# CEFUR-DUO INJECTION
## *(Ceftiofur HCL & Ketoprofen)*

**SUMMARY OF PRODUCT CHARACTERISTICS**

**1 NAME OF THE VETERINARY MEDICINAL PRODUCT**

CEFUR-DUO INJECTION

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each ml contains:
Ceftiofur (as hydrochloride)…… 50.0 mg
Ketoprofen……. 150.0 mg

**3. PHARMACEUTICAL FORM**

Injectable Suspension.

**4. CLINICAL INFORMATION**

**4.1. Target species**

Cattle

**4.2. Indications for use specifying the target species**

For the treatment of bovine respiratory disease (BRD) caused by Mannheimia haemolytica and Pasteurella multocida sensitive to ceftiofur and the reduction of clinical symptoms associated with inflammation and piresia.

**4.3. Contraindications**

Non use in cases of resistance to other cephalosporins or beta-lactam antibiotics.
Do not use in cases of hypersensitivity to ceftiofur and other $\beta$-lactam antibiotics.
Do not use in cases of hypersensitivity to ketoprofen.
Non-administration with other non-steroidal anti-inflammatory drugs (NSAIDs) and concomitant corticosteroids within 24 hours of the last administration.
Do not use in animals affected by cardiac, hepatic or renal pathology, and the possibility of ulceration or gastrointestinal bleeding exists, in case of obvious blood dyscrasia.

**4.4. Special warnings for each target species**

None.

**4.5. Special precautions for use**

**Special precautions for safe use in the target species**:

The veterinary medicinal product can select resistant strains, such as bacteria producing extended-spectrum beta-lactamases (ESBLs), and may pose a risk to human health if

these strains spread to humans, for example, through food. For this reason, the veterinary medicinal product should be reserved for the treatment of clinical conditions that have responded poorly, or will respond poorly (and refers to very serious cases, when treatment must be initiated without bacteriological diagnosis) to first-line treatment.

Once the inflammation or fever has subsided, the veterinarian should switch to a veterinary medicinal product containing only ceftiofur to cover the 3-5 days of follow-up antibiotic treatment. Treatment for an adequate period of time is important to limit the development of resistance.

The official, national, and regional antimicrobial policies should be taken into account when using the veterinary medicinal product. Excessive use, including the use of veterinary medicinal products other than the instructions given in the Product Summary, can increase the prevalence of resistance. Whenever possible, the veterinary medicinal product should be used only based on sensitivity testing.

The veterinary medicine is indicated for the treatment of individual animals. Do not use for the prevention of disease outbreaks or as part of herd health programs. Treatment of groups of animals must be strictly limited to ongoing epidemics according to the approved conditions of use.

The concomitant use of diuretics or coagulants must be based on a benefit/risk assessment by the responsible veterinarian.

Avoid intra-arterial and intravenous injections.

Avoid use in dehydrated, hypovolemic animals or if there is a risk of increased renal toxicity

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

Penicillins and cephalosporins can cause hypersensitivity (allergy) following injection, inhalation, ingestion, or skin contact. Hypersensitivity to penicillins can lead to cross-reactions to cephalosporins and vice versa. Ketoprofen can cause hypersensitivity. An allergic reaction to these substances can occasionally be serious.

Do not handle this veterinary medicinal product if you are known to be sensitive to the active substances or any of the excipients, or if you have been advised not to handle these preparations.

Wash your hands after use.

Avoid contact with eyes and skin. In case of contact, wash immediately with water.

If symptoms occur after contact, such as a skin rash, immediately consult a doctor and show him or her this warning.

Swelling of the face, lips, eyes, or difficulty breathing are more serious symptoms and require urgent medical treatment.

In case of accidental self-injection, seek immediate medical attention and show the leaflet, illustration, or label.

**4.6. Adverse reactions (frequency and seriousness)**

| | |
|---|---|
| (1 to 10 animals out of 100 animals treated): | Inflammation at the injection site (i.e., injection site edema)1 |
| Very rare<br>(<1 animal / 10,000 animals treated, including<br>isolated reports): | Hypersensitivity reactions (e.g. anaphylaxis, allergic skin reaction)2<br>Stomach disorder of ruminants3<br>Renal pathology3<br>Alteration of the color of the skin and/or alteration of the color of the muscle tissue |

1Mild and painless in most cases. [1]In case of an allergic reaction, treatment must be interrupted.
2 Not dose-related. [3]A common effect of all NSAIDs due to their inhibitory action on prostaglandin synthesis.

