SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dehinel Plus Flavour Tablets for dogs (Czech Republic, Hungary, Estonia, Latvia, Lithuania, Poland, Romania, Slovenia, Slovakia)
Endogard Plus Flavour Tablets for dogs (United Kingdom, Austria, Belgium, Germany, Denmark, Greece, Ireland, Netherlands, Portugal)
Endogard Sabor Tablets for dogs (Spain)
Endogard Flavour Tablets for dogs (Italy)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:

Praziquantel	50 mg
Pyrantel embonate	144 mg
Febantel	150 mg

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.
Round, yellow, uncoated tablets with visible darker spots and bevelled edges with cross line on one side and plain on other side.
The tablets can be divided into equal halves or equal quarters.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs (small and medium size)

4.2 Indications for use, specifying the target species

For the treatment of mixed infestations with the following roundworms and tapeworms in adult dogs and puppies:

Nematodes
Ascarids: *Toxocara canis*, *Toxascaris leonina* (late immature forms and mature forms)
Hookworms: *Uncinaria stenocephala*, *Ancylostoma caninum* (adults)
Cestodes
Tapeworms: *Taenia* spp., *Dipylidium caninum*

4.3 Contraindications

Do not use simultaneously with piperazine compounds.
Do not exceed the stated dosage when treating pregnant bitches.
Do not use in animals with a known hypersensitivity to the active substance or to any of excipients.
Not for use in dogs younger than 2 weeks of age and/or weighing less than 2 kg.

4.4 Special warnings for each target species

Fleas serve as intermediate hosts for one common type of tapeworm – *Dipylidium caninum*. Tapeworm infestation is certain to re-occur unless control of intermediate hosts such as fleas, mice etc. is undertaken.

4.5 Special precautions for use

Special precautions for use in animals
Any part-used tablets should be discarded.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In the interests of good hygiene, persons administering the tablet directly to a dog or by adding it to the dog's food should wash their hands afterwards.
In case of accidental ingestion, seek medical advice and show the package leaflet to the physician.

4.6 Adverse reactions (frequency and seriousness)

In rare cases transient loose faeces, diarrhoea and/or vomiting may occur in some puppies. In adult dogs, very rare cases of vomiting, with or without diarrhoea, may occur.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Consult a veterinary surgeon before treating pregnant animals for roundworms.
The product may be used during lactation (see Sections 4.3 and 4.9).
Do not use in bitches during the first two-thirds of pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with piperazine as the anthelmintic effects of pyrantel and piperazine (used in many worming products for dogs) may be antagonized.
Concurrent use with other cholinergic compounds can lead to toxicity.

4.9 Amounts to be administered and administration route

For oral administration.

Dosage
The recommended dose rates are: 15 mg/kg bodyweight febantel, 14.4 mg/kg pyrantel and 5 mg/kg praziquantel. This is equivalent to 1 tablet per 10 kg bodyweight.
Tablets may be halved/quartered to allow accuracy of dosing.

Administration and Duration of Treatment
The tablet(s) can be given directly to the dog or disguised in food. No restriction of access to food is required either before or after administration of the product.
To ensure administration of a correct dose, body weight should be determined as accurately as possible.
Puppies may be wormed with this product from 2 weeks of age and every 2 weeks until 12 weeks of age. Thereafter they should be treated at 3 monthly intervals. It is advisable to treat the bitch at the same time as the puppies.
For the control of *Toxocara*, nursing bitches should be dosed 2 weeks after giving birth and every 2 weeks until weaning.
For routine control a single dose is recommended at 3 monthly intervals.
In the event of a heavy roundworm infestation, a repeat dose should be given after 14 days.

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

Benzimidazoles possess wide safety margin. Pyrantel is not absorbed systematically to any extent. Praziquantel also has a wide safety margin, of up to five times the recommended dose.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anthelmintics, Benzimidazoles and related substances, ATCvet code: QP52AC55

5.1 Pharmacodynamic properties

The product contains anthelmintics active against roundworms and tapeworms. The product contains three active substances: febantel, pyrantel embonate (pamoate) and praziquantel, a partially hydrogenated pyrazino-isoquinoline derivative used widely as an anthelmintic for both human and veterinary use. Pyrantel acts as a cholinergic agonist. Its mode of action is to stimulate nicotinic cholinergic receptors of the parasite, induce spastic paralysis and thereby allow removal from the gastro-intestinal (GI) system by peristalsis.
With the mammalian system febantel undergoes ring closure forming fenbendazole and oxfendazole. It is these chemical entities which exert the anthelmintic effect by inhibition of tubulin polymerization. Formation of microtubules is thereby prevented,

resulting in disruption to structures vital to the normal functioning of the helminth. Glucose uptake, in particular, is affected, leading to depletion in cell ATP. The parasite dies upon exhaustion of its energy reserves, which occurs 2 – 3 days later. Praziquantel is very rapidly absorbed and distributed throughout the parasite. Both *in vitro* and *in vivo* studies have shown that praziquantel causes severe damage to the parasite integument, resulting in contraction and paralysis. There is an almost instantaneous tetanic contraction of the parasite musculature and a rapid vacuolisation of the syncytial tegument. This rapid contraction has been explained by changes in divalent cation fluxes, especially calcium.

