

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DOLAGIS 50 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

One tablet contains:

Carprofen 50 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

Clover-shaped scored beige tablet

The tablet can be divided into four equal parts.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

In the dog:

Reduction of inflammation and pain caused by musculo-skeletal disorders and degenerative joint disease.

As a follow-up to parenteral analgesia in the management of post-operative pain.

4.3 Contraindications

Do not use in pregnant and lactating bitches.

Do not use in dogs aged less than 4 months in the absence of specific data.

Do not use in cats.

Do not use in dogs, suffering from cardiac, hepatic or renal disease, when there is a possibility of gastrointestinal ulceration or bleeding or where there is evidence of blood dyscrasia.

Do not use in case of hypersensitivity to the active substance, to other NSAIDs and to any of the excipients.

4.4 Special warnings for each target species

See sections 4.3 and 4.5.

4.5 Special precautions for use

Special precautions for use in animals

Use in dogs less than 6 weeks of age, or in aged dogs, may involve additional risk. If such a use cannot be avoided, dogs may require a reduced dosage and careful clinical management.

Avoid use in any dehydrated, hypovolaemic or hypotensive dog, as there is a potential risk of increased renal toxicity.

Concurrent administration of potential nephrotoxic drugs should be avoided.

NSAIDs can cause inhibition of phagocytosis and hence in the treatment of inflammatory conditions associated with bacterial infection, appropriate concurrent antimicrobial therapy should be instigated.

As with other NSAIDs, photodermatitis during treatment with carprofen has been observed in laboratory animals and in humans. These skin reactions have never been observed in dogs.

Do not administer other NSAIDs concurrently or within 24 hours of each other. Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs, which can lead to toxic effects.

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

In case of accidental ingestion, seek medical advice immediately and show the package leaflet to the physician.

Wash hands after handling the product.

4.6 Adverse reactions (frequency and seriousness)

Typical undesirable effects associated with NSAIDs, such as vomiting, soft faeces/diarrhea, faecal occult blood, loss of appetite and lethargy have been reported. These adverse reactions generally occur within the first treatment week and are in most cases transient and disappear following termination of the treatment but in very rare cases may be serious or fatal.

If adverse reactions occur, use of the product should be stopped and the advice of a veterinarian should be sought.

As with other NSAIDs there is a risk of rare renal or idiosyncratic hepatic adverse events.

4.7 Use during pregnancy and lactation

Studies in laboratory species (rat and rabbit) have shown evidence of foetotoxic effects of carprofen at doses close to the therapeutic dose. The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Do not use in pregnant or lactating bitches.

For breeding animals, do not use during reproduction period.

4.8 Interaction with other medicinal products and other forms of interaction

Carprofen is highly bound to plasma proteins and compete with other highly bound drugs, which can increase their respective toxic effects.

Do not use this veterinary medicinal drug concurrently with other NSAIDs or with glucocorticoids.

Concurrent administration of potentially nephrotoxic drugs (e.g. aminoglycoside antibiotics) should be avoided.

Refers also to section 4.5

4.9 Amounts to be administered and administration route

For oral administration.

4 mg carprofen per kg bodyweight per day.

An initial dose of 4 mg carprofen per kg bodyweight per day given as a single daily dose. The analgesic effect from each dose persists for at least 12 hours.

The daily dose may be reduced, subject to clinical response.

Duration of treatment will be dependant upon the response seen. Long term treatment should be under regular veterinary supervision.

To extend analgesic and anti-inflammatory cover post-operatively parenteral pre-operative treatment with an injectable carprofen may be followed with carprofen tablets at 4 mg/kg/day for 5 days.

Do not exceed the stated dose.

The breakability method is the following: Put the tablet on a plain surface, with its scored side facing the surface (convex face up).

With the tip of forefinger, exert a slight vertical pressure on the middle of the tablet to break it in its width into halves. In order to obtain quarters, then exert a slight pressure on the middle of one half with forefinger to break it in its length.

