1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Convenia Veterinary

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each vial of lyophilised powder contains 852 mg cefovecin (as sodium salt)

When reconstituted according to label instruction, the solution for injection contains 80.0 mg/ml cefovecin (as sodium salt)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.
The powder is off-white to yellow and the diluent (solvent) is a clear, colourless liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and Cats.

4.2 Indications for use, specifying the target species

For use only for the following infections which require prolonged treatment. The antimicrobial activity of Convenia following a single injection lasts for up to 14 days.
Dogs:
For the treatment of skin and soft tissue infections including pyoderma wounds and abscesses associated with Staphylococcus intermedius beta-haemolytic streptococci escherichia coli and/or pasteurella multocida.
For the treatment of urinary tract infections associated with Escherichia coli and/or Proteus spp.
As adjunctive treatment to mechanical or surgical periodontal therapy of severe infections of the gingival and periodontal tissues associated with Porphyromonas spp. and Prevotella spp.
Cats:
For the treatment of skin and soft tissue abscesses and wounds associated with pasteurella multocida fusobacterium spp. bacteroides spp. prevotella oralis beta-haemolytic streptococci and/or staphylococcus intermedius.
For the treatment of urinary tract infections associated with escherichia coli.

4.3 Contraindications

Do not use in cases of hypersensitivity to cephalosporin or penicillin antibiotics.
Do not use in small herbivores (including guinea pigs and rabbits).
Do not use in dogs and cats less than 8 weeks old.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals:

It is prudent to reserve third generation cephalosporins for the treatment of clinical conditions, which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials or first generation cephalosporins. Use of the product should be based on susceptibility testing and take into account official and local antimicrobial policies.

The fundamental requirement of the treatment of periodontal disease is mechanical and/or surgical intervention by the veterinarian.

The safety of Convenia has not been assessed in animals suffering from severe renal dysfunction.

Pyoderma is often secondary to an underlying disease. It is, therefore, advisable to determine the underlying cause and to treat the animal accordingly.

Caution should be exercised in patients that have previously shown hypersensitivity reactions to cefovecin, other cephalosporins, penicillins, or other drugs. If an allergic reaction occurs, no further administrations of cefovecin should be administered and appropriate therapy for beta-lactam hypersensitivity should be instituted. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamine, corticosteroids, and airway management, as clinically indicated. Veterinarians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Occasionally, cephalosporins have been associated with myelotoxicity, thereby creating a toxic neutropenia. Other haematological reactions seen with cephalosporins include neutropenia, anemia, hypoprothrombinemia, thrombocytopenia, prolonged prothrombin time (PT) and partial thromboplastin time (PTT), platelet dysfunction.

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

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious. Do not handle this product if you know you are sensitised or if you have been advised not to work with such preparations.

Handle this product with care to avoid exposure, taking all recommended precautions.

If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

If you know you are allergic to penicillins or cephalosporins, avoid contact with contaminated litter. In the event of contact, wash skin with soap and water.

4.6 Adverse reaction (frequency and seriousness)

Gastrointestinal signs, including emesis, diarrhoea and/or anorexia have been observed on very rare occasions.
Neurological signs (ataxia, convulsion or seizure) and injection site reactions have been reported in very rare cases after the use of the product.
Hypersensitivity reactions (e.g. anaphylaxis, dyspnoea, circulatory shock) may occur very rarely.
If such a reaction occurs, appropriate treatment should be administered without delay (see also 4.5 Special precautions for use in animals)
The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(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).

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form http://sideeffects.health.gov.il/

4.7 Use during pregnancy, lactation or lay

The safety of Convenia in dogs and cats has not been established during pregnancy and lactation. Treated animals should not be used for breeding for 12 weeks after the last administration.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent use of other substances that have a high degree of protein binding (e.g., furosemide, ketoconazole or non-steroidal anti-inflammatory drugs (NSAIDs)) may compete with cefovecin binding and thus may cause adverse effects.

4.9 Amounts to be administrated and administration route

Skin and soft tissue infections in dogs:
A single subcutaneous injection of 8 mg/kg bodyweight (1 ml per 10 kg bodyweight). If required, treatment may be repeated at 14-day intervals up to a further three times. In accordance with good veterinary practice, treatment of pyoderma should be extended beyond complete resolution of clinical signs.

