1.3.1 Summary of Product Characteristics

1. **Name of the medicinal product**
   Levofloxacin Film coated Tablets USP 500mg

2. **Qualitative and quantitative composition**
   Each Film coated tablet contains:
   Levofloxacin Hemihydrate USP
   Eq.to Levofloxacin ..... 500 mg
   Excipient .....q. s.
   Colours: Off-white

3. **Pharmaceutical form**

   Film coated tablet
   Description: - Off-white colour, round shape, standard convex Film coated tablet having break line on one side and other side is plain

4. **Clinical particulars**

4.1 Therapeutic Indications:
Levofloxacin Tablets 500mg is an antibiotic medication that is commonly used to treat a variety of bacterial infections.

4.2 Posology and Method of administration:
The posology (dosage) and method of administration for levofloxacin tablets can vary depending on the specific infection being treated, patient age, weight, and other factors. Always follow your healthcare provider's instructions and the dosing information on the prescription label. Here are some general guidelines for the posology and method of administration of levofloxacin tablets:

Posology

Adults:
- For most infections, the typical starting dose of levofloxacin for adults is 500 mg once daily, taken by mouth.
- In some cases, a higher dosage of 750 mg once daily may be prescribed, especially for more severe infections or specific types of pneumonia.
- Your healthcare provider will determine the appropriate dosage based on the type and severity of the infection.

Children:
- The pediatric dosage of levofloxacin is determined based on the child's weight, the type of infection, and the child's overall health.

Method of Administration:

- Levofloxacin tablets are meant to be taken by mouth and should be swallowed whole with a full glass of water.
- They can be taken with or without food. However, it's important to follow your healthcare provider's specific instructions regarding food or antacid restrictions. In some cases, it's recommended to take the medication either 1 hour before or 2 hours after meals or other medications.

Do not crush, break, or chew the tablets; swallow them whole

- If you are prescribed a once-daily dosage, try to take the tablet at approximately the same time each day to maintain a consistent level of the medication in your system.

If you miss a dose, take it as soon as you remember. If it's close to the time for the next dose, skip the missed dose and continue with your regular dosing schedule. Do not double up on doses

4.3 Contraindications:

The concurrent administration of levofloxacin with drugs that prolong the QT interval is contraindicated.

It is also contraindicated in patients with documented hypersensitivity to the drug or excipients, as cases of anaphylaxis have been reported. Fluoroquinolones, including levofloxacin, are contraindicated in pregnancy. Research has suggested that risk is highest during the first trimester; levofloxacin administration should typically be discouraged during pregnancy and lactation unless a safer alternative is not available. More research is needed to establish the role of fluoroquinolone during pregnancy. It is recommended to avoid levofloxacin and other fluoroquinolone antibiotics in patients with myasthenia gravis due to an increased risk of exacerbation of existing muscle weakness.

Boxed Warning: FDA has alerted a boxed warning for using levofloxacin and other fluoroquinolones due to increased risk of disabling and irreversible side effects, including tendinitis and tendon rupture, peripheral neuropathy, and CNS effects (e.g., seizures, increased intracranial pressure) in all ages. Older patients > 60 years, those taking corticosteroids and with kidney, heart, or lung transplants, are at increased risk of severe tendon disorders.

4.4 Special warnings and precautions for use

Levofloxacin is a potent antibiotic medication, and there are several special warnings and precautions to be aware of when using levofloxacin tablets. It's important to follow your healthcare provider's instructions and discuss any concerns you may have. Here are some key special warnings and precautions for the use of levofloxacin tablets:

