grat 320mg

گریٹ ۳۲۰ ملی گرام

(جیمی فلوکساسن)

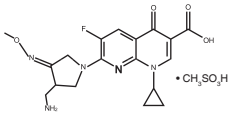
ٹیبلٹس یو۔ایس۔پی۔

(Gemifloxacin)
Tablets U.S.P.

DESCRIPTION:

Grat (Gemifloxacin) is a synthetic broad spectrum antibacterial agent for oral administration. Gemifloxacin is related to the fluoroquinolone class of antibiotics, available as the mesylate salt in the sesquihydrate form. Chemically, Gemifloxacin is (R,S)-7-[(4Z)-3-(aminomethyl)-4-(methoxyimino)-1-pyrro lidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid ($C_{18}H_{20}FN_5O_4.CH_4O_3S$)

Its unique structure confers enhanced activity against gram+ve pathogens without significant compromising gram -ve & atypical pathogens activity as compare to other fluoroquinolones.



COMPOSITION:

Each film-coated tablet contains:
Gemifloxacin Mesylate eq. to
Gemifloxacin... 320mg

CLINICAL PHARMACOLOGY

Mechanism of Action : Gemifloxacin inhibits two specific enzymes, DNA gyrase and DNA topoisomerase IV, which aid in bacterial DNA replication. Gemifloxacin displays strong binding affinity at both of these target sites, which helps maintain high potency against resistant S pneumoniae. This dual targeting with Gemifloxacin is achievable at therapeutic drug levels.

Pharmacokinetics: The pharmacokinetics of Gemifloxacin are approximately linear over the dose range from 40mg to 640mg. There was minimal accumulation of Gemifloxacin following multiple oral doses up to 640mg a day for 7 days (mean accumulation <20%). Following repeat oral administration of 320mg Gemifloxacin once daily, steady-state is achieved by the third day of dosing.

Absorption and Bioavailability: Gemifloxacin is rapidly absorbed from the gastrointestinal tract. Peak plasma concentrations of Gemifloxacin were observed between 0.5 and 2 hours following oral tablet administration and the absolute bioavailability of the 320mg tablet averaged approximately 71% (95% CI 60%-84%). Following repeat oral doses of 320mg to healthy subjects, the mean ± SD maximal Gemifloxacin plasma concentrations (Cmax) and systemic drug exposure (AUC(0-24)) were 1.61 ± 0.51 g/mL (range 0.70-2.62 g/mL) and 9.93 ± 3.07 g/mL (range 4.71-20.1 g /mL), respectively. In patients with respiratory and urinary tract infections (n=1423), similar estimates of systemic drug exposure were determined using a population pharmacokinetics analysis (geometric mean AUC(0-24), 8.36 g/mL; range 3.2 – 47.7 g/mL. The pharmacokinetics of Gemifloxacin were not significantly altered when a 320mg dose was administered with a high-fat meal. Therefore Grat tablets 320mg may be administered without regard to meals.

Distribution:

Tissues	Concentration (mean +- SD)	Ratio vs plasma (mean +- SD)
Plasma	1.40 (0.442) ug/mL	----------
Bronchoalveolar Macrophages	107 (77) ug/g	90.54 (106.3)
Epithelial Lining fluid	2.69 (1.96) ug/mL	1.99 (1.32)
Bronchial Mucosa	9.52 (5.15) ug/g	7.21 (4.03)

Metabolism: Gemifloxacin is metabolized to a limited extent by the liver. The unchanged compound is the predominant drug-related component detected in plasma (approximately 65%) up to 4 hours after dosing. All metabolites formed are minor (<10% of the administered oral dose); the principal ones are N-acetyl gemifloxacin, the E-isomer of Gemifloxcin and the carbamyl glucuronide of Gemifloxcin. Cytochrome P450 enzymes do not play an important role in Gemifloxcin metabolism, and the metabolic activity of these enzymes is not significantly inhibited by Gemifloxcin.

Excretion: Gemifloxcin and its metabolites are excreted via dual routes of excretion. Following oral administration of Gemifloxcin to healthy subjects, a mean (±SD) of 61 ± 9.5% of the dose was excreted in the feces and 36 ± 9.3% in the urine as unchanged drug and metabolites. The mean (±SD) renal clearance following repeat doses of 320mg was approximately 11.6 ± 3.9 L/hr (range 4.6-17.6 L/hr), which indicates active secretion is involved in the renal excretion of Gemifloxcin. The mean (±SD) plasma elimination half-life at steady state following 320mg to healthy subjects was approximately 7 ± 2 hours (range 4-12 hours).

Hepatic Insufficiency: The pharmacokinetics following a single 320mg dose of Gemifloxcin were studied in patients with mild to moderate liver disease. There was a mean increase in AUC (0-24) of 34% and a mean increase in Cmax of 25% in these patients with hepatic impairment compared to healthy volunteers. The pharmacokinetics of a single 320mg dose of Gemifloxcin were also studied in patients with severe hepatic impairment. There was a mean increase in AUC (0-inf) of 45% and a mean increase in Cmax of 41% in these subjects with hepatic impairment compared to healthy volunteers. These average pharmacokinetic increases are not considered to be clinically significant. There was no significant change in plasma elimination half-life in the mild, moderate or severe hepatic impairment patients. No dosage adjustment is recommended in patients with mild, moderate or severe hepatic impairment.

