The format of this leaflet was determined by the Ministry of Health
and its contents checked and approved in May 2016

CONSUMER PACKAGE INSERT FOR A VETERINARY PREPARATION

The medicine is only dispensed with a veterinarian's prescription
For veterinary use only

1. Zuprevo 40 mg/ml veterinary Solution for Intramuscular Injection for Pigs

2. **COMPOSITION:**

Each 1 ml contains:
Active ingredient:
Tildipirosin 40 mg

A detailed list of inactive ingredients can be found in the section "Further Information".

3. **WHAT IS THE MEDICINE INTENDED FOR:**

For treatment and prevention of swine respiratory disease (SRD) associated with the causative:
Actinobacillus pleuropneumonia, *Pasteurella multocida*, *Bordetella bronchiseptica* and *Haemophilus parasuis,* which are sensitive to tildipirosin.

The presence of the disease in the herd must be confirmed before prophylactic treatment.

Therapeutic group: Macrolide antibacterials for systemic use.

4. **CONTRAINDICATIONS:**

Do not use in the case of known sensitivity to macrolide antibiotics or to any of the inactive ingredients.
Do not administer intravenously in swine.

5. **ADVERSE REACTIONS:**

The frequency of adverse reactions is defined as follows:

- Very common (more than 1/10 animals displaying adverse reactions during the course of one treatment)
- Common (more than 1/100 but less than 10/100 animals displaying adverse reactions during the course of one treatment)
- Uncommon (more than 1/1,000 but less than 10/1,000 animals displaying adverse reactions during the course of one treatment)
- Rare (more than 1/10,000 but less than 10/10,000 animals displaying adverse reactions during the course of one treatment)
- Very rare (less than 1/10,000 animals, including isolated incidences)

In very rare cases, severe allergic (shock) reactions with a potentially fatal outcome might occur.

In very rare cases, transient sleepiness, lethargy in piglets has been observed.

During clinical trials, pain at the injection site, as well as swellings, were very common in

treated pigs. The swelling disappeared within 1 to 6 days.

In target animal safety studies, administration of the maximum recommended dose (5 ml) very commonly caused slight swellings at the injection site that were not painful on palpation, and persisted for up to 3 days. Injection site reactions resolved completely within 21 days following injection.

If a serious side effect occurs or other effect not mentioned in this leaflet, inform the veterinarian.

Pain at the injection site, as well as swellings, were very common during clinical trials in treated pigs. The swelling disappeared within 1 to 6 days.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

6. **TARGET SPECIES:**

Pigs.

7. **METHOD OF ADMINISTRATION AND DOSAGE:**

Intramuscular use

Administer 4 mg tildipirosin/kg body weight (equivalent to 1 ml/10 kg body weight) **once only**.

It is recommended to treat animals in the early stages of the disease and to evaluate the response to treatment within 48 hours after injection. If the clinical signs of the respiratory disease persist or increase, or if relapse occurs, treatment should be with another antibiotic until clinical signs have resolved.

Strictly administer intramuscularly. Special attention should be paid in selecting the injection site and to use the appropriate needle diameter and length, adjusted to the size and weight of the animal.

The recommended injection site is at the highest point of the base of the ear, behind the ear, at the transition from bald to hairy skin.

Injection should be given in a horizontal direction and a 90° angle to the body axis.

Recommended needle size and diameter:

	Needle length (cm)	Needle diameter (mm)
Piglet, newborn	1.0	1.2
Piglet, 3-4 weeks	1.5 – 2.0	1.4
Growing	2.0 – 2.5	1.5
Growing-growth completion	3.5	1.6
Growth completion/ sows/boars	4.0	2.0

Do not inject more than 5 ml per injection site.

The rubber stopper of the vial may be safely punctured up to 20 times. Otherwise, the use of a multiple-dose syringe is recommended.

To ensure correct dosage, body weight should be determined as accurately as possible to avoid underdosing.

8. **WITHDRAWAL PERIOD:**

Meat: 9 days.

9. **WARNINGS:**

- Special precautions regarding use in the target animal

Prophylactic use in herds is only recommended in severe outbreaks of swine respiratory disease (SRD) confirmed to be caused by the indicated pathogens. Prophylactic treatment implies that clinically healthy animals in close contact with diseased animals are administered the product at the same time as treatment of the clinically diseased animals, to reduce the risk for development of clinical signs.

