Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Zelys 1.25 mg chewable tablets for dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:
Pimobendan 1.25 mg

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

3 PHARMACEUTICAL FORM

Chewable tablet
Round in shape beige to light brown tablet, with single score line on one side.
The tablets can be divided into two equal parts.

4 CLINICAL PARTICULARS

4.1 Target Species

Dogs

4.2 Indications for use, specifying the target species

For the treatment of canine congestive heart failure originating from valvular insufficiency (mitral and/or tricuspid valve regurgitation) or dilated cardiomyopathy.
(See also section 4.9).

4.3 Contraindications

Do not use pimobendan in hypertrophic cardiomyopathies or in diseases in which an improvement in cardiac output cannot be achieved for functional or anatomical reasons (e.g. aortic stenosis).
Since pimobendan is metabolised mainly via the liver, it should not be used in dogs with severe impairment of liver function.
(See also section 4.7).

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
The blood glucose should be tested regularly during treatment in dogs with existing diabetes mellitus.
Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan (See also section 4.6)
The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.
Unused part-tablets should be returned to the open blister space, or to the bottle and inserted back into the outer packaging.
Keep in a safe place out of the sight and reach of children.
Close bottle tightly with cap directly after removal of the required number of tablets or part-tablets.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

In rare cases a slight positively chronotropic effect (rise in heart rate) and vomiting can occur. However, these effects are dose-dependent and can be avoided by reducing the dose.
In rare cases transient diarrhoea, anorexia or lethargy have been observed.
Although a relationship with pimobendan has not been clearly established, in very rare cases, signs of effects on primary haemostasis (petechiae on mucous membranes, subcutaneous haemorrhages) may be observed during treatment. These signs disappear when the treatment is withdrawn. In rare cases, an increase in mitral valve regurgitation has been observed during chronic pimobendan treatment in dogs with mitral valve disease.
The frequency of adverse reactions is defined using the following convention:
- very common (*more than 1 in 10 animals treated displaying adverse reactions(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

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic or foetotoxic effects. However, these studies have shown evidence of maternotoxic and embryotoxic effects at high doses, and have also shown that pimobendan is excreted into milk. The safety of the product has not been assessed in pregnant or nursing bitches. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interactions

In pharmacological studies no interaction between the cardiac glycosides strophanthin and pimobendan was observed. The pimobendan-induced increase in cardiac contractility is attenuated by the calcium antagonists verapamil and diltiazem and by the β-antagonist propranolol.

4.9 Amounts to be administered and administration route

Do not exceed the recommended dosage.
Determine the bodyweight accurately before treatment to ensure correct dosage.
The tablets should be administered orally at a dose range of 0.2 mg to 0.6 mg pimobendan/kg body weight per day. The preferable daily dose is 0.5 mg pimobendan/kg body weight. The dose should be divided into two administrations (0.25 mg/kg body weight each), using a suitable combination of whole, half or quarter of tablets. One half of the dose in the morning and the other half approximately 12 hours later.
Each dose should be given approximately one hour before feeding. Spontaneous intake by the animal or place the tablet behind the lingual torus.
This corresponds to:
One 1.25 mg chewable tablet in the morning and one 1.25 mg chewable tablet in the evening for a body weight of 5 kg.

Tablets are divisible in 4 for the 5 and 10 mg and are divisible in 2 for the 1.25 mg tablet.
The product may be combined with a diuretic treatment such as furosemide.

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

In the case of overdose, a positive chronotropic effect, vomiting, apathy, ataxia, heart murmurs or hypotension may occur. In this situation, the dosage should be reduced and appropriate symptomatic treatment should be initiated.
In prolonged exposure (6 months) of healthy beagle dogs at 3 and 5 times the recommended dose, mitral valve thickening and left ventricular hypertrophy were observed in some dogs. These changes are of pharmacodynamic origin.

4.11 Withdrawal period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Cardiac stimulant, Excl. Cardiac Glycosides, phosphodiesterase inhibitor.
ATC vet code: QC01CE90.

5.1 Pharmacodynamic properties

Pimobendan, a benzimidazole-pyridazinone derivative, is a non-sympathomimetic, non-glycoside inotropic substance with potent vasodilatative properties.

Pimobendan exerts its stimulatory myocardial effect by a dual mechanism of action: increase in calcium sensitivity of cardiac myofilaments and inhibition of phosphodiesterase (type III). It also exhibits a vasodilating action through an inhibitory action on phosphodiesterase III activity. Thus the positive inotropism is triggered neither by an action similar to that of the cardiac glycosides nor sympathomimetically.

When used in cases of symptomatic valvular insufficiency in conjunction with furosemide the product has been shown to improve the quality of life and extend life expectancy in treated dogs.
When used in a limited number of cases of symptomatic dilated cardiomyopathy in conjunction with furosemide, enalapril and digoxin, the product has been shown to improve the quality of life and to extend life expectancy in treated dogs.

5.2 Pharmacokinetic particulars

Absorption:
Following oral administration of pimobendan, the absolute biovailability of the active principle is 60 - 63 %. Since this bioavailability is considerably reduced when pimobendan is administered with food or shortly thereafter, it is recommended to treat animals approximately 1 hour before feeding.
After oral administration of 0.25 mg/kg b.w of pimobendan, the maximal plasma concentration was 17.4 µg/L (mean C_{max}) and AUC was 20.9 h*µg/L (mean AUC_{0-t}).

Distribution:
The volume of distribution is 2.6 l/kg, indicating that pimobendan is distributed readily into the tissues. The mean plasma protein binding is 93 %.

Metabolism:
The compound is oxidatively demethylated to its major active metabolite (UD-CG 212). Further metabolic pathways are phase II conjugates of UD-CG 212, in essence glucuronides and sulfates.

Elimination:
The plasma elimination half-life of pimobendan is 0.4 hours, consistent with the high clearance of 90 ml/min/kg and a short mean residence time of 0.5 hours.
The main active metabolite is eliminated with a plasma elimination half-life of 2.0 hours. Almost the entire dose is eliminated via faeces.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica colloidal anhydrous
Stearic acid
Copovidone
Croscarmellose sodium
Malic acid
Maize starch
Cellulose microcrystalline
Lactose monohydrate
Dried Yeast (from *Saccharomyces cerevisiae*)
Pig liver powder

6.2 Major incompatibilities

Not applicable.

6.3 Shelf-life

For blisters: Shelf life of the veterinary medicinal product as packaged for sale: 2 years

For bottle: Shelf life of the veterinary medicinal product as packaged for sale: 2 years

Shelf life after first opening the immediate packaging: 2 months

6.4 Special precautions for storage

For blisters: Any unused tablet portion should be returned to the blister and be used for the next administration.
Do not store above 30 °C.

For bottle: Keep the bottle tightly closed in order to protect from moisture.
Any unused tablet portion should be returned to the bottle and be used for the next administration.
Do not store above 25 °C.

6.5 Nature and composition of immediate packaging

For blisters: Polyamide-Aluminium-Polyvinyl chloride / aluminium heat sealed blisters.
Cardboard box with 3 or 8 blisters of 12 tablets.

For bottle: High density polyethylene screw bottles with a polypropylene child-resistant closure –twist off cap.
35 ml bottle contains 60 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Ceva Santé Animale
10, avenue de La Ballastière
33500 Libourne
France

8 MARKETING AUTHORISATION NUMBER(S)

VPA10815/046/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 June 2018

10 DATE OF REVISION OF THE TEXT

April 2021