FACTIVE®

(gemifloxacin mesylate)

ACTION

Factive (gemifloxacin mesylate) is a synthetic broad-spectrum antibacterial agent for oral administration. Gemifloxacin, a compound related to the fluoroquinolone class of antibiotics, is available as the mesylate salt in the sesquihydrate form.

INDICATIONS

Factive is indicated for the treatment of infections caused by susceptible strains of the following microorganisms:

Aerobic Gram-positive:

Streptococcus pneumoniae (including penicillin, macrolide and most ofloxacin/ levofloxacin resistant and MDRSP; multi-drug resistant streptococcus pneumonia formerly known as penicillin resistant streptococcus pnuemoniae) *Streptococcus pyogenes* (including macrolide resistant), *Streptococcus viridans, Streptococcus agalactiae, Streptococcus milleri, Streptococcus anginosius, Streptococcus constellatus, Streptococcus mitis, Streptococcus* species, *Staphylococcus aureus* (methicillin sensitive), *Staphylococcus epidermidis, Staphylococcus saprophyticus, Staphylococcus haemolyticus, Staphylococcus* species, *Enterococcus faecalis, Enterococcus faecium, Enterococcus* species.

Aerobic Gram-negative:

Haemophilus influenzae (beta lactamase positive and negative), *Haemophilus parainfluenzae, Haemophilus* species, *Moraxella catarrhalis* (beta lactamase positive and negative), *Moraxella* species, *Klebsiella pneumoniae, Klebsiella oxytoca, Klebsiella* species, *Escherichia coli, Neisseria gonorrhoeae, Neisseria* species, *Acinetobacter lwof , Acinetobacter anitratus, Acinetobacter calcoaceticus, Acinetobacter haemolyticus, Acinetobacter* species, *Citrobacter freundii, Citrobacter koseri, Citrobacter* species, *Salmonella* species, *Shigella* species, *Enterobacter cloacae, Enterobacter aerogenes, Enterobacter* species, *Serratia marcescens, Serratia* species, *Proteus mirabilis, Proteus vulgaris, Proteus* species, *Providencia* species, *Morganella morganii, Morganella* species, *Yersinia* species, *Pseudomonas aeruginosa, Pseudomonas* species, *Bordetella pertussis, Bordetella* species.

Atypicals:

Coxiella burnetti, Coxiella species, *Mycoplasma pneumoniae, Mycoplasma* species, *Legionella pneumophila, Legionella* species, *Chlamydia pneumoniae, Chlamydia* species.

Anaerobes:

Peptostreptococcus species, *Clostridium non-perfringens, Clostridium perfringens, Clostridium* species, *Fusobacterium* species, *Porphyromonas* species, *Prevotella* species.

Factive is indicated for the treatment of infections caused by susceptible microorganisms in the following conditions:

- Acute bacterial exacerbation of chronic bronchitis
- Community-acquired pneumonia
- Acute bacterial sinusitis

DOSAGE AND ADMINISTRATION

Factive can be taken with or without food and should be swallowed whole with a liberal amount of liquid. The recommended dose of Factive is 320 mg daily, as the following:

- ***Acute bacterial exacerbation of chronic bronchitis:*** One 320 mg tablet daily for 5 days.
- ***Community-acquired pneumonia (CAP):*** One 320 mg tablet daily from 5 to 7 days.
- ***Acute bacterial sinusitis:*** One 320 mg tablet daily for 5 days.

The recommended dose and duration of Factive should not be exceeded.

- ***Renally Impaired Patients:*** Dose adjustment in patients with creatinine clearance > 40 mL/min is not required. Modification of the dosage is recommended for patients with creatinine clearance ≤ 40 mL/min. (i.e, to take160 mg every 24h).
- ***Use in Hepatically Impaired Patients or elderly:*** No dosage adjustment is required.

CONTRAINDICATIONS

Gemifloxacin is contraindicated in patients with a history of hypersensitivity to gemifloxacin, fluoroquinolone antibiotic agents, or any of the product components.

WARNINGS

QT Effects: Fluoroquinolones may prolong the QT interval in some patients. Gemifloxacin should be avoided in patients with a history of prolongation of the QTc interval, patients with uncorrected electrolyte disorders (hypokalemia or hypomagnesemia), and patients receiving some kinds of antiarrhythmic agents such as quinidine.

Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving fluoroquinolone therapy. These reactions may occur following the first dose.

Gemifloxacin should be discontinued immediately at the appearance of any sign of an immediate type I hypersensitivity skin rash or any other manifestation of a hypersensitivity reaction; the need for continued fluoroquinolone therapy should be evaluated.

Tendon Effects: Ruptures of the shoulder, hand, Achilles tendon or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones. Gemifloxacin should be discontinued if the patient experiences pain, inflammation, or rupture of a tendon.