The efficacy of the prophylactic use of Zuprevo was demonstrated in a multi-center field study, when outbreak of clinical disease was confirmed (i.e. animals in at least 30% of the pens sharing the same airspace showed clinical signs of SRD, including at least 10% animals per pen within 1 day; 20% within 2 days; 30% within 3 days). Following metaphylactic use, approximately 86% of the healthy animals remained free of clinical signs of disease (as compared to 65% of animals in the untreated control group).

- Special safety precautions regarding use of the medicine in animals

Whenever possible, the use of a veterinary medicinal product should only be based on susceptibility testing. Local regulations (assuming they exist) should be taken into account when administering antimicrobial medicines to farm animals.

Strictly administer intramuscularly. Special attention should be paid to selection of the injection site and to use the appropriate needle diameter and length (adjusted to the size and weight of animal) in accordance with Good Veterinary Practice.

- Special safety precautions to be taken by the person handling the product

Special caution should be taken to avoid accidental self-injection, as toxicology studies in laboratory animals have shown cardiovascular effects after intramuscular administration of tildipirosin. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label of the medicine to the attending doctor.

Do not use in automatically powered syringes which have no protective system against accidental injection.

Tildipirosin may cause sensitization by skin contact. If accidental skin exposure occurs, wash the exposed area immediately with soap and water.

If accidental eye exposure occurs, flush eyes immediately with clean water.

Wash hands after use.

- Pregnancy and lactation in the treated animal

Safety of the use of this medicine during pregnancy or lactation has not been tested during pregnancy or lactation. However, there has been no evidence for any developmental or reproductive effects in any of the laboratory studies.

Use only according to the benefit-risk assessment by the attending veterinarian.

- Interaction with other medicinal products and other forms of interaction

  Cross resistance with other macrolides is known.
  The product should not be administered with antimicrobials with a similar mode of action such as other macrolides or lincosamides.

- Overdose

  In piglets, intramuscular administration of tildipirosin, on three occasions at intervals of 4 days, at 8, 12 and 20 mg/kg bodyweight (2, 3 and 5 times of the recommended clinical dose), resulted in transient slightly behavioral changes (subdued behavior) in one piglet each from the 8 and 12 mg/kg bodyweight group, and 2 piglets from the 20 mg/kg bodyweight group following the first or second injection.

  Muscle tremors to the hind legs were observed following the first treatment in one pig each from the 12 and 20 mg/kg bodyweight group. At 20 mg/kg bodyweight one of eight animals showed transient generalized body tremors with inability to stand after the first administration and the animal showed transient unsteadiness on its feet after the third administration. Another animal developed treatment related shock after the first administration and was euthanized. Mortality was observed at doses of 25 mg/kg body weight and higher.

- Incompatibility

  In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

10. **STORAGE INSTRUCTIONS:**

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach of children and/or infants in order to avoid poisoning.
- Do not use the medicine after the expiry date (exp. Date) that appears on the package/bottle.
- The expiry date refers to the last day of that month.
- Storage Conditions

  Store below 25°C

  Shelf life after first opening - 28 days.

11. **INSTRUCTIONS FOR THE DISPOSAL OF THE PRODUCT/UNUSED PRODUCT AFTER USE:**

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of as toxic waste; do not discard into the wastewater.

12. **FURTHER INFORMATION:**

- In addition to the active ingredient(s), the medicine also contains:

  Propylene glycol
  Citric acid monohydrate
  Water for injection

- What does the medicine look like and what are the contents of the package:

  Clear to yellow solution for injection.

  Type I amber glass vials with a chlorobutyl rubber stopper.

- The package contains 1 vial of 50, 100 or 250 ml.
  Not all package sizes may be marketed.

- **License holder and address:**

  Intervet Israel Ltd., Neve-Neeman Industrial Zone, Hod Hasharon 45240.

- **Manufacturer and address:**
  Intervet International GmbH, Feldstrasse 1a, 85716 Unterschleissheim, Germany

- **This leaflet was checked and approved by the Ministry of Health in**
  May 2016.

- **Registration number of the medicine in the National Drug Registry of the Ministry of Health**
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