drug has a persistent action and protects cattle for a certain duration against infection or re-infection with the following parasites for the period indicated:

Species	**Protection period (days)**
Dictyocaulus viviparus	120
Ostertagia ostertagi	120
Haemonchus placei	90
Oesophagostomum radiatum	150
Trichostrongylus axei	90
Linognathus vituli	133

The product is effective against Hypoderma larvae at the time of treatment but its persistent activity against Hypoderma has not been evaluated.
If the product is given before the end of the fly season complimentary treatment with a product effective against Hypoderma may be required.

Persistent efficacy periods have not been established for parasite species other than those included in the above list. Therefore, re-infection of animals on pasture contaminated by parasites other than these remains possible before the end of the 90 day minimum persistency period demonstrated for specific species.

4.3 Contraindications

Do not use in animals less than 100 kg bodyweight or greater than 500 kg.
Do not inject the product by intravascular route. Intravascular injection may result in ataxia, paralysis, convulsions, collapse and death. To prevent any intravascular injection, carefully follow the administration procedure described in item “Amounts to be administered and administration route”.

4.4 Special warnings

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 bodyweight, 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.

4.5 Special precautions for use

Special precautions for use in animals

In order to prevent abscesses, a strict aseptic technique is recommended.
The veterinary medicinal product has been formulated specifically for subcutaneous injection in dorsal surface of the ear of cattle and must not be given by any other route of administration or to any other species.
To avoid possible secondary reactions by the death of Hypoderma larvae in the spine or the oesophagus of animals, it is recommended to administer a product effective against Hypoderma larvae after the end of fly activity and before the larvae reach their resting sites. Consult your veterinary surgeon on the correct timing of this treatment.

Immunity to nematodes depends on adequate exposure to infection. Although not normally the case, circumstances could occur in which anthelmintic control measures might increase the vulnerability of cattle to re-infection. Animals may be at risk towards the end of their first grazing season, particularly if the season is long, or in the following year if they move onto heavily contaminated pasture. In such instances, further control measures may be necessary.

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

Avoid direct contact with skin and eyes.
Wash hands after use.
Do not smoke, drink or eat while handling the product.
Take care to avoid self-injection. Advice to Medical Practitioners in case of accidental self injection: Treat symptomatically.

Other precautions regarding impact on the environment

Moxidectin fulfils the criteria for a (very) persistent, bioaccumulative and toxic (PBT) substance; therefore, exposure of the environment to moxidectin must be limited to the extent possible. Treatments should be administered only when necessary and should be based on faecal egg counts or evaluation of the risk of infestation at the animal and/or herd level.

Like other macrocyclic lactones, moxidectin has the potential to adversely affect non-target organisms:

- Faeces containing moxidectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of cattle with the product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period more than 4 weeks and may decrease dung fly abundance during that period. It has been established in laboratory tests that moxidectin may temporarily affect dung beetle reproduction; however, field studies indicate no long-term effects. Nevertheless, in case of repeated treatments with moxidectin (as with products of the same anthelmintic class) it is advisable not to treat animals every time on the same pasture to allow dung fauna populations to recover.
- Moxidectin is inherently toxic to aquatic organisms including fish. The product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the injectable formulation, treated animals should not have access to watercourses during the 10 days after treatment.

4.6 Adverse reactions (frequency and seriousness)

On rare occasions, immediate or delayed swelling can be observed at the injection site, these swellings may further develop into abscesses (approx. 1% of cases). The frequency of injection site swellings tends to be higher in the heavier animals. These side effects generally disappear without treatment , within 14 days after administration, some may persist for up to 5 weeks in a number of animals (<5%) and in very rare occasions longer.

On rare occasions, depression and ataxia can be observed after injection.
In case of hypersensitivity reactions, a symptomatic treatment should be applied.

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

Can be used during pregnancy. However, note 4.11, Withdrawal periods.

4.8 Interaction with other medicinal products and other forms of interaction

The effects of GABA agonists are increased by moxidectin

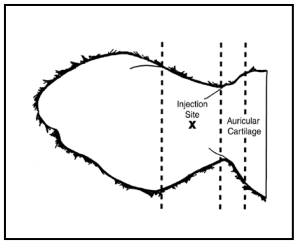
4.9 Amounts to be administered and administration route

Dosage is 0.5 ml/50 kg bodyweight, equivalent to 1.0 mg moxidectin/kg bodyweight, given by a single subcutaneous injection in the ear using an 18 gauge, 25 – 40 mm hypodermic needle. The 50ml vial stoppers must not be broached more than 20 times. Use automatic syringe equipment for the 200 ml vial. To ensure administration of a correct dosage, bodyweight should be determined as accurately as possible: accuracy of the dosage should be checked.
The injection should be given subcutaneously in the loose tissues on the dorsal surface of the ear, just distal to the distal edge of the auricular cartilage.
The dorsal (outer) surface of the ear should first be cleansed with antiseptic and allowed to briefly air dry. Palpate the edge of the auricular cartilage closest to the head, on the dorsal (hairy) surface of the ear. From this landmark, taking care to avoid blood vessels (artery, vein), the needle should be inserted subcutaneously starting at a point approximately 3 to 3.5 cm distal to this edge (away from the head), and directed towards the base of the ear, and the needle advanced to the hub. At this point, gently aspirate the syringe to confirm that the needle is not in a blood vessel.
Upon injection, the resulting depot should reside just distal to the edge of the auricular cartilage.
Following administration, the needle is withdrawn from the skin as pressure is applied for several seconds with the thumb at the point of insertion.