Reporting of adverse events is important because it allows continuous monitoring of the safety of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to the marketing authorisation holder or its local representative, or to the national competent authority via the national reporting system. See the package leaflet for contact details.

**4.7. Use during pregnancy and lactation or lay**

Pregnancy and lactation: Laboratory studies with ceftiofur or ketoprofen have not shown any teratogenic effects, abortion, or influence on reproduction. The safety of veterinary medicine during pregnancy has not been established.

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

**4.8. Interaction with other veterinary medicinal products and other forms of interaction**

Certain FANS can bind strongly to all plasma proteins and compete for binding to other pharmaceuticals, with consequent toxic effects. Non-concomitant administration with other non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, diuretics, nephrotoxic substances or anticoagulants. The bactericidal properties of beta-lactams are neutralized by the contemporary use of bacteriostatic antibiotics (macrolides, sulfonamides and tetracyclines).

**4.9. Dosage and administration route**

**Intramuscular use.**
1 mg of ceftiofur/kg/day is 3 mg of ketoprofen/kg/day per intramuscular injection corresponding to 1 ml/ 50 kg per each injection. The veterinary medicinal product should be used only when the disease is associated with clinical signs of inflammation or pyrexia. The veterinary medicinal product may be administered for 1 to 5 consecutive days depending on the clinical response on a case-by-case basis. The duration of antibiotic treatment should not be lower than 3-5 days, therefore, when the inflammation is febrile and attenuated, the veterinary doctor should switch to a veterinary medicine containing only ceftiofur per cover and 3-5 days of antibiotic treatment. Only a few animals will need to administer a fourth or fifth injection with the combined product.

To ensure a homogeneous suspension, vigorously shake the bottle for 20 seconds before use. Re-suspension of the product could be longer when stored at low temperatures.
To ensure correct dosage and avoid underdosing, determine body weight as accurately as possible.
The user must use the bottles of the most suitable dimensions based on the number of animals to be treated. The 50 ml and 100 ml bottles should not be perforated more than 10 times and the 250 ml bottles should not be perforated more than 10 times. of 18 volts. It is recommended to use a suction needle to avoid an excessive perforation of the plug.

Successive intramuscular injections must be given in different sites. Do not administer more than 16 ml per inoculum sieve.

Preferably use a 14 gauge needle.

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

Systemic toxicity symptoms were not observed when the veterinary medicine was administered at a dose 5 times higher than the one recommended for 15 consecutive days.

**4.11. Special restrictions on use and special conditions of use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products, in order to limit the risk of development of resistance**

Do not use in poultry (including eggs) due to the risk of spreading antimicrobial resistance to humans.

**4.12. Withdrawal period:**

Meat and offal: 8 days.
Latte: zero hours.

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:

ATCvet Code: QJ01DD99

### 5.1. Pharmacodynamics properties

Ceftiofur is a third-generation cephalosporin, active against many Gram-positive and Gram-negative bacteria. Ceftiofur, like other beta-lactams, inhibits the synthesis of the bacterial cell wall, exerting therefore bactericidal properties.
Cell wall synthesis depends on enzymes called penicillin-binding proteins (PBPs). Bacteria can develop resistance to all cephalosporins through four basic mechanisms: 1) altering or acquiring penicillin-binding proteins insensitive to other effective β-lactams; 2) altering the permeability of the cellular membrane of β-lactams; 3) production of β-lactamases that cleave the β-lactam ring of the molecule; or 4) active efflux.
Certain beta-lattamases, documented in Gram-negative enteric bacteria, MIC elevate per the various cephalosporins of the third and fourth generation, as well as penicillin, ampicillin, and combinations of b-lactam inhibitors and cephalosporins of the first and second generation.
Ceftiofur is active against the following microorganisms that are involved in respiratory diseases of cattle: *Pasteurella multocida*, *Mannheimia haemolytica* (ex *Pasteurella haemolytica*).
The minimum inhibitory concentrations (MIC) were determined for ceftiofur in European isolates of batteri bersaglio, isolated from sick animals between 2014 and 2016.