In this fixed combination product pyrantel and febantel act synergistically against all relevant nematodes (ascarids and hookworms) in dogs. In particular, the activity spectrum covers *Toxocara canis*, *Toxascaris leonina*, *Uncinaria stenocephala* and *Ancylostoma caninum.* The spectrum of activity of praziquntel covers also cestode species in dogs, in particular all *Taenia* spp.and *Dipylidium caninum*,. Praziquantel acts against adult and immature forms of these parasites.

5.2 Pharmacokinetic particulars

Perorally administered praziquantel is absorbed almost completely from the intestinal tract. After absorption, the drug is distributed to all organs. Praziquantel is metabolized into inactive forms in the liver and secreted in bile. It is excreted within 24 hours to more than 95% of the administered dosage. Only traces of non-metabolised praziquantel are excreted.

The pamoate salt of pyrantel has low aqueous solubility, an attribute that reduces absorption from the gut and allows the drug to reach and be effective against parasites in the large intestine. Because of the low systemic absorption of pyrantel pamoate, there is very little danger of adverse reactions/toxicity in the host. Following absorption, pyrantel pamoate is quickly and almost completely metabolized into inactive metabolites that are excreted rapidly in the urine.

Febantel is absorbed relatively rapidly and metabolized to a number of metabolites including fenbendazole and oxfendazole, which have anthelmintic activity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Povidone K-30
Sodium laurilsulfate
Microcrystalline cellulose (E460)
Colloidal anhydrous silica
Magnesium stearate (E572)
Meat flavour

6.2 Incompatibilities

None known.

6.3 Shelf life

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

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Nature of container: Print and perforated Alu-Alu blister: 2 tablets (1 blister with 2 tablets), in a box.
Print and perforated Alu-Alu blister: 4 tablets (2 blisters with 2 tablets), in a box.
Print and perforated Alu-Alu blister: 10 tablets (1 blister with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 30 tablets (3 blisters with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 50 tablets (5 blisters with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 100 tablets (10 blisters with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 300 tablets (30 blisters with 10 tablets), in a box.
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.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

Vm 01656/4017

9. DATE OF FIRST AUTHORISATION

02 June 2011

10. DATE OF REVISION OF THE TEXT

June 2016

Approved: 23 June 2016

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dehinel Plus XL Tablets for dogs (Czech Republic, Hungary, Estonia, Latvia, Lithuania, Poland, Romania, Slovenia, Slovakia)
Endogard Plus XL Tablets for dogs (United Kingdom, Austria, Belgium, Germany, Denmark, Greece, Ireland, Netherlands, Portugal)
Endogard para perros grandes (Spain)
Endogard per cani grandi (Italy)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:

Praziquantel	175 mg
Pyrantel embonate	504 mg
Febantel	525 mg

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets
Oval, biconvex tablets with bevelled edges and scored on both sides. Slightly greenish-yellow.
The tablets can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs (large and extra large size)

4.2 Indications for use, specifying the target species

For the treatment of mixed infestations with the following roundworms and tapeworms in adult dogs:
Nematodes:
Ascarids: *Toxocara canis*, *Toxascaris leonina* (late immature forms and mature forms)
Hookworms: *Uncinaria stenocephala*, *Ancylostoma caninum* (adults)
Cestodes:
Tapeworms: *Taenia* spp., *Dipylidium caninum*

4.3 Contraindications

Do not use simultaneously with piperazine compounds.
Do not use in animals with a known hypersensitivity to the active substance or to any of excipients.
Do not exceed the stated dosage when treating pregnant bitches.

4.4 Special warnings for each target species

Fleas serve as intermediate hosts for one common type of tapeworm – *Dipylidium caninum*. Tapeworm infestation is certain to re-occur unless control of intermediate hosts such as fleas, mice etc. is undertaken.

4.5 Special precautions for use

Special precautions for use in animals
This product is not recommended for use in dogs under 17.5 kg body weight.
Any part-used tablets should be discarded.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In the interests of good hygiene, persons administering the tablet directly to a dog or by adding it to the dog's food, should wash their hands afterwards.
In case of accidental ingestion, seek medical advice and show the package leaflet to the physician.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases vomiting, with or without diarrhoea, may occur.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Consult a veterinary surgeon before treating pregnant animals for roundworms.
The product may be used during lactation (see also Sections 4.3 and 4.9).
Do not use in bitches during the first two-thirds of pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with piperazine as the anthelmintic effects of pyrantel and piperazine (used in many worming products for dogs) may be antagonized.
Concurrent use with other cholinergic compounds can lead to toxicity.

