**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zubrin 50 mg oral lyophilisates for dogs
Zubrin 100 mg oral lyophilisates for dogs
Zubrin 200 mg oral lyophilisates for dogs

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Active substance**

| | |
|---|---|
| Tepoxalin | 50 mg / oral lyophilisate |
| Tepoxalin | 100 mg / oral lyophilisate |
| Tepoxalin | 200 mg / oral lyophilisate |

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Oral lyophilisates

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Dogs

### 4.2 Indications for use

Reduction of inflammation and relief of pain caused by acute and chronic musculoskeletal disorders.

### 4.3 Contraindications

Do not use in pregnant or lactating dogs or in bitches intended for breeding.
Use is contraindicated in animals suffering from cardiac or hepatic disease, or where there is a history of gastrointestinal ulceration, or bleeding, or where there is hypersensitivity to the product.
Do not use in dehydrated, hypovolaemic or hypotensive dogs, as there is an increased risk of renal toxicity.

### 4.4 Special warnings

Special care should be taken when treating dogs with marked renal insufficiency.

### 4.5 Special precautions for use

**Special precautions for use in animals**

Use in animals less than 6 months of age, with a weight below 5 kg, or in aged animals, may involve additional risk. If such use cannot be avoided, close veterinary supervision to monitor for gastrointestinal blood loss is necessary.
If side effects occur, treatment should be discontinued and the advice of a veterinary surgeon should be sought.
The recommended dose should not be exceeded.

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

Tepoxalin is not water-soluble and becomes very sticky upon wetting. If the oral lyophilisate disintegrates prematurely, wash hands thoroughly.
In case of ingestion of a number of oral lyophilisates by a person, the advice of a doctor should be sought immediately.

## 4.6 Adverse reactions (frequency and seriousness)

Vomiting or diarrhoea may occur due to treatment. Alopecia and erythema may also occur occasionally.
Typical undesirable side-effects associated with NSAIDs are vomiting, soft faeces/diarrhoea, blood in faeces, reduced appetite, lethargy and renal disorders. If there are such undesirable effects, treatment should be discontinued immediately. In rare cases, particularly in older or in sensitive dogs, these undesirable effects may be serious or fatal.
During clinical trial testing of the product, the incidence of gastrointestinal reactions (diarrhoea/vomiting) was 10%.

## 4.7 Use during pregnancy, lactation or lay

Do not use in pregnant or lactating bitches.

## 4.8 Interaction with other medicinal products and other forms of interaction

Tepoxalin must not be administered in conjunction with other NSAIDs or glucocorticosteroids. Other NSAIDs, diuretics, anticoagulants and substances with high plasma protein binding may compete for binding leading to potentially toxic effects.

## 4.9 Amounts to be administered and administration route

10 mg tepoxalin per kg bodyweight once daily. The duration of treatment is dependent on clinical response. After a treatment period of 7-10 days, the condition of the dog should be re-evaluated in order to establish the need for continuation of treatment. Long term treatment should be under regular veterinary supervision.
The weight of the animal should be accurately determined before start of treatment.
Peel back foil to reveal a single oral lyophilisate in the form of a round tablet. Ensure hands are dry to prevent the tablet from sticking to fingers. Push the bottom of the blister and the tablet will pop out. Place the tablet in the dog's mouth. The tablet will disintegrate upon contact with moisture. Keep the mouth of the dog closed for a few seconds to ensure complete tablet wetting. Administer to dogs within 1-2 hours after feeding. When this is not possible, or when dogs resist having the product placed directly into the mouth, put the tablet immediately before administration into a small amount of moistened food, or in a moist treat. Ensure the food or treat containing the medication is completely consumed.

## 4.10 Overdose (symptoms, emergency procedures, antidotes)

At doses of 30 mg/kg and above, oral administration of tepoxalin is associated with discoloured faeces ranging in colour from white to yellow, which is the result of unabsorbed drug.
NSAID overdosage is characterised by vomiting, soft faeces/diarrhoea, blood in faeces, reduced appetite and lethargy. In the case of overdosage discontinue therapy. If gastrointestinal bleeding is suspected, administer gastric protectants. If vomiting continues, administer anti-emetics. Monitor the hematocrit frequently. Maintain the animal on intravenous fluids and, if necessary, administer whole blood.