- **Tendon Rupture**: Levofloxacin has been associated with an increased risk of tendonitis and tendon rupture, particularly in the Achilles tendon. This risk is higher in people over 60 years of age, those taking corticosteroids, and those with a history of tendon disorders. If you experience tendon pain, swelling, or inflammation, discontinue the medication and consult your healthcare provider immediately.
- **Central Nervous System Effects**: Levofloxacin can have adverse effects on the central nervous system, which may include dizziness, confusion, tremors, hallucinations, and seizures. If you experience any of these symptoms, contact your healthcare provider.
- **Photosensitivity**: Levofloxacin may make your skin more sensitive to sunlight. It's important to limit sun exposure and use sunscreen or protective clothing while taking the medication.
- **Cardiovascular Effects**: Levofloxacin may prolong the QT interval, which can lead to a potentially life-threatening irregular heart rhythm (arrhythmia). It should be used with caution in individuals with a history of heart conditions or those taking medications that affect heart rhythm.
- **Hypersensitivity Reactions**: Some people may experience severe allergic reactions to levofloxacin, including skin rash, itching, swelling, and breathing difficulties. If you have a hypersensitivity reaction, discontinue the medication and seek medical attention.
- **Muscle Weakness**: Levofloxacin can cause muscle weakness, especially in people with myasthenia gravis, a neuromuscular disorder. Use with caution in such cases.
- **Psychiatric Effects**: Levofloxacin has been associated with mental health effects, such as anxiety, depression, and even suicidal thoughts. If you experience any changes in mood or behavior, consult your healthcare provider.

- **Peripheral Neuropathy**: Levofloxacin can cause peripheral neuropathy, which may result in pain, numbness, tingling, or weakness in the extremities. If you notice any of these symptoms, notify your healthcare provider.

- **Kidney and Liver Function**: People with impaired kidney or liver function should use levofloxacin with caution, as it is primarily eliminated from the body through the kidneys and metabolized by the liver.
- **Interactions**: Levofloxacin can interact with other medications, including antacids, dairy products, and certain other antibiotics. It's important to inform your healthcare provider about all medications and supplements you are taking.
- **Pregnancy and Breastfeeding**: Levofloxacin should generally be avoided during pregnancy and while breastfeeding, as it may have adverse effects on fetal development and can be excreted in breast milk.

4.5 Interaction with other medicinal products and other forms of interaction

Levofloxacin can interact with other medicinal products and substances, which can affect its effectiveness and safety. It's essential to inform your healthcare provider about all medications, supplements, and medical conditions you have before starting levofloxacin treatment. Here are some important interactions and forms of interaction to be aware of:

- **Antacids, Iron, Calcium, and Magnesium Supplements**: These substances can interfere with the absorption of levofloxacin in the digestive system. To avoid this interaction, take antacids or supplements containing iron, calcium, or magnesium at least 2 hours before or 2 hours after taking levofloxacin.
- **Warfarin and Other Blood Thinners**: Levofloxacin can enhance the anticoagulant effect of drugs like warfarin, increasing the risk of bleeding. Your healthcare provider may need to monitor your blood clotting time more closely and adjust the dosage of your blood thinner.
- **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**: Levofloxacin can increase the risk of CNS (central nervous system) side effects when taken with NSAIDs, such as ibuprofen or naproxen. Be cautious if using these drugs together.
- **Theophylline**: Concurrent use of levofloxacin with theophylline, a medication for respiratory conditions, can lead to increased theophylline levels in the blood, potentially causing side effects. Theophylline levels may need to be monitored and adjusted.
- **Corticosteroids**: Using levofloxacin with corticosteroids can increase the risk of tendon problems, such as tendon rupture. This combination should be used with caution, especially in older adults.
- **QT Prolonging Medications**: Levofloxacin can prolong the QT interval on an electrocardiogram (ECG), which can increase the risk of arrhythmias. Avoid concurrent use of other medications that can prolong the QT interval, such as certain antiarrhythmics, antipsychotics, and antidepressants.
- **Caffeine**: Levofloxacin may enhance the stimulant effects of caffeine, leading to nervousness, restlessness, and increased heart rate. Limit caffeine intake or be cautious with caffeine-containing products while on levofloxacin.
- **Other Antibiotics**: Concurrent use of levofloxacin with other antibiotics may interfere with their effectiveness. Use in combination with other antibiotics should be based on the specific clinical situation and guidance from your healthcare provider.
- **Diabetes Medications**: Levofloxacin can affect blood sugar levels. If you have diabetes, monitor your blood sugar closely while taking levofloxacin, and inform your healthcare provider.
- **Vitamins and Minerals**: High doses of levofloxacin can interfere with the absorption of some vitamins and minerals. Discuss this with your healthcare provider if you are concerned.