Renal Insufficiency: Studies with repeated 320mg doses indicate the clearance of Gemifloxacin is reduced and the plasma elimination is prolonged, leading to an average increase in AUC values of approximately 70% in patients with renal insufficiency. In the pharmacokinetic studies, Gemifloxacin Cmax was not significantly altered in subjects with renal insufficiency. 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. Hemodialysis removes approximately 20 to 30% of an oral dose of Gemifloxacin from plasma.

Drug Interactions: Administration of repeat doses of Gemifloxacin had no effect on the repeat dose pharmacokinetics of theophylline, digoxin or an ethinylestradiol/levonorgestrol oral contraceptive product in healthy subjects. Concomitant administration of Gemifloxacin 320mg and calcium carbonate, cimetidine, omeprazole, or an estrogen/progesterone oral contraceptive produced minor changes in the pharmacokinetics of gemifloxacin, which

were considered to be without clinical significance. Concomitant administration of Grat 320mg with probenecid resulted in a 45% increase in systemic exposure to Gemifloxacin. Gemifloxacin had no significant effect on the anticoagulant effect of warfarin in healthy subjects on stable warfarin therapy. However, because some quinolones have been reported to enhance the anticoagulant effects of warfarin or its derivatives in patients, the prothrombin time or other suitable coagulation test should be closely monitored if a quinolone antimicrobial is administered concomitantly with warfarin or its derivatives. 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, multivitamin preparations containing zinc or other metal cations, or didanosine should not be taken within 3 hours before or 2 hours after Grat 320mg . Sucralfate should not be taken within 2 hours of Grat (Gemifloxacin).

INDICATIONS AND DOSAGE:

Indication	Dose	Durations
Acute sinusitis	320mg O.D	5 days
Acute bacterial exacerbation of chronic bronchitis		5 days
Community-acquired pneomonia (of mild to moderate severity)		7 days
Uncomplicated urinary tract infections		3 days
Acute pyelonephritis		10 days

Adverse Effects: Drug-related adverse events, classified as possibly or probably related with a frequency of Gemifloxacin 1% for patients receiving 320mg of Gemifloxacin versus comparator drug (beta-lactam antibiotics, macrolides or other fluoroquinolones) are as follows: diarrhoea 3.6% vs. 4.6%; rash 2.8% vs. 0.6%; nausea 2.7% vs. 3.2%; headache 1.2% vs. 1.5%; abdominal pain 0.9% vs. 1.1%; vomiting 0.9% vs. 1.1%; dizziness 0.8% vs. 1.5%; and taste perversion 0.3% vs. 1.9%. Gemifloxacin appears to have a low potential for photosensitivity. Additional drug-related adverse events (possibly or probably related) in >0.1% to 1% of patients who received 320 mg of Gemifloxacin were: abdominal pain, anorexia, arthralgia, constipation, dermatitis, dizziness, dry mouth, dyspepsia, fatigue, flatulence, fungal infection, gastritis, genital moniliasis, hyperglycemia, insomnia, leukopenia, moniliasis, pruritus, somnolence, taste perversion, , urticaria, vaginitis, and vomiting.

PRECAUTIONS

General: Prescribing Moxifloxacin tablets in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Rash: In clinical studies, the overall rate of drug-related rash was 2.8%. The most common form of rash associated with Grat was described as maculopapular and mild to moderate in severity; 0.3% was described as urticarial in appearance. There were no documented cases in the clinical trials of more serious skin reactions known to be associated with significant morbidity or mortality. Rash was observed in patients <40 years of age, especially females and post-menopausal females taking hormone replacement therapy. Prolonging duration of therapy beyond 7 days causes the incidence of rash to increase significantly in all subgroups except men over the age of 40. Gemifloxacin therapy should be discontinued in patients developing a rash while on treatment.

Hepatic Effects: There were no clinical symptoms associated with these liver enzyme elevations. The recommended dose of Gemifloxacin 320 mg daily should not be exceeded. Alteration of the dosage regimen is necessary for patients with impairment of renal function (creatinine clearance 40 mL/min). Adequate hydration of patients receiving Gemifloxacin should be maintained to prevent the formation of a highly concentrated urine.

Pregnancy: The safety of Gemifloxacin in pregnant women has not been established. Gemifloxacin tablets 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: There is no information on excretion of Gemifloxacin into human milk. Therefore, Grat (Gemifloxacin) 320mg tablets should not be used in lactating women unless the potential benefit to the mother outweighs the risk.

INSTRUCTIONS:

Store below 30°C. Protect from heat, light & moisture.
Keep all medicines out of the reach of children.

PRESENTATION

Grat (Gemifloxacin) 320mg tablets are available in Alu-Alu blister pack of 1x7's.

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
روشنی، گرمی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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