Severe infections of the gingival and periodontal tissues in dogs:
A single subcutaneous injection of 8 mg/kg bodyweight (1 ml per 10 kg bodyweight).

Skin and soft tissue abscesses and wounds in cats:
A single subcutaneous injection of 8 mg/kg bodyweight (1 ml per 10 kg bodyweight). If required, an additional dose may be administered 14 days after the first injection.

Urinary tract infections in dogs and cats:
A single subcutaneous injection of 8 mg/kg bodyweight (1 ml per 10 kg bodyweight).

To reconstitute, withdraw the required volume of the supplied diluent from its vial (for 23 ml vial containing 852 mg of lyophilised powder reconstitute using 10 ml of diluent) and add to the vial containing the lyophilised powder. Shake the vial until the powder is seen to have fully dissolved.

Dosing Table

Animal Weight (Dogs and Cats)	Volume to be Administered
2.5 kg	0.25 ml
5 kg	0.5 ml
10 kg	1.0 ml
20 kg	2.0 ml
40 kg	4.0 ml
60 kg	6.0 ml

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

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

Repeated dosing (eight administrations) in 14-day intervals at five times the recommended dose was tolerated well in young dogs. Slight and transient injection site swellings were observed after the first and second administration. A single administration of 22.5 times the recommended dose caused transient oedema and discomfort at the injection site.
Repeated dosing (eight administrations) in 14-day intervals at five times the recommended dose was tolerated well in young cats. A single administration of 22.5 times the recommended dose caused transient oedema and discomfort at the injection site.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPRTIES

Pharmacotherapeutic group: Antibacterial for systemic use (cephalosporins).
ATCvet code: QJ01DD91.

5.1 Pharmacodynamic properties

Cefovecin is a third-generation cephalosporin with a broad spectrum of activity against Gram-positive and Gram-negative bacteria. It differs from other cephalosporins in that it is highly protein bound and has a long duration of activity. As with all cephalosporins, the action of cefovecin results from the inhibition of bacterial cell wall synthesis; cefovecin has bactericidal activity.
Cefovecin exhibits *in-vitro* activity against *Staphylococcus pseudintermedius* and *Pasteurella multocida* which are associated with canine and feline skin infections. Anaerobic bacteria such as *Bacteroides* spp. and *Fusobacterium* spp. collected from feline abscesses were shown to be susceptible. *Porphyromonas gingivalis* and *Prevotella intermedia* collected from canine periodontal

disease were also shown to be susceptible. In addition, cefovecin exhibits *in-vitro* activity against *Escherichia coli* which is associated with canine and feline urinary tract infections.
In-vitro activity against these pathogens as well as against other skin and urinary tract pathogens collected during a European (Denmark, France, Germany, Italy and United Kingdom) MIC survey (1999 – 2000) and during European (France, Germany, Spain and United Kingdom) clinical efficacy and safety field studies (2001 – 2003) are listed below. Periodontal isolates were collected during a European (France and Belgium) clinical efficacy and safety field study (2008).

Bacterial Pathogen	Origin	No. of Isolates	cefovecin MIC (µg/ml)			
			Min	Max	MIC_{50}[1]	MIC_{90}[2]
Staphylococcus pseudintermedius	Dog Cat	226 44	≤0.06 ≤0.06	8 8	0.12 0.12	0.25 0.25
B haemolytic *Streptococcus* spp.	Dog Cat	52 34	≤0.06 ≤0.06	16 1	≤0.06 ≤0.06	0.12 0.12
Coagulase negative *Staphylococcus* spp.[4]	Cat	16	0.12	32	0.25	8
Staphylococcus aureus[3, 4]	Dog[4] Cat[4]	16 20	0.5 0.5	1 >32	1 1	1 16
Coagulase positive *Staphylococcus* spp.[3, 4]	Dog[4] Cat[4]	24	0.12	>32	0.25	0.5
Escherichia coli	Dog Cat	167 93	0.12 0.25	>32 8	0.5 0.5	1 1
Pasteurella multocida	Dog Cat	47 146	≤0.06 ≤0.06	0.12 2	≤0.06 ≤0.06	0.12 0.12
Proteus spp.	Dog Cat[4]	52 19	0.12 0.12	8 0.25	0.25 0.12	0.5 0.25
Enterobacter spp.[4]	Dog[4] Cat[4]	29 10	0.12 0.25	>32 8	1 2	>32 4
Klebsiella spp.[4]	Dog[4] Cat[4]	11	0.25	1	0.5	1
Prevotella spp. (2003 survey)	Dog[4] Cat	25 50	≤0.06 ≤0.06	8 4	0.25 0.25	2 0.5
Fusobacterium spp.	Cat	23	≤0.06	2	0.12	1
Bacteroides spp.	Cat	24	≤0.06	8	0.25	4
Prevotella spp. (periodontal 2008)	Dog	29	≤0.008	4	0.125	1
Porphyromonas spp.	Dog	272	≤0.008	1	0.031	0.062

