SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Santiola 50 mg/ml solution for injection for cattle and sheep (BG, CZ, EE, GB, HR, HU, IE, LT, LV, RO, SI, SK)
Santiola vet 50 mg/ml solution for injection for cattle and sheep (DK, SE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains

Active substance:
Closantel 50 mg
(equivalent to closantel sodium dihydrate 54.375 mg)

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Clear light yellow to yellow or brown yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and sheep

4.2 Indications for use, specifying the target species

For treatment of the following trematodes (fluke), gastro-intestinal nematodes and arthropods if sensitive to closantel.

Sheep

Trematodes
Fasciola hepatica (adult)
Fasciola gigantica (adult and 8 weeks immature)

Nematodes
Haemonchus contortus (adult and immature)
Oesophagostomum columbianum (adult and immature)
Gaigeria pachyscelis (adult and immature)
Chabertia ovina (adult and immature)

Arthropods
Oestrus ovis (1st, 2 nd and 3rd instar)

Cattle

Trematodes
Fasciola hepatica (adult)
Fasciola gigantica (adult and 8 week immature)

Nematodes
Haemonchus placei (adult and immature)
Bunostomum phlebotomum (adult and immature)
Oesophagostomum radiatum (adult and immature)

Arthropods
Hypoderma bovis (dermal stages)
Hypoderma lineatum (dermal stages)

4.3 Contraindications

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

4.4 Special warnings for each target species

Do not exceed the stated dose.

Care should be taken to ensure that all injection procedures are correctly carried out and body weights accurately assessed.

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.

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

Safe and efficacious use of this product at a dose of 2.5 mg/kg is dependent on accurate species level parasitological diagnosis of risks at farm level. Where this is unavailable, the dose rate of 5 mg/kg must be used

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

Wash hands after administration.
Take care to avoid accidental self-administration.

Other precautions
Closantel is toxic to dung fauna.
To reduce the risk for the dung fauna, treated and untreated animals should be grazed on the same field.
In order to reduce the risk to aquatic organisms, treated animals should be kept out of water for at least 48 hours after treatment.

4.6 Adverse reactions (frequency and seriousness)

The solution contains polyvidone. This substance may in very rare cases induce hyperacute anaphylactic reactions in cattle.

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 and lactation.
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

Route of administration:
Cattle: subcutaneous route
Sheep: subcutaneous route

To ensure administration of a correct dose, body weight should be determined as accurately as possible.
When large volumes have to be injected (more than 20 ml), divide the total volume equally over both neck sides.
Do not exceed 20 broachings per vial. If more than 20 broachings are required, use of a draw off needle is recommended.
If treatment is to be repeated, a minimum interval of 11 weeks for cattle and 107 days for sheep must be observed in order to avoid accumulation of residues.

Dose:
Cattle

2.5 mg/kg BW (1 ml/20 kg BW)	Adults	Immatures
Fasciola hepatica	X	
Fasciola gigantica	X	
Haemonchus placei	X	X
Bunostomum phlebotomum	X	
Oesophagostomum radiatum	X	

5.0 mg/kg BW (1 ml/10 kg BW)	Adults	Immatures
Fasciola hepatica	X	
Fasciola gigantica	X	From 8 weeks after
Haemonchus placei	X	infection
Bunostomum phlebotomum	X	X
Oesophagostomum radiatum	X	X
Hypoderma bovis	Dermal stages	X
Hypoderma lineatum	Dermal stages	

Sheep

2.5 mg/kg BW (1 ml/20 kg BW)	Adults	Immatures
Haemonchus contortus	X	X
Gaigeria pachyscelis	X	X
Oestrus ovis	1st, 2nd and 3rd instar	

5.0 mg/kg BW (1 ml/10 kg BW)	Adults	Immatures
Fasciola hepatica	X	
Fasciola gigantica	X	From 8 weeks after
Haemonchus contortus (+ BZ-resistant strains)	X	infection
Oesophagostomum columbianum	X	X
	X	X
Chabertia ovina		X

Because of its long half-life, closantel will protect for several weeks against re-infections with the following nematodes:

Cattle

Residual Activity	Dose (mg/kg)	Protection Period
Haemonchus placei	2.5	4 weeks
	5	6 weeks
Bunostomum phlebotomum	5	3 weeks
Oesophagostomu radiatum	5	2 weeks

Sheep

Residual Activity	Dose (mg/kg)	Protection Period
Haemonchus contortus	2.5	2 weeks
	5	7 weeks
Gaigeria pachyscelis	2.5	3 weeks
	5	8 weeks
Oestrus ovis	5	8 weeks

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

Symptoms of acute overdosage are decreased vision or blindness, anorexia, incoordination and general weakness.

4.11 Withdrawal period(s)

Cattle: meat and offal: 77 days
Sheep: meat and offal: 107 days

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.
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: anthelmintics, phenol derivatives, including salicylanilides
ATCvet code: QP52AG09

5.1 Pharmacodynamic properties

The product contains the salicylanilide closantel, a synthetic antiparasitic agent with high efficacy against liver fluke (*Fasciola gigantica and Fasciola hepatica*), haematophagous nematodes (*Bunostomum phlebotomum, Chabertia ovina, Gaigeria pachyscelis, Haemonchus contortus* – including benzimidazole-resistant strains, *Haemonchus placei, Oesophagostomum columbianum*, and *Oesophagostomum radiatum*) and larval stages of some arthropods (*Hypoderma bovis, Hypoderma lineatum,* and *Oestrus ovis*) in sheep and cattle.
Closantel is an uncoupler of mitochondrial oxidative phosphorylation resulting in inhibition of ATP synthesis. This induces a marked change in the energy metabolism and finally leads to death of the parasite.

5.2 Pharmacokinetic particulars

Closantel is rapidly absorbed into the systemic circulation with peak plasma levels at 24-48 hours after dosing. In plasma, closantel is bound 99% to albumin. As a result, tissue distribution is very limited. On average, tissue levels are 15 times lower than plasma levels. The elimination half-life of closantel from plasma and tissues is

approximately 2 to 4 weeks in sheep and 9 to 21 days in cattle. The drug is poorly metabolised and the main excretion route is in the faeces via the bile. Urinary excretion is negligible.

Environmental properties
Closantel has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of closantel may take place over a period of several weeks. Faeces containing closantel excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.
Closantel may affect aquatic organisms (aquatic invertebrates, sediment dwellers and fish).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol (E1520)
Povidone K 12
Citric acid monohydrate
Sodium hydroxide
Water for injections

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

6.4 Special precautions for storage

Store below 30 °C.
Store in the original container in order to protect from light.
Once opened, store below 25 °C.

6.5 Nature and composition of immediate packaging

Container or pack size: 1 or 4 type I amber glass vials.
Closure: bromobutyl rubber.
Contents of each vial: 250 ml solution.
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 materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

The product should not enter water courses as this may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

KRKA d.d., Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

8. MARKETING AUTHORISATION NUMBER

Vm 01656/4118

9. DATE OF FIRST AUTHORISATION

06 March 2018

10. DATE OF REVISION OF THE TEXT

August 2019

Approved: 08 August 2019