CNS Effects: In clinical studies with gemifloxacin, central nervous system (CNS) effects have been reported infrequently. As with other fluoroquinolones, gemifloxacin should be used with caution in patients with CNS diseases such as epilepsy or patients predisposed to convulsions.

Antibiotic Associated Colitis: Pseudomembranous colitis has been reported with nearly all antibacterial agents, including gemifloxacin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of any antibacterial agent.

PRECAUTIONS

Pregnancy: Pregnancy Category C; the safety of gemifloxacin in pregnant women has not been established. Gemifloxacin should not be used in pregnant women unless the potential benefit to the mother outweighs the risk to the fetus. There are no adequate and well-controlled studies in pregnant women.

Nursing Mothers: Gemifloxacin is excreted in the breast milk of rats. There is no information on excretion of gemifloxacin into human milk. Therefore, gemifloxacin should not be used in lactating women unless the potential benefit to the mother outweighs the risk.

Pediatric Use: Safety and effectiveness in children and adolescents less than 18 years of age have not been established.

Rash: In clinical studies, the overall rate of drug-related rash was 2.8%. The most common form of rash associated with gemifloxacin was described as maculopapular and mild to moderate in severity. Rash usually appeared 8 to 10 days after start of therapy; 60% of the rashes resolved within 7 days, and 80% resolved within 14 days.

Photosensitivity reactions have been reported very rarely in clinical trials with Factive.

Hepatic Effects: Liver enzyme elevations (increased ALT and/or AST) occurred at similar rates in patients receiving gemifloxacin 320 mg daily relative to comparator antimicrobial agents (ciprofloxacin, levofloxacin, clarithromycin, cefuroxime axetil, amoxicillin / clavulanate potassium, and ofloxacin).

There were no clinical symptoms associated with these liver enzyme elevations. The liver enzyme elevations resolved following cessation of therapy.

Drug Interactions

Concomitant administration of Factive and calcium carbonate, cimetidine, omeprazole, or combined estrogen / progesterone oral contraceptives produced minor changes in the pharmacokinetics of gemifloxacin, which were considered to be without clinical significance.

Concomitant administration of Factive with probenecid resulted in a 45% increase in systemic exposure to gemifloxacin.

Factive had no significant effect on the anticoagulant effect of warfarin in healthy subjects on stable warfarin therapy.

Quinolones form chelates with alkaline earth and transition metals. The absorption of oral gemifloxacin is significantly reduced by the concomitant administration of an antacid containing aluminum and magnesium. Magnesium- and/or aluminum-containing antacids, products containing ferrous sulfate (iron), multivitamin preparations containing zinc or other metal cations, or didanosine chewable/ buffered tablets or the pediatric powder for oral solution should not be taken within 3 hours before or 2 hours after Factive. Sucralfate should not be taken within 2 hours of Factive.

SIDE EFFECTS

Factive is generally well tolerated. The majority of adverse reactions experienced by patients in clinical trials were considered to be of mild to moderate severity. And may include:

- ***Body as a Whole:*** occasional fungal overgrowth could occur, such as oral thrush, and vaginitis.
- ***Central Nervous System / Psychiatric:*** headache, occasional dizziness and insomnia could occur.
- ***Gastrointestinal:*** diarrhea, occasional abdominal pain, nausea, and vomiting could occur.
- ***Hepatic:*** occasional asymptomatic transient elevations in liver enzymes could occur.
- ***Skin:*** occasional rash, urticaria, and pruritus could occur. A diffuse maculopapular or erythematous skin rash was reported in some patients taking Factive in clinical trials. The rash mainly occurred after one week, was generally mild to moderate and appeared to be a reversible type IV hypersensitivity reaction. It is recommended that treatment with Factive should be discontinued if a patient experiences rash, unless the opinion of the physician dictates otherwise.
- ***Other:*** isolated cases of the following adverse events were observed: elevated bilirubin, tendonitis, thrombocytopenia, and photosensitivity reaction.

OVERDOSE

Any sign or symptom of overdosage should be treated symptomatically. No specific antidote is known. In the event of acute oral overdosage, the stomach should be emptied by inducing vomiting or by gastric lavage; the patient should be carefully observed and treated symptomatically with appropriate hydration maintained.

Toxic signs after administration of a single high oral dose (400 mg/kg) of gemifloxacin to rodents included ataxia, lethargy, piloerection, tremor, and clonic convulsions.

STORAGE

Store at tightly closed container at room temperature, below 25°C.

PRESENTATION

Tablets:

FACTIVE: Gemifloxacin mesylate 426.39 mg equivalent to 320 mg of gemifloxacin.

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of the reach of children

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