The tablet is divisible and can be used as follows:

Number of tablets per day	Dog weight (kg)		
$\frac{1}{4}$	> 3	-	< 6
$\frac{1}{2}$	≥ 6	-	< 9
$\frac{3}{4}$	≥ 9	-	< 12.5
1	≥ 12.5	-	< 15.5
1 $\frac{1}{4}$	≥ 15.5	-	< 18.5
1 $\frac{1}{2}$	≥ 18.5	-	< 21.5
1 $\frac{3}{4}$	≥ 21.5	-	< 25
2	≥ 25	-	< 28
2 $\frac{1}{4}$	≥ 28	-	< 31
2 $\frac{1}{2}$	≥ 31	-	< 34
2 $\frac{3}{4}$	≥ 34	-	< 37
3	≥ 37	-	< 40
3 $\frac{1}{4}$	≥ 40	-	< 43
3 $\frac{1}{2}$	≥ 43	-	< 45

The tablets are flavoured, and are accepted by dogs, but they may be administered directly in the mouth of the dog or added to food if necessary.

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

Bibliographic data report that carprofen is well tolerated in dogs at twice the recommended dosage for 42 days.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

ATCvet code: QM01AE91

Pharmacotherapeutic group: anti-inflammatory, NSAID, aryl proprionic acids

5.1 Pharmacodynamic properties

Carprofen is a non-steroidal anti-inflammatory drug (NSAID), of the 2-aryl propionic acid class and possesses anti-inflammatory, analgesic and antipyretic activities.

The mechanism of action of carprofen, is not well known. However, it was shown that the inhibition of the cyclo-oxygenase enzyme by carprofen is relatively weak at the recommended dosage. Moreover, it was shown that carprofen doesn't inhibit the generation of thromboxane (TX) B₂ in dog clotting blood and neither prostaglandin (PG) E₂ nor 12-hydroxyeicosatetraenoic acid (HETE) in inflammatory exudate are inhibited. This suggests the mechanism of action of carprofen is not the inhibition of the eicosanoids. Some authors suggested an activity of carprofen on one or numerous inflammatory mediators not yet identified but no clinical evidence could be shown.

Carprofen exists in two enantiomeric forms, R(-)-carprofen and S(+)-carprofen and the racemic form is the one marketed. Laboratory animal studies suggest that the S(+) enantiomer possesses greater anti-inflammatory potency.

Ulcerogenic potential of carprofen has been shown in the rodents but not in the dogs.

5.2 Pharmacokinetic particulars

After a single oral administration of 4 mg of carprofen per kg of bodyweight in dog, the time to obtain a maximum plasma concentration of 23 µg/ml is about 2 hours. The oral bioavailability is more than 90% of the total dose. Carprofen is more than 98% bound to plasma proteins and its volume of distribution is low.

Carprofen is excreted in the bile with 70 % of an intra-venous dose of carprofen being eliminated in the faeces, mainly as the glucuronide conjugate. Carprofen undergoes an enantioselective enterohepatic cycle in dog, with only the S(+) enantiomer being significantly recycled. The plasma clearance of the S(+) carprofen is about twice that of the R(-) carprofen. The biliary clearance of S(+) carprofen seems to be subject to stereoselectivity too as it is about three times higher than that of R(-) carprofen.

Environmental properties

No studies have been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pig liver flavour
Yeast,
Croscarmellose sodium,
Copovidone,
Magnesium stearate,
Anhydrous colloidal silica,
Microcrystalline cellulose,
Lactose monohydrate.

6.2 Incompatibilities

None

6.3 Shelf life

36 months.

6.4. Special precautions for storage

Do not store above 30°C.
Protect from light

6.5 Nature and composition of immediate packaging

Blister complex: PVDC-PVC/Aluminium heat sealed blisters with 10 tablets / blister.
Cardboard box with 2 blisters of 10 tablets
Cardboard box with 10 blisters of 10 tablets
Cardboard box with 20 blisters of 10 tablets
Cardboard box with 30 blisters of 10 tablets
Cardboard box with 40 blisters of 10 tablets
Cardboard box with 50 blisters of 10 tablets

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

Vm 20749/4005

9. DATE OF FIRST AUTHORISATION

31/01/2008

10. DATE OF REVISION OF THE TEXT

April 2009

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be completed in accordance with national requirements