4.9 Amounts to be administered and administration route

For oral administration.

Dosage

The recommended dose rates are: 15 mg/kg bodyweight febantel, 14.4 mg/kg pyrantel and 5 mg/kg praziquantel. This is equivalent to 1 tablet per 35 kg bodyweight.

Tablets may be halved to allow accuracy of dosing.

Administration and Duration of Treatment

No restriction of access to food is required either before or after administration of the product. The tablet(s) can be given directly to the dog or disguised in food.
To ensure administration of a correct dose, bodyweight should be determined as accurately as possible.
For the control of *Toxocara*, nursing bitches should be dosed 2 weeks after giving birth and every 2 weeks until weaning.
In the event of a heavy roundworm infestation, a repeat dose should be given after 14 days.
For routine control adult dogs should be treated every 3 months.

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

The product is well tolerated in dogs. In safety studies, doses of up to five times the recommended dose gave rise to occasional vomiting.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anthelmintics, Benzimidazoles and related substances, ATCvet code: QP52AC55

5.1 Pharmacodynamic properties

The product contains anthelmintics active against roundworms and tapeworms. The product contains three active substances: febantel, pyrantel embonate (pamoate) and praziquantel, a partially hydrogenated pyrazino-isoquinoline derivative used widely as an anthelmintic for both human and veterinary use.
Pyrantel acts as a cholinergic agonist. Its mode of action is to stimulate nicotinic cholinergic receptors of the parasite, induce spastic paralysis and thereby allow removal from the gastro-intestinal (GI) system by peristalsis.
With the mammalian system febantel undergoes ring closure forming fenbendazole and oxfendazole. It is these chemical entities which exert the anthelmintic effect by inhibition of tubulin polymerization. Formation of microtubules is thereby prevented, resulting in disruption to structures vital to the normal functioning of the helminth.

Glucose uptake, in particular, is affected, leading to depletion in cell ATP. The parasite dies upon exhaustion of its energy reserves, which occurs 2 – 3 days later.
Praziquantel is very rapidly absorbed and distributed throughout the parasite. Both *in vitro* and *in vivo* studies have shown that praziquantel causes severe damage to the parasite integument, resulting in contraction and paralysis. There is an almost instantaneous tetanic contraction of the parasite musculature and a rapid vacuolisation of the syncytial tegument. This rapid contraction has been explained by changes in divalent cation fluxes, especially calcium.

In this fixed combination product pyrantel and febantel act synergistically against all relevant nematodes in dogs. In particular, the activity spectrum covers *Toxocara canis*, *Toxascaris leonina*, *Uncinaria stenocephala* and *Ancylostoma caninum*. The spectrum of activity of praziquntel covers also cestode species in dogs, in particular all *Taenia* spp. and *Dipylidium caninum*. Praziquantel acts against adult and immature forms of these parasites.

5.2 Pharmacokinetic particulars

Perorally administered praziquantel is absorbed almost completely from the intestinal tract. After absorption, the drug is distributed to all organs. Praziquantel is metabolized into inactive forms in the liver and secreted in bile. It is excreted within 24 hours to more than 95% of the administered dosage. Only traces of non-metabolised praziquantel is excreted.

The pamoate salt of pyrantel has low aqueous solubility, an attribute that reduces absorption from the gut and allows the drug to reach and be effective against parasites in the large intestine. Because of the low systemic absorption of pyrantel pamoate, there is very little danger of adverse reactions/toxicity in the host. Following absorption, pyrantel pamoate is quickly and almost completely metabolized into inactive metabolites that are excreted rapidly in the urine.

Febantel is absorbed relatively rapidly and metabolized to a number of metabolites including fenbendazole and oxfendazole, which have anthelmintic activity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Povidone K-30
Sodium laurilsulfate
Microcrystalline cellulose (E460)
Colloidal anhydrous silica
Magnesium stearate (E572)

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Print and perforated Alu-Alu blister: 2 tablets (1 blister with 2 tablets), in a box.
Print and perforated Alu-Alu blister: 4 tablets (2 blisters with 2 tablets), in a box.
Print and perforated Alu-Alu blister: 10 tablets (1 blister with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 12 tablets (2 blisters with 6 tablets), in a box.
Print and perforated Alu-Alu blister: 24 tablets (4 blisters with 6 tablets), in a box.
Print and perforated Alu-Alu blister: 30 tablets (3 blisters with 10 tablets or 5 blisters with 6 tablets), in a box.
Print and perforated Alu-Alu blister: 50 tablets (5 blisters with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 60 tablets (10 blisters with 6 tablets or 6 blisters with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 100 tablets (10 blisters with 10 tablets), in a box.
Print and perforated Alu-Alu blister: 102 tablets (17 blisters with 6 tablets), in a box.
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.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

Vm 01656/4018

9. DATE OF FIRST AUTHORISATION

June 2011

10. DATE OF REVISION OF THE TEXT

January 2016

Approved: 26 January 2016