| Species (number of strains) | MIC range (ÿg/ml) | MIC50 (ÿg/ml) | MIC90 (ÿg/ml) |
|---|---|---|---|
| ***Mannheimia haemolytica*** 0.002 - 4 (91) | | 0.015 | 0.06 |
| ***Pasteurella multocida*** (155) | 0.008 – 0.25 | 0.015 | 0.03 |

The MICs of the target respiratory pathogens showed mono-modal distribution profiles with good sensitivity to ceftiofur. The clinical breakpoints (documento CLSI VET08 (5) and VET06 (6)) for ceftiofur are established for the bovine respiratory disease defined as M. haemolytica, P. multocida: sensitive: ÿ 2 µg/ml; intermediate: 4 µg/ml; Resistant: ÿ 8 µg/ml. According to this breakpoint, resistant strains of respiratory pathogens were not observed.

Ketoprofene is a derivative of phenylpropionic acid it belongs to the group of non steroid antiinfiammatori drugs. The mechanism of action is correlated to the ability of ketoprofen to interfere with the synthesis of prostaglandins and precursors such as arachidonic acid. Although ketoprofen does not have any direct effect on endotoxins after they have been produced, it reduces the production of prostaglandins and therefore also reduces many effects of the prostaglandin cascade. The prostaglandins are part of the complex processes involved in the development of endotoxic shock. Like all similar substances, its main pharmacological actions are anti-inflammatory, analgesic and antipyretic.

### 5.2 Pharmacokinetic information

After administration, ceftiofur is quickly metabolized into desfuroylceftiofur, the main active metabolite. Desfuroylceftiofur has an antimicrobial activity equivalent to ceftiofur against the main bacteria bersaglio in animals. The active metabolite is reversibly bound to all plasma proteins.

Due to transport by these proteins, the metabolite concentrates at the infection site, is active, and remains active in the presence of necrotic tissue and debris.
Ceftiofur after intramuscular administration is completely bioavailable.
After a single dose of 1 mg/kg of ceftiofur (as hydrochloride) administered intramuscularly to cattle, the maximum plasma concentrations of ceftiofur and the related metabolite desfuroylceftiofur are 6.11 ± 1.56 µg /mL (Cmax) and are reached within 5 hours (Tmax). The apparent half-life (t ½) of ceftiofur and related metabolites desfuroylceftiofur is 22 hours.
The elimination occurs mainly through the urine (more than 55%); il 31 % of dose in feces. After intramuscular administration, ketoprofen is completely bioavailable.
After a single dose of 3 mg/kg of ketoprofen administered intramuscularly to cattle, maximum plasma concentrations of ketoprofen of 5.55 ± 1.58 µg /ml (Cmax) are reached within 4 hours (Tmax). The apparent half-life (t ½) of ketoprofen is 3.75 hours.

In cattle, ketoprofene is strongly bound to all proteins (97 %). The elimination takes place mainly via the urine (90% of the dose), as a metabolite.

## 6. PHARMACEUTICAL INFORMATION

### 6.1 Incompatibilities

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

### 6.2. Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2years.
Shelf life after first opening the container: use within 28 days, do not store.

### 6.3. Special precautions for storage

Store below 25°C.
Protect from light and moisture.
Shake well before use
Keep out of the reach of children.
To be used as directed by the registered veterinary practitioner only.

### 6.4. Nature and composition of primary conditioning

Cardboard box with glass bottle.
Amber Glass bottle is tightly packed with a screw tight cap.
**Pack sizes:** 100ml

SPECIAL PRECAUTIONS FOR THE DISPOSAL OF WASTE MATERIALS UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS

Any unused veterinary medicinal products or waste materials derived from such medicinal products should be disposed of in accordance with local requirements and placed in appropriate collection and disposal systems for unused or expired medicinal products.

**7. MARKETING AUTHORISATION HOLDER**

Nawan Laboratories (Pvt.) Ltd.
Plots No. 136-138, Sector-15,
Korangi Industrial Area, Karachi-74900, Pakistan.

**8. MARKETING AUTHORISATION NUMBER**

Reg. No.: 130410

**9. DATE OF FIRST AUTHORISATION**

Date of Reg.: 29-10-2025

**10. DATE OF REVISION OF THE TEXT**

1-01-2026