## 4.11 Withdrawal period

Not applicable

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-inflammatory Products, Non Steroids
ATCvet code: QM01AE92

### 5.1 Pharmacodynamic properties

Tepoxalin is a dual cyclooxygenase / 5-lipoxygenase inhibitor with anti-inflammatory activity. Oral administration of 10 mg tepoxalin / kg bodyweight results in inhibition of prostaglandin and leukotriene synthesis.

### 5.2 Pharmacokinetic properties

Tepoxalin is rapidly ($T_{max}$ of approximately 2 hours) absorbed after oral administration in dogs. At a therapeutic dose of 10 mg/kg, the $C_{max}$ of tepoxalin was 1.08 ± 0.37 μg/ml in dogs fed a low fat meal and 1.19 ± 0.29 μg/ml in dogs fed a high fat meal. Absorption of tepoxalin is facilitated via administration to dogs in a fed state. Tepoxalin is extensively converted to its acid metabolite. The acid metabolite is a potent, active cyclooxygenase inhibitor and prolongs the activity of the parent compound. Plasma concentrations of the acid metabolite are higher than those of the parent compound in the dog. No accumulation of tepoxalin or its acid metabolite was detected after multiple dosing over a broad dose range. Tepoxalin and its metabolites are highly protein-bound, more than 98%. Tepoxalin and its metabolites are excreted in the faeces (99%).

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Gelatin
Mannitol

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

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

Zubrin oral lyophilisates are supplied in boxes with foil blisters. Each blister contains 10 oral lyophilisates.

The oral lyophilisates are available in the following pack sizes:
50 mg, 100 mg: 1 box containing 1 or 3 blisters.
200 mg: 1 box containing 1, 3 or 6 blisters.

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 products should be disposed of in accordance with the local requirements.

## 7. MARKETING AUTHORISATION HOLDER

Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

## 8. MARKETING AUTHORISATION NUMBER(S)

EU/2/00/028/002-008

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13 March 2001

## 10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

## PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable

**ANNEX II**

**A. MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE**

**B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE**

**C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO SAFE AND EFFECTIVE USE**

**D. STATEMENT OF THE MRLs**

## A. MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

S-P Veterinary Ltd
Breakspear Road South
Harefield
Uxbridge UB9 6LS
United Kingdom

## B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

To be supplied only on veterinary prescription.

## C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE PRODUCT

Not applicable

## D. STATEMENT OF THE MRLs

Not applicable

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

**A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

{50 mg oral lyophilisate}

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zubrin 50 mg oral lyophilisates for dogs

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Tepoxalin 50 mg / oral lyophilisate

## 3. PHARMACEUTICAL FORM

Oral lyophilisates

## 4. PACKAGE SIZE

10 oral lyophilisates (EU/2/00/028/002)
30 oral lyophilisates (EU/2/00/028/003)

## 5. TARGET SPECIES

Dogs

## 6. INDICATION(S)

Reduction of inflammation and relief of pain caused by acute and chronic musculoskeletal disorders.

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

10 mg/kg of body weight once daily.
The duration of treatment is dependent on clinical response. After a treatment period of 7-10 days, the condition of the dog should be re-evaluated in order to establish the need for continuation of treatment. Long term treatment should be under regular veterinary supervision.
The weight of the animal should be accurately determined before start of treatment.

Administer to dogs within 1-2 hours after feeding. When this is not possible, or when dogs resist having the product placed directly into the mouth, put the tablet immediately before administration into a small amount of moistened food, or in a moist treat. Ensure the food or treat containing the medication is completely consumed.

Read the package leaflet before use.

## 8. SPECIAL WARNING(S), IF NECESSARY

Ensure hands are dry to prevent the oral lyophilisate from sticking to fingers

Do not use in pregnant or lactating dogs or in bitches intended for breeding.
The recommended dose should not be exceeded.
If side effects occur, treatment should be discontinued and the advice of a veterinary surgeon should be sought.

