Safety Data Sheet

Levofloxacin Tablet USP

Strength:250/500/750 mg. **Pack Size:**50/100/500 Tablets per bottle (250mg)
50/100/500/1000 Tablets per bottle (500mg)
20/30/50/100/500 Tablets per bottle (750mg)

Revision No.: 00

EMERGENCY OVERVIEW

Levofloxacin Tablets contain Levofloxacin and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

Section 1. Identification

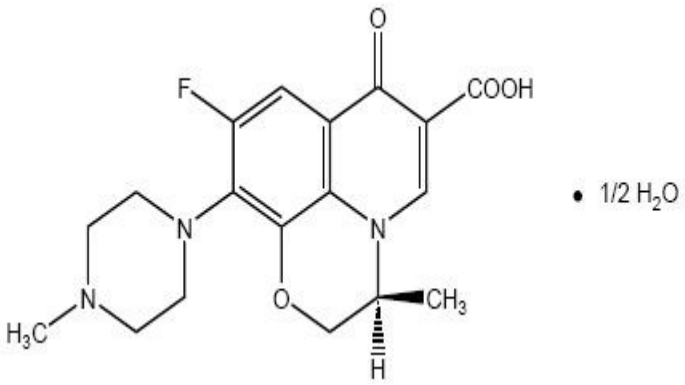
Identification of the product

Product name: Levofloxacin Tablet

Formula: $C_{18}H_{20}FN_3O_4 \cdot ½ H_2O$

Chemical Name: (-)-(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid hemihydrate.

Therapeutic Category Antibacterial



Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd. Ahmedabad, India**

Address: Sarkhej – Bavla. N.H. 8A, Moraiya. Tal. Sanand. Dist. Ahmedabad – 382210. State: Gujarat. India

Contact for information: Tel.: +91 79 666200

Emergency Telephone No. Tel.: +91 79 666200

Recommended use / Therapeutic Category Antibacterial

Restriction on Use / Contraindications: Levofloxacin tablet is contraindicated in persons with known hypersensitivity to levofloxacin, or other quinolone antibacterials.

Section 2. Hazard(s) Information

Dose and Administration

Dosage in Adult Patients with Normal Renal Function

The usual dose of levofloxacin tablets is 250 mg, 500 mg, or 750 mg administered orally every 24 hours, as indicated by infection and described in below Table.

These recommendations apply to patients with creatinine clearance ≥ 50 mL/min. For patients with creatinine clearance < 50 mL/min, adjustments to the dosing regimen are required

Type of Infection*	Dose Every 24 hours	Duration (days)†
Nosocomial Pneumonia	750 mg	7 to 14
Community Acquired Pneumonia‡	500 mg	7 to 14
Community Acquired Pneumonia§	750 mg	5
Acute Bacterial Sinusitis	750 mg	5
	500 mg	10 to 14
Acute Bacterial Exacerbation of Chronic Bronchitis	500 mg	7
Complicated Skin and Skin Structure Infections (SSSI)	750 mg	7 to 14
Uncomplicated SSSI	500 mg	7 to 10
Chronic Bacterial Prostatitis	500 mg	28
Complicated Urinary Tract Infection or Acute Pyelonephritis (AP)¶	750 mg	5
Complicated Urinary Tract Infection or Acute Pyelonephritis (AP)#	250 mg	10
Uncomplicated Urinary Tract Infection	250 mg	3
Inhalational Anthrax (Post-Exposure) Adults and Pediatric Patients > 50 kg and ≥ 6 months of age Þ,ß Pediatric Patients < 50 kg and ≥ 6 months of age Þ,ß	500 mg 8 mg/kg BID (not to exceed 250 mg/dose)	60 ß 60 ß
Plague, adult and pediatric patients weighing 50 kgà or greater Pediatric patients weighing 30 kg to < 50 kgà	500 mg	10 to 14

* Due to the designated pathogens.

† Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.