1 Lowest concentration, which completely inhibits visible growth of at least 50 % of isolates.
2 Lowest concentration, which completely inhibits visible growth of at least 90 % of isolates.
3 Some of these pathogens (e.g., *S. aureus*) exhibited natural *in vitro* resistance to cefovecin.
4 The clinical significance of these *in vitro* data has not been demonstrated.

5.2 Pharmacokinetic particulars

Cefovecin has unique pharmacokinetic properties with extremely long elimination half-lives in both dogs and cats.

In dogs, when cefovecin was administered as a single subcutaneous dose of 8 mg/kg bodyweight, absorption was rapid and extensive; peak plasma concentration at 6 hours was 120 µg/ml and bioavailability approximately 99 %. Peak concentrations in tissue cage fluid of 31.9 µg/ml were measured 2 days after administration. Fourteen days after administration, the mean cefovecin concentration in plasma was 5.6 µg/ml. Plasma protein binding is high (96.0 % to 98.7 %) and the volume of distribution is low (0.1 l/kg). Elimination half-life is long – approximately 5.5 days. Cefovecin is primarily eliminated unchanged via the kidneys. At fourteen days after administration, urine concentrations were 2.9 µg/ml.

In cats, when cefovecin was administered as a single subcutaneous dose of 8 mg/kg bodyweight, absorption was rapid and extensive; peak plasma concentration at 2 hours was 141 µg/ml and bioavailability approximately 99 %. Fourteen days after administration the mean cefovecin concentration in plasma was 18 µg/ml. Plasma protein binding is high (more than 99 %) and the volume of distribution is low (0.09 l/kg). Elimination half-life is long – approximately 6.9 days. Cefovecin is primarily eliminated unchanged via the kidneys. At ten and fourteen days after administration, urine concentrations were 1.3 µg/ml and 0.7 µg/ml, respectively. Following repeated administrations at the recommended dose, elevated concentrations of cefovecin were observed in plasma.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Citrate Dihydrate b
Methylparaben
Propylparaben
Citric Acid Monohydrate
Sodium Hydroxide
Hydrochloric Acid
The dilutant contains:
Benzyl Alcohol
Water for Injection

6.2 Major incompatibilities

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

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials. The expiry date refers to the last day of that month.

Shelf life after reconstitution according to directions: 28 days.

6.4 Special precautions for storage

Before reconstitution:
Store in a refrigerator (2^0C – 8^0C). Do not freeze.
Store in the original package in order to protect from light.
After reconstitution:
Store in a refrigerator (2^0C – 8^0C). Do not freeze.
Store in the original package in order to protect from light.

6.5 Nature and composition of immediate packaging

Powder:
Type I glass vial of 23 ml with butyl rubber stopper sealed with an aluminium flip-off seal.

Diluent:
Type I glass vial of 10 ml with chlorobutyl rubber stopper sealed with an aluminium flip-off seal.

Pack size: 1 vial of powder and 1 vial of diluent

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 from such veterinary medicinal products should be disposed of as a toxic waste. Do not dispose of in the sewage system.

7. MARKETING AUTHORISATION HOLDER

Zoetis Israel Holding B.V. 5 Atir Yeda Street, Kfar Saba, Israel

8. MARKETING AUTHORISATION NUMBER

144-77-92447-01

9. MANUFACTURER

Haupt Pharma Latina S.R.L, Italy, S.S. 156 KM, 04010 Borgo San Michele, Latina, Italy

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