4.6 Pregnancy and Lactation

Fertility:
Levofloxacin has not been shown to have a direct impact on fertility. However, if you are planning to conceive or are experiencing fertility issues, it's advisable to discuss your medication with a healthcare provider. Some antibiotics, including levofloxacin, can affect sperm quality in rare cases.

Pregnancy:

- Levofloxacin falls into pregnancy category C, which means that it should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks to the fetus.
- Animal studies have shown an increased risk of musculoskeletal and joint disorders in offspring exposed to quinolone antibiotics, like levofloxacin. While animal studies may not directly translate to human outcomes, this is a concern.
- Levofloxacin can cross the placenta, potentially affecting the developing fetus. It is generally recommended to avoid levofloxacin during pregnancy, particularly during the first trimester when fetal development is most critical.

Lactation:

- Levofloxacin can be excreted in breast milk, which may pose risks to a breastfeeding infant. There have been reports of adverse effects in breastfed infants whose mothers were taking quinolone antibiotics, so breastfeeding while using levofloxacin is usually discouraged.
- If levofloxacin is deemed necessary for the mother's health, it may be advisable to temporarily discontinue breastfeeding and provide expressed breast milk or use an alternative feeding method for the duration of treatment to minimize the infant's exposure to the medication. Discuss this with a healthcare provider.

4.7 Effects on ability to drive and use machines

Levofloxacin can cause certain side effects that may impair your ability to perform tasks that require alertness, concentration, and coordination. Some of these effects include:

- **Dizziness or Lightheadedness**: Levofloxacin may cause dizziness, which can affect your balance and ability to focus, making activities like driving or operating heavy machinery risky.
- **Tiredness or Fatigue**: Some people experience tiredness or fatigue as a side effect, which can significantly impair reaction times and concentration, thus affecting driving or machine operation.
- **Visual Disturbances**: Although not very common, Levofloxacin can cause blurred vision or other visual disturbances in some individuals, which would make driving dangerous.

4.8 Undesirable effects

Levofloxacin, like any medication, can have undesirable or adverse effects. It's essential to be aware of these potential side effects and to consult with your healthcare provider if you experience any of them. Common and less common undesirable effects associated with levofloxacin tablets include

Common Undesirable Effects (may affect up to 1 in 10 people):

- **Nausea**: Feeling sick to your stomach.
- **Diarrhea**: Changes in bowel habits, including loose stools.
- **Headache**: A common side effect that can vary in intensity.

Less Common Undesirable Effects (may affect up to 1 in 100 people):

- **Vomiting**: Throwing up.
- **Dizziness**: Feeling lightheaded or unsteady.
- **Abdominal Pain**: Discomfort or pain in the abdomen.
- **Rash**: Skin reactions, which can include itching or hives.
- **Insomnia**: Difficulty falling asleep or staying asleep.
- **Altered Sense of Taste**: A metallic or bitter taste in the mouth.
- **Increased Liver Enzymes**: Affecting liver function (usually reversible).

Rare and Serious Undesirable Effects (may affect up to 1 in 1,000 people):

- **Tendon Disorders**: Such as tendonitis or tendon rupture, particularly in the Achilles tendon. This can be a severe and potentially disabling side effect.
- **Central Nervous System Effects**: Including confusion, hallucinations, tremors, and seizures. These effects are relatively rare but can be serious.
- **Photosensitivity**: An increased sensitivity to sunlight, which can lead to sunburn.
- **Cardiovascular Effects**: Prolongation of the QT interval, potentially leading to arrhythmias (irregular heart rhythms).
- **Allergic Reactions**: Including skin rash, itching, swelling of the face or throat, and difficulty breathing. Severe allergic reactions are rare but can be life-threatening.
- **Peripheral Neuropathy**: Nerve damage that can cause pain, tingling, or weakness in the extremities.
- **Blood Disorders**: Such as anemia or low white blood cell count, which can affect the body's ability to fight infections.
- **Hypoglycemia**: A decrease in blood sugar levels, particularly in people with diabetes.