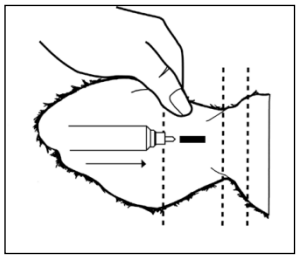
Due to the long lasting protection against *Dictyocaulus viviparus* and the stomach worms, *Ostertagia ostertagi* and *Haemonchus placei*, a single treatment with the formulation at turn-out helps control parasitic bronchitis (lungworm) and parasitic gastro-enteritis throughout the grazing season by reducing the build-up of infective larvae on pasture associated with these parasites. For best results the injection should be given to each calf of target weight to be grazed together immediately prior to being turned out to pasture. Animals should be set stocked throughout the grazing season or moved to a pasture which has not been grazed by other cattle earlier in the season.

Shake vigorously before use.

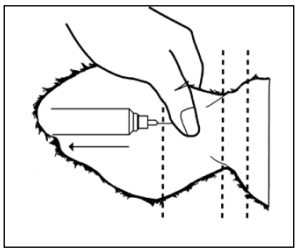
Diagram: Ear injection procedure



- The injection site is approximately 3.5 cm (1.5 inches) distal to the distal edge of the auricular cartilage.



- **Use one hand to grasp and steady the ear.**
- Inject subcutaneously using an 18 gauge x 1 inch needle.



- **Inject contents. Depot should be just distal to the distal edge of the auricular cartilage.**
- Apply pressure at the point of insertion as the needle is withdrawn from the skin to help seal the opening.

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

Reactions at the injection site have to be expected more frequently and severe depending on the injected volume. Systemic signs of overdoses are consistent with the mode of action of moxidectin. These signs are manifested as transient salivation, depression, drowsiness and ataxia 24 to 36 hours post-treatment. The systemic signs usually disappear within 36 to 72 hours without treatment. At doses >3 times the recommended dose divided on both ears, the systemic signs included recumbency, muscle tremor, ruminal tympany and dehydration, which were resolved after treatment with fluids. The systemic signs can last for a few days to ten days. There is no specific antidote.

4.11 Withdrawal period(s)

Meat and offal: 108 days.
Milk: Not permitted for use in lactating animals producing milk for human consumption or industrial purposes or within 80 days of expected parturition.

The withdrawal period is based solely on a single injection at the ear site of injection.

5. PHARMACOLOGICAL PROPERTIES

ATCvet Code QP54AB02

Moxidectin is an endectocide active against a wide range of internal and external parasites and is a second generation macrocyclic lactone of the milbemycin family.

5.1 Pharmacodynamic properties

Moxidectin interacts with GABA receptors and chloride channels.
The net effect is to open the chloride channels on the postsynaptic junction to allow the inflow of chloride ions and induce an irreversible resting state. This results in flaccid paralysis and eventual death of parasites exposed to the drug.

5.2 Pharmacokinetic particulars

Moxidectin is absorbed following subcutaneous injection with maximum blood concentrations being achieved 24 to 48 hours post injection. The drug is distributed throughout the body tissues but due to its lipophilicity it is concentrated mainly in the fat. The depletion half life in fat is 26 – 32 days.

Moxidectin undergoes limited biotransformation by hydroxylation in the body. The only significant route of excretion is the faeces.

5.3 Environmental properties

Moxidectin fulfils the criteria for a (very) persistent, bioaccumulative and toxic (PBT) substance. In particular, in acute and chronic toxicity studies with algae, crustaceans and fish, moxidectin showed toxicity to these organisms, yielding the following endpoints:

Organism		EC50	NOEC
Algae	*S. capricornutum*	>86.9 µg/l	86.9 µg/l
Crustaceans (Water fleas)	*Daphnia magna* (acute)	0.0302 µg/l	0.011 µg/l
	Daphnia magna (reproduction)	0.0031 µg/l	0.010 µg/l
Fish	*O. mykiss*	0.160 µg/l	Not determined
	L. macrochirus	0.620 µg/l	0.52 µg/l
	P. promelas (early life stages)	Not applicable	0.0032 µg/l
	Cyprinus carpio	0.11 µg/l	Not determined

EC50: the concentration which results in 50% of the test species individuals being adversely affected, i.e. both mortality and sub-lethal effects.
NOEC: the concentration in the study at which no effects are observed.

This implies that when allowing moxidectin to enter water bodies, this may have a severe and lasting impact on aquatic life. To mitigate this risk, all precautions for use and disposal must be adhered to.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Sorbitan monooleate
Propylene glycol dicaprylocaprate

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: 3 years
Shelf-life after first opening the immediate packaging: 28 days

6.4 Special precautions for storage

Do not store above 25°C.

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

6.5 Nature and composition of immediate packaging

Nature of the primary container:
HDPE vial
Flurotec coated chlorinated butyl rubber stopper
Aluminium flip off seal (50 ml vial)
Aluminium seal (200 ml)
Presentations to be sold and identification numbers:
- Box containing 1 vial of 50ml size
- Box 1 vial of 200ml size

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 material derived from such veterinary medicinal products should be disposed of in accordance with local requirements. Do not contaminate watercourses with the product. Extremely dangerous for fish and aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

Zoetis UK Limited
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8. MARKETING AUTHORISATION NUMBER

Vm 42058/4172

9. DATE OF FIRST AUTHORISATION

19 November 2009

10. DATE OF REVISION OF THE TEXT

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Approved 22 October 2019