## 9. EXPIRY DATE

EXP {month/year}

## 10. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with the local requirements.

## 11. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription.

## 12. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

## 13. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

**Marketing Authorisation Holder**

Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

## 14. MARKETING AUTHORISATION NUMBER(S)

EU/2/00/028/002 (1 blister)
EU/2/00/028/003 (3 blisters)

## 15. MANUFACTURER'S BATCH NUMBER

Batch {number}

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

{100 mg oral lyophilisate}

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zubrin 100 mg oral lyophilisates for dogs

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Tepoxalin 100 mg / oral lyophilisate

## 3. PHARMACEUTICAL FORM

Oral lyophilisates

## 4. PACKAGE SIZE

10 oral lyophilisates (EU/2/00/028/004)
30 oral lyophilisates (EU/2/00/028/005)

## 5. TARGET SPECIES

Dogs

## 6. INDICATION(S)

Reduction of inflammation and relief of pain caused by acute and chronic musculoskeletal disorders.

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

10 mg/kg of body weight once daily.
The duration of treatment is dependent on clinical response. After a treatment period of 7-10 days, the condition of the dog should be re-evaluated in order to establish the need for continuation of treatment. Long term treatment should be under regular veterinary supervision.
The weight of the animal should be accurately determined before start of treatment.

Administer to dogs within 1-2 hours after feeding. When this is not possible, or when dogs resist having the product placed directly into the mouth, put the tablet immediately before administration into a small amount of moistened food, or in a moist treat. Ensure the food or treat containing the medication is completely consumed.

Read the package leaflet before use.

## 8. SPECIAL WARNING(S), IF NECESSARY

Ensure hands are dry to prevent the oral lyophilisate from sticking to fingers

Do not use in pregnant or lactating dogs or in bitches intended for breeding.
The recommended dose should not be exceeded.
If side effects occur, treatment should be discontinued and the advice of a veterinary surgeon should be sought.

## 9. EXPIRY DATE

EXP {month/year}

## 10. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with the local requirements.

## 11. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription.

## 12. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

## 13. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

**Marketing Authorisation Holder**

Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

## 14. MARKETING AUTHORISATION NUMBER(S)

EU/2/00/028/004 (1 blister)
EU/2/00/028/005 (3 blisters)

## 15. MANUFACTURER'S BATCH NUMBER

Batch {number}

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

{200 mg oral lyophilisate}

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zubrin 200 mg oral lyophilisates for dogs

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

| | |
|---|---|
| Tepoxalin | 200 mg / oral lyophilisate |

## 3. PHARMACEUTICAL FORM

Oral lyophilisates

## 4. PACKAGE SIZE

10 oral lyophilisates (EU/2/00/028/006)
30 oral lyophilisates (EU/2/00/028/007)
60 oral lyophilisates (EU/2/00/028/008)

## 5. TARGET SPECIES

Dogs

## 6. INDICATION(S)

Reduction of inflammation and relief of pain caused by acute and chronic musculoskeletal disorders.

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

10 mg/kg of body weight once daily.
The duration of treatment is dependent on clinical response. After a treatment period of 7-10 days, the condition of the dog should be re-evaluated in order to establish the need for continuation of treatment. Long term treatment should be under regular veterinary supervision.
The weight of the animal should be accurately determined before start of treatment.

Administer to dogs within 1-2 hours after feeding. When this is not possible, or when dogs resist having the product placed directly into the mouth, put the tablet immediately before administration into a small amount of moistened food, or in a moist treat. Ensure the food or treat containing the medication is completely consumed.

Read the package leaflet before use.

## 8. SPECIAL WARNING(S), IF NECESSARY

Ensure hands are dry to prevent the oral lyophilisate from sticking to fingers

Do not use in pregnant or lactating dogs or in bitches intended for breeding.
The recommended dose should not be exceeded.
If side effects occur, treatment should be discontinued and the advice of a veterinary surgeon should be sought.

## 9. EXPIRY DATE

EXP {month/year}

## 10. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with the local requirements.

## 11. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription

## 12. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

## 13. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

**Marketing Authorisation Holder**

Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

## 14. MARKETING AUTHORISATION NUMBER(S)

EU/2/00/028/006 (1 blister)
EU/2/00/028/007 (3 blisters)
EU/2/00/028/008 (6 blisters)

## 15. MANUFACTURER'S BATCH NUMBER

Batch {number}

**MINIMUM PARTICULARS TO APPEAR ON BLISTER**

{50 mg}{100 mg}{200 mg}

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zubrin 50 mg oral lyophilisates for dogs
Zubrin 100 mg oral lyophilisates for dogs
Zubrin 200 mg oral lyophilisates for dogs
Tepoxalin