‡ Due to methicillin-susceptible Staphylococcus aureus, Streptococcus Pneumonia (including multi-drug-resistant strains [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydophila pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae

§ Due to Streptococcus pneumoniae (excluding multi-drug-resistant Strains [MDRSP]), Haemophilus influenzae, Haemophilus parainfluenzae, Mycoplasma pneumoniae, or Chlamydophila pneumoniae [see Indications and Usage.

¶ This regimen is indicated for cUTI due to Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis and AP due to E. coli, including cases with concurrent bacteremia.

This regimen is indicated for cUTI due to Enterococcus faecalis, Enterococcus cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa; and for AP due to E. coli.

Þ Drug administration should begin as soon as possible after suspected or confirmed exposure to aerosolized B. anthracis. This indication is based on a surrogate endpoint. Levofloxacin plasma concentrations achieved in humans are reasonably likely to predict clinical benefit.

ß The safety of levofloxacin tablets in adults for durations of therapy beyond 28 days or in pediatric patients for durations beyond 14 days has not been studied. An increased incidence of musculoskeletal adverse events compared to controls has been observed in pediatric patients [see Warnings and Precautions, Use in Specific Populations and Clinical Studies. Prolonged levofloxacin tablets therapy should only be used when the benefit outweighs the risk.

à Drug administration should begin as soon as possible after suspected or confirmed exposure to *Yersinia pestis*. Higher doses of levofloxacin tablet typically used for treatment of pneumonia can be used for treatment of plague, if clinically indicated.

Adverse Effects

The following serious and otherwise important adverse drug reactions are discussed in greater detail in other sections of labeling:

- Disabling and Potentially Irreversible Serious Adverse Reactions
- Tendinitis and Tendon Rupture
- Peripheral Neuropathy
- Central Nervous System Effects
- Exacerbation of Myasthenia Gravis
- Other Serious and Sometimes Fatal Reactions
- Hypersensitivity Reactions
- Hepatotoxicity
- Risk of Aortic Aneurysm and Dissection
- *Clostridium difficile*-Associated Diarrhea

- Prolongation of the QT Interval
- Musculoskeletal Disorders in Pediatric Patients
- Blood Glucose Disturbances
- Photosensitivity/Phototoxicity
- Development of Drug Resistant Bacteria

Crystalluria and cylindruria have been reported with quinolones, including levofloxacin. Therefore, adequate hydration of patients receiving levofloxacin should be maintained to prevent the formation of a highly concentrated urine.

Over Dose Effect

In the acute overdosage, the stomach should be emptied .The patient should be observed and appropriate hydration maintained. Levofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis. Levofloxacin exhibits a low potential for acute toxicity.

Medical Conditions

Disabling and Potentially Irreversible Serious Adverse Reactions Including Tendinitis and Tendon Rupture, Peripheral Neuropathy, and Central Nervous System Effects

Fluoroquinolones, including levofloxacin, have been associated with disabling and potentially irreversible serious adverse reactions from different body systems that can occur together in the same patient. Commonly seen adverse reactions include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). These reactions can occur within hours to weeks after starting levofloxacin. Patients of any age or without pre-existing risk factors have experienced these adverse reactions

Discontinue levofloxacin immediately at the first signs or symptoms of any serious adverse reaction. In addition, avoid the use of fluoroquinolones, including levofloxacin, in patients who have experienced any of these serious adverse reactions associated with fluoroquinolones.

Tendinitis and Tendon Rupture

Fluoroquinolones, including levofloxacin, have been associated with an increased risk of tendinitis and tendon rupture in all ages. This adverse reaction most frequently involves the Achilles tendon and has also been reported with the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendon sites. Tendinitis or tendon rupture can occur within hours or days of starting levofloxacin or as long as several months after completion of fluoroquinolone therapy. Tendinitis and tendon rupture can occur bilaterally.

The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is increased in patients over 60 years of age, in those taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Other factors that may independently increase the risk of tendon rupture include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis.

Tendinitis and tendon rupture have been reported in patients taking fluoroquinolones who do not have the above risk factors.