4.9 Overdose

An overdose of levofloxacin can be a serious medical emergency and may lead to a range of symptoms and complications. If you suspect or have ingested more levofloxacin tablets than prescribed, or if someone else has done so, you should seek immediate medical attention. Here are some steps to take in the event of a suspected overdose:

- **Contact Emergency Services**: If you or someone else is experiencing symptoms of an overdose or has ingested a potentially toxic amount of levofloxacin, call emergency services (e.g., 911 in the United States) immediately. Seek urgent medical help.
- **Inform Medical Professionals**: Provide information about the overdose, including the number of tablets taken, the strength of the tablets, and the time of ingestion. This information will assist healthcare providers in determining the appropriate treatment.
- **Go to the Nearest Hospital**: Transport the person to the nearest hospital or emergency room for prompt evaluation and treatment. Levofloxacin overdose can have serious effects on the body and may require medical intervention.
- **Treatment**: Treatment for a levofloxacin overdose may involve measures to remove the drug from the body and manage symptoms. Treatment can include:
  - Gastric Lavage: The stomach may be pumped to remove any unabsorbed levofloxacin.
  - Activated Charcoal: This may be administered to help absorb and reduce the absorption of the medication.
  - Intravenous (IV) Fluids: IV fluids may be given to maintain hydration and support kidney function.
  - Monitoring: Vital signs, kidney function, and cardiac activity will be closely monitored.
- **Symptomatic Care**: Treatment may be based on managing specific symptoms or complications resulting from the overdose.
- **Supportive Care**: Supportive care, such as addressing dehydration or electrolyte imbalances, may be necessary.
- **Consult a Poison Control Center**: In some cases, you may be advised to contact a poison control center for further guidance. They can provide information on the specific actions to take based on the situation.

Levofloxacin overdose can lead to symptoms such as dizziness, confusion, hallucinations, seizures, and potential cardiac arrhythmias. The severity of symptoms can vary based on the amount ingested and the individual's health status. Rapid medical intervention is essential to minimize the risk of complications and ensure the best possible outcome.

Please remember that this information is for general guidance, and it's important to follow the advice of healthcare professionals and emergency services in the event of an overdose. If you have any concerns about a potential overdose, do not hesitate to seek medical assistance immediately.

5.0 Pharmacological properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group- Antibacterial Agent

ATC Code- J01MA12

Levofloxacin is a **fluoroquinolone antibiotic** with broad-spectrum antibacterial activity. Its pharmacodynamics are characterized by its **mechanism of action**, **antimicrobial spectrum**, and **effect on bacterial resistance**.

Mechanism of action

- Levofloxacin works by inhibiting the activity of DNA gyrase and topoisomerase IV, which are enzymes involved in the replication and repair of bacterial DNA. By interfering with these essential processes, levofloxacin prevents bacterial DNA from unwinding and replicating properly, ultimately leading to bacterial cell death.

Pharmacodynamic effects

Levofloxacin is a **fluoroquinolone antibiotic** that exerts its therapeutic effects through **bactericidal** action against a broad range of bacteria. The pharmacodynamic effects of Levofloxacin are primarily due to its mechanism of action on bacterial enzymes involved in DNA replication and transcription. Below is an overview of its key **pharmacodynamic effects**:

Bactericidal Action
Levofloxacin is **bactericidal**, meaning it kills bacteria rather than just inhibiting their growth. This is due to its inhibition of two key bacterial enzymes:

- **DNA Gyrase (Topoisomerase II)**
- **Topoisomerase IV**

These enzymes are essential for maintaining the supercoiling and uncoiling of bacterial DNA, a process vital for DNA replication and cell division. By inhibiting these enzymes, **Levofloxacin disrupts DNA synthesis**, leading to bacterial cell death.

- **Effect on DNA Gyrase**: Levofloxacin binds to the **DNA gyrase complex**, preventing it from relieving the strain on the DNA, which is crucial for replication.
- **Effect on Topoisomerase IV**: Inhibition of **Topoisomerase IV** interferes with bacterial chromosome separation, leading to impaired cell division.