## 2. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B. V.

## 3. EXPIRY DATE

EXP {month/year}

## 4. BATCH NUMBER

Batch {number}

## 5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only

**B. PACKAGE LEAFLET**

**PACKAGE LEAFLET**

Zubrin oral lyophilisates for dogs

## 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

**Marketing Authorisation Holder:**

Intervet International B. V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

**Manufacturer for the Batch Release:**

S-P Veterinary Ltd
Breakspear Road South
Harefield
Uxbridge UB9 6LS
United Kingdom

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zubrin 50 mg oral lyophilisates for dogs
Zubrin 100 mg oral lyophilisates for dogs
Zubrin 200 mg oral lyophilisates for dogs

## 3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

**Active substance**

| | |
|---|---|
| Tepoxalin | 50 mg / oral lyophilisate |
| Tepoxalin | 100 mg / oral lyophilisate |
| Tepoxalin | 200 mg / oral lyophilisate |

## 4. INDICATIONS

Reduction of inflammation and relief of pain caused by acute and chronic musculoskeletal disorders.

## 5. CONTRAINDICATIONS

Do not use if your dog

- is pregnant or lactating or in bitches intended for breeding
- has cardiac or hepatic disease
- has had gastrointestinal ulceration or bleeding
- is hypersensitive to the product
- is dehydrated, hypovolaemic or hypotensive, as there is an increased risk of renal toxicity.

## 6. ADVERSE REACTIONS

Vomiting or diarrhoea may occur due to treatment. Alopecia and erythema may also occur occasionally.
Typical undesirable side-effects associated with NSAIDs are vomiting, soft faeces/diarrhoea, blood in faeces, reduced appetite, lethargy and renal disorders. If there are such undesirable effects, treatment should be discontinued immediately. In rare cases, particularly in older or in sensitive dogs, these undesirable effects may be serious or fatal.
During clinical trial testing of the product, the incidence of gastrointestinal reactions (diarrhoea/vomiting) occurred in 1 out of 10 animals.
If you notice any other side effects, please inform your veterinary surgeon.

## 7. TARGET SPECIES

Dogs

## 8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

**10 mg/kg once daily.**
The weight of the animal should be accurately determined before start of treatment.
Peel back foil to reveal a single oral lyophilisate in the form of a round tablet. Push the bottom of the blister and the tablet will pop out. Place the tablet in the dog's mouth. The tablet will disintegrate upon contact with moisture. Keep the mouth of the dog closed for a few seconds to ensure complete tablet wetting. Administer to dogs within 1-2 hours after feeding. When this is not possible, or when dogs resist having the product placed directly into the mouth, put the tablet immediately before administration into a small amount of moistened food, or in a moist treat. Ensure the food or treat containing the medication is completely consumed.

## 9. ADVICE ON CORRECT ADMINISTRATION

The duration of treatment is dependent on clinical response. After a treatment period of 7-10 days, the condition of the dog should be re-evaluated in order to establish the need for continuation of treatment. Long term treatment should be under regular veterinary supervision.
Ensure hands are dry to prevent the oral lyophilisate from sticking to fingers. Tepoxalin is not water-soluble and becomes very sticky upon wetting. If the oral lyophilisate disintegrates prematurely, wash hands thoroughly.

## 10. WITHDRAWAL PERIOD

Not applicable

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
This veterinary medicinal product does not require any special storage conditions.
Do not use after the expiry date, which is stated on the blister.

## 12. SPECIAL WARNINGS

The recommended dose should not be exceeded.
Use in animals less than 6 months of age, with a weight below 5 kg, or in aged animals, may involve additional risk. If such use cannot be avoided, close veterinary supervision to monitor for gastrointestinal blood loss is necessary.
Special care should be taken when treating dogs with marked renal insufficiency

Tepoxalin must not be administered in conjunction with other NSAIDs or glucocorticosteroids, diuretics or anticoagulants.
If side effects occur, treatment should be discontinued and the advice of a veterinary surgeon should be sought.
In case of ingestion of a number of oral lyophilisates by a person, the advice of a doctor should be sought immediately.

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this product is available on the website of the European Medicines Agency http://www.ema.europa.eu

## 15. OTHER INFORMATION

Not all pack sizes may be marketed.