Discontinue levofloxacin immediately if the patient experiences pain, swelling, inflammation or rupture of a tendon. Patients should be advised to rest at the first sign of tendinitis or tendon rupture, and to contact their healthcare provider regarding changing to a non-quinolone antimicrobial drug. Avoid levofloxacin in patients who have a history of tendon disorders or tendon rupture.

Peripheral Neuropathy

Fluoroquinolones, including levofloxacin, have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving fluoroquinolones, including levofloxacin. Symptoms may occur soon after initiation of levofloxacin and may be irreversible in some patients.

Discontinue levofloxacin immediately if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation. Avoid fluoroquinolones, including levofloxacin, in patients who have previously experienced peripheral neuropathy .

Central Nervous System Effects
Psychiatric Adverse Reactions

Fluoroquinolones, including levofloxacin, have been associated with an increased risk of psychiatric adverse reactions, including: toxic psychoses, hallucinations, or paranoia; depression, or suicidal thoughts; anxiety, agitation, restlessness, or nervousness; confusion, delirium, disorientation, or disturbances in attention; insomnia or nightmares; memory impairment. Attempted or completed suicide has been reported, especially in patients with a medical history of depression, or an underlying risk factor for depression. These reactions may occur following the first dose. If these reactions occur in patients receiving levofloxacin tablets, discontinue levofloxacin tablets and institute appropriate measures.

Central Nervous System Adverse Reactions

Fluoroquinolones, including levofloxacin, have been associated with an increased risk of seizures (convulsions), increased intracranial pressure (including pseudotumor cerebri), tremors, and lightheadedness. As with other fluoroquinolones, levofloxacin tablets should be used with caution in patients with a known or suspected central nervous system (CNS) disorder that may predispose them to seizures or lower the seizure threshold (e.g., severe cerebral

Arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose them to seizures or lower the seizure threshold (e.g., certain drug therapy, renal dysfunction). If these reactions occur in patients receiving levofloxacin tablets, discontinue levofloxacin tablets and institute appropriate measures.

Exacerbation of Myasthenia Gravis
Fluoroquinolones, including levofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Postmarketing serious adverse reactions, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Avoid levofloxacin in patients with a known history of myasthenia gravis.

Other Serious and Sometimes Fatal Adverse Reactions
Other serious and sometimes fatal adverse reactions, some due to hypersensitivity, and some due to uncertain etiology, have been reported rarely in patients receiving therapy with fluoroquinolones, including levofloxacin. These events may be severe and generally occur following the administration of multiple doses. Clinical manifestations may include one or more of the following:

- Fever, rash, or severe dermatologic reactions (e.g., toxic epidermal Necrolysis, Stevens - Johnson syndrome);
- Vasculitis; arthralgia; myalgia; serum sickness;
- Allergic pneumonitis;
- Interstitial nephritis; acute renal insufficiency or failure;
- Hepatitis; jaundice; acute hepatic necrosis or failure;
- Anemia, including hemolytic and aplastic; thrombocytopenia,

including thrombotic thrombocytopenic purpura; leukopenia; agranulocytosis; pancytopenia; and/or other hematologic abnormalities.
Discontinue levofloxacin immediately at the first appearance of skin rash, jaundice, or any other sign of hypersensitivity and institute supportive measures.

Hypersensitivity Reactions
Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving therapy with fluoroquinolones, including levofloxacin. These reactions often occur following the first dose. Some reactions have been accompanied by cardiovascular collapse, hypotension/ shock, seizure, loss of consciousness, tingling, angioedema (including tongue, laryngeal, throat, or facial edema/swelling), airway obstruction (including bronchospasm, shortness of breath, and acute respiratory distress), dyspnea, urticaria, itching, and other serious skin reactions. Levofloxacin should be discontinued immediately at the first appearance of a skin rash or any other sign of hypersensitivity.

Serious acute hypersensitivity reactions may require treatment with epinephrine and other resuscitative measures, including oxygen, intravenous fluids, antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

Hepatotoxicity

Post-marketing reports of severe hepatotoxicity (including acute hepatitis and fatal events) have been received for patients treated with levofloxacin.