Clinical efficacy

Levofloxacin is effective in treating a range of bacterial infections, including:

- **Community-acquired pneumonia (CAP)**
- **Chronic bronchitis exacerbations**
- **Urinary tract infections (UTIs)**
- **Skin and soft tissue infections**
- **Acute bacterial sinusitis**

- **Prostatitis**
- **Anthrax** (post-exposure prophylaxis)

Resistance

Bacterial resistance to levofloxacin can occur through several mechanisms:

- **Mutations in DNA Gyrase or Topoisomerase IV**: Changes in these target enzymes can reduce the binding affinity of Levofloxacin, leading to resistance.
- **Efflux pumps**: Some bacteria have efflux pumps that can pump out the antibiotic from the cell before it exerts its effect.
- **Reduced permeability**: In some gram-negative bacteria, the outer membrane may become less permeable to Levofloxacin.

Paediatric population>

- Levofloxacin, as a **fluoroquinolone antibiotic**, is generally **not recommended** for **routine use in children and adolescents** unless other treatment options are not available or appropriate. This is due to concerns about **potential adverse effects**, especially related to the developing musculoskeletal system.

5.2 Pharmacokinetic Properties

➢ **Absorption**: Levofloxacin is well absorbed after oral administration. It reaches peak plasma concentrations within 1 to 2 hours of taking the medication.
➢ **Distribution**: Levofloxacin has good tissue penetration, allowing it to reach various body tissues and fluids, such as the lungs, kidneys, skin, and prostate. It can also penetrate into cerebrospinal fluid, making it effective in treating certain infections of the central nervous system.
➢ **Protein Binding**: Levofloxacin binds moderately to plasma proteins, primarily albumin.
➢ **Metabolism**: Levofloxacin has minimal metabolism in the liver, with the majority of the drug excreted unchanged in the urine.
➢ **Elimination**: The elimination half-life of levofloxacin is approximately 6 to 8 hours in adults. It is mainly eliminated through renal excretion, with approximately 85% of the dose excreted in the urine as unchanged drug. A smaller portion is eliminated in feces

5.3 Preclinical safety data

Preclinical safety data, which includes information from laboratory and animal studies conducted before a drug is tested in humans, provide valuable insights into the safety profile of medications. Levofloxacin has been subjected to preclinical studies to assess its safety and potential adverse effects. Here are some key points from the preclinical safety data for levofloxacin tablets:

General Toxicity Studies:

- Standard toxicology studies in animals, such as rats and dogs, were conducted to assess the effects of levofloxacin on various organs and systems.
- These studies typically include examining the effects of the drug on the cardiovascular system, nervous system, liver, kidneys, and gastrointestinal tract.
- Results from general toxicity studies help determine the maximum tolerated dose and potential dose-related adverse effects.

Reproductive and Developmental Toxicity:

- Levofloxacin was assessed for its effects on reproduction and fetal development.
- Studies in animals (such as rats and rabbits) examined the impact of levofloxacin on fertility, embryo-fetal development, and postnatal development.

Carcinogenicity:

- Levofloxacin was evaluated for its potential to cause cancer (carcinogenicity) in long-term animal studies.
- Results from these studies can indicate whether there is an increased risk of cancer associated with the drug.

Genotoxicity:

- Genotoxicity studies investigate whether levofloxacin has the potential to damage genetic material.
- These studies include assessments of mutagenicity (the ability to cause mutations) and chromosomal damage.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipient

Lactose Monohydarate, MCCP-101, Maize starch, Sodium Starch Glycolate, PVPK 30, Sodium Benzoate, Purified water, Sodium Starch Glycolate, Aerosil 200, Talcum, C.C.S. Disolwell, Magnesium Stearate, Mediicoatt-Uni- (WT335) white Universal, Red Oxide of Iron, Titanium Dioxide, Isopropyl Alcohol, Methylene Di Chloride.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at temperature not exceeding 30ºC. Protect from light and moisture.

6.5 Nature and contents of container

1 x 10 Blister

6.6 Special precautions for disposal < and other handling>

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Applicant/Manufactured by :-

Marine Medicare Pvt. Ltd.,
Vill. Kulhariwala, P.O. Mandhala,Distt Solan,
Baddi [H.P]-174103. INDIA