No evidence of serious drug-associated hepatotoxicity was detected in clinical trials of over 7,000 patients. Severe hepatotoxicity generally occurred within 14 days of initiation of therapy and most cases occurred within 6 days. Most cases of severe hepatotoxicity were not associated with hypersensitivity. The majority of fatal hepatotoxicity reports occurred in patients 65 years of age or older and most were not associated with hypersensitivity. Levofloxacin should be discontinued immediately if the patient develops signs and symptoms of hepatitis.

Risk of Aortic Aneurysm and Dissection

Epidemiologic studies report an increased rate of aortic aneurysm and dissection within two months following use of fluoroquinolones, particularly in elderly patients. The cause for the increased risk has not been identified. In patients with a known aortic aneurysm or patients who are at greater risk for aortic aneurysms, reserve levofloxacin for use only when there are no alternative antibacterial treatments available.

Clostridium difficile-Associated Diarrhea

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including levofloxacin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile,* and surgical evaluation should be instituted as clinically indicated.

Prolongation of the QT Interval

Some fluoroquinolones, including levofloxacin, have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. Rare cases of torsade de pointes have been spontaneously reported during post marketing surveillance in patients receiving fluoroquinolones, including levofloxacin. Levofloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving Class IA (quinidine, procainamide), or Class III (amiodarone, sotalol) antiarrhythmic agents. Elderly patients may be more susceptible to drug-associated effects on the QT interval.

Musculoskeletal Disorders in Pediatric Patients and Arthropathic Effects in Animals

Levofloxacin is indicated in pediatric patients (6 months of age and older) only for the prevention of inhalational anthrax (post-exposure) and for plague.

An increased incidence of musculoskeletal disorders (arthralgia, arthritis, tendinopathy, and gait abnormality) compared to controls has been observed in pediatric patients receiving levofloxacin.

In immature rats and dogs, the oral and intravenous administration of levofloxacin resulted in increased osteochondrosis. Histopathological examination of the weight-bearing joints of immature dogs dosed with levofloxacin revealed persistent lesions of the cartilage. Other fluoroquinolones also produce similar erosions in the weight-bearing joints and other signs of arthropathy in immature animals of various species.

Blood Glucose Disturbances

Fluoroquinolones, including levofloxacin, have been associated with disturbances of blood glucose, including symptomatic hyperglycemia and hypoglycemia, usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glyburide) or with insulin. In these patients, careful monitoring of blood glucose is recommended. Severe cases of hypoglycemia resulting in coma or death have been reported. If a hypoglycemic reaction occurs in a patient being treated with levofloxacin tablets, discontinue levofloxacin tablets and initiate appropriate therapy immediately.

Photosensitivity/Phototoxicity

Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g., burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, “V” area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of fluoroquinolones after sun or UV light exposure.

Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if photosensitivity/phototoxicity occurs.

Development of Drug Resistant Bacteria

Prescribing levofloxacin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Contraindications Levofloxacin tablet is contraindicated in persons with known hypersensitivity to levofloxacin, or other quinolone antibacterial.

Pregnancy Comments Published information from case reports, case control studies and observational studies on levofloxacin administered during pregnancy have not identified any drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

In animal reproduction studies, oral administration of levofloxacin to pregnant rats and rabbits during organogenesis at doses up to 9.4 times and 1.1 times the maximum recommended human dose (MRHD), respectively, did not result in teratogenicity. Fetal toxicity was seen in the rat study, but was absent at doses up to 1.2 times the maximum recommended human dose.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Pregnancy Category C

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component :		
Levofloxacin hemihydrate equivalent to levofloxacin	Not Found	138199-71-0
Inactive ingredients :		
Crospovidone	Not Found	9003-39-8
Hypromellose	Not Found	9004-65-3
Magnesium stearate	Not Found	577-04-0
Microcrystalline cellulose	Not Found	9004-34-6
Polyethylene glycol 6000	Not Found	25322-68-0
Talc	Not Found	14807-96-6
Titanium dioxide.	Not Found	13463-67-7

Section 4. First aid measures

General

Inhalation

Remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen. Seek medical attention.

contact with skin

Immediately wash skin with soap and copious amounts of water for at least 15 minutes. If irritation persists, seek medical attention.

contact with eyes
Immediately flush eyes with copious amounts of water for at least 15 minutes. Seek medical advice

Ingestion
If swallowed, wash out mouth with water, provided person is concious. Seek medical advice

Remove and wash/dispose of contaminated clothing promptly.

Overdose Treatment

In the event of an acute overdosage, the stomach should be emptied. The patient should be observed and appropriate hydration maintained.

Section 5. Fire – fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable Limit:**	Not Found
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.	**Fire and Explosion Hazard**	This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with the dry material to dissipate the potential buildup of static electricity.

Fire Fighting Procedure As with all fires, evacuate personnel to a safe area. Fire fighter should use self-contained breathing equipment and protective clothing.

Section 6. Accidental Release Measures

Spill Response Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Section 7. Handling and Storage

Storage Store at 20° to 25° C (68° to 77° F)

Incompability No data available.

Section 8. Exposure controls / personal protection

Respiratory Protection Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.

Skin Protection Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.

Eye protection Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.

Protective Clothing Protective clothing is not normally necessary, however it is good practice to use apron.

Section 9. Physical and chemical properties

Appearance

Levofloxacin Tablets, **250 mg** are white to off white, modified capsule shaped, biconvex, film-coated tablets debossed with logo of 'ZC55' on one side and plain on other side and are supplied as follows:

In bottles of 50 tablets
In bottles of 100 tablets
In bottles of 500 tablets

Levofloxacin Tablets, **500 mg** are white to off white, modified capsule shaped, biconvex, film-coated tablets debossed with logo of 'ZC56' on one side and plain on other side and are supplied as follows:

In bottles of 50 tablets
In bottles of 100 tablets
In bottles of 500 tablets
In bottles of 1,000 tablets

Levofloxacin Tablets, **750 mg** are white to off white, modified capsule shaped, biconvex, film-coated tablets debossed with logo of 'ZC57' on one side and plain on other side and are supplied as follows:

In bottles of 20 tablets
In bottles of 30 tablets
In bottles of 50 tablets
In bottles of 100 tablets
In bottles of 500 tablets

Solubility in water	No Data Available	**Odour**	Odourless
Boiling point	No Data Available	**Melting Point**	No Data Available
Evaporation rate	No Data Available	**Vapour density**	No Data Available
Reactivity in water	No Data Available	**Evaporation rate**	No Data Available
% Volatile by volume	No Data Available	**Specific gravity**	No Data Available
Vapour pressure	No Data Available		

Other information

Levofloxacin tablets are synthetic antibacterial agents for oral administration. Chemically, levofloxacin, a chiral fluorinated carboxyquinolone, is the pure (-)-(S)-enantiomer of the racemic drug substance ofloxacin. The chemical name is (-)-(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid hemihydrate.
Its molecular formula is $C_{18}H_{20}FN_3O_4 \cdot \frac{1}{2} H_2O$ and the molecular weight is 370.38. Levofloxacin, USP is a light yellowish–white to yellow–white crystals or crystalline powder. The molecule exists as a zwitterion at the pH conditions in the small intestine.

Section 10. Stability and Reactivity

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Stable under normal ambient and anticipated storage and handling conditions.
Decomposition Products	No Data Available	**Hazardous Reaction**	No data available.
Incompatibilities	No data available.		

Section 11. Toxicological information

General Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target organ Eye contact, Skin contact and inhalation is not great risk as this product is tablet.

Other Not Applicable

Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil

Section 13. Disposal Consideration

Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. Regulatory Information

Generic Medicine. Approved by USFDA & the ANDA Number is 077652

Section 16. Other information

None

NFPA Rating: These ratings are based on NFPA code 704 and are intended for use by emergency personnel to determine the immediate hazards of a material.

Health	1
Flammability	0
Instability	0
Physical Hazards	NA

Date of issue: 18/12/21 **Supersedes edition of:** Nil

The information contained herein is based on the state of our knowledge. It Characterises the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.