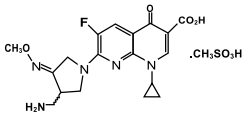
Renova 320mg Tablets

(Gemifloxacin)

COMPOSITION:
Each film coated tablet contains:
Gemifloxacin mesylate
equivalent to Gemifloxacin ……..320mg

DESCRIPTION:
Gemifloxacin is a synthetic broad-spectrum fluoroquinolone antibiotic for oral administration. It is available as mesylate salt in the sesquihydrate form. Chemically, gemifloxacin is (R,S)-7-[(4Z)-3-(aminomethyl) - 4-methoxyimino-pyrrolidinyl] - 1-cyclopropyl-6-fluoro-4-oxo-1, 8-naphthyridine-3-carboxylic acid ($C_{18}H_{20}FN_5O_4.CH_4O_3S$)



CLINICAL PHARMACOLOGY:
Mechanism of Action
Gemifloxacin acts by inhibiting DNA synthesis through inhibition of two specific enzymes, DNA gyrase and DNA topoisomerase IV. Both of these enzymes are essential for bacterial growth. Gemifloxacin exhibits strong binding affinity with both of these enzymes which helps to maintain high potency against resistant *S. pneumoniae*. Most strains of streptococci showing mutations in both DNA gyrase and topoisomerase IV are resistant to all fluoroquinolones in clinical use. However, gemifloxacin maintains activity against most of these double mutants. Gemifloxacin is highly selective for bacterial rather than human topoisomerase II

PHARMACOKINETIC PROPERTIES:
Absorption and Bioavailability
Following oral administration, gemifloxacin is rapidly absorbed from gastrointestinal tract. Peak plasma concentration achieved during 0.5 – 2.0 hours post dose and absolute bioavailability is 71% approximately. The pharmacokinetics of gemifloxacin are linear over the dose range 40mg to 640mg. Accumulation of gemifloxacin following multiple doses of 640mg a day for 7 days is minimum (Mean accumulation <20%). Steady state achieved by the 3rd day of dosing after repeat oral administration. Gemifloxacin absorption does not affected by food intake
Distribution
The mean plasma protein bound fraction, in vivo, is approximately 55% - 73% and is concentration independent. The steady-state volume of distribution is approximately 3.5L/kg which exceeds total body water indicating high level of distribution into various body tissues
Penetration into Tissues and Body Fluids
Gemifloxacin is rapidly distributed into target tissues and body fluids like lungs (Epithelial lining fluid, alveolar macrophages, bronchial tissue) and nasal secretions
Metabolism
Gemifloxacin is partly metabolized and the compound itself is the predominant drug-related component detected in plasma (*ca* 65%) up to 4hrs. after dosing. All metabolites formed are minor of which the principal ones are N-acetyl gemifloxacin, the E-isomer of gemifloxacin and the carbamoyl glucuronide of gemifloxacin
Elimination
Approximately 36% and 61% of the dose is excreted as unchanged drug and metabolites in the urine and faeces, respectively after gemifloxacin oral administration. Renal clearance of gemifloxacin (*ca* 160mL/min) is slightly greater than the glomerular filtration rate of 120mL/min, and indicates active renal secretion is involved in the elimination of gemifloxacin. The plasma and urinary elimination half-lives are approximately 8 and 15hours, respectively

SPECIAL POPULATION:
Elderly
The pharmacokinetics of gemifloxacin is unaffected with age. Dose adjustment is not required
Gender
AUC values were generally slightly higher (Approx. 10%) in women than in men. This small difference is not clinical significant and therefore no dose adjustment is required based on gender
Renal Insufficiency
The plasma clearance of gemifloxacin is reduced by approximately 50% in severe renal impairment patients with creatinine clearance <40mL/min and patients undergoing dialysis or CAPD. Gemifloxacin is not notably removed by dialysis. Dose adjustment is not required in mild/moderate renal impairment patients with creatinine clearance ≥ 40mL/min. For severe renal impairment patients, haemodialysis patients and CAPD patients the dose should be reduced to 160mg
Hepatic Insufficiency
No dose adjustment of gemifloxacin is required in patients with hepatic impairment
Pregnancy and Lactation: (Pregnancy category C); see contra-indications
The safety and efficacy of gemifloxacin in pregnant or lactating women have not been established. Gemifloxacin should not be used in pregnant or lactating women unless the potential benefits outweighs the potential risk

INDICATIONS:
Gemifloxacin is indicated for the treatment of the following bacterial infections in adults caused by sensitive organisms as follows:

Respiratory Tract Infections:
- **Community acquired pneumonia (CAP)** caused by S. pneumoniae, C. pneumoniae, M. pneumoniae, H. influenzae, M. catarrhalis, L. pneumophila
- **Acute exacerbations of chronic bronchitis (AECB)** caused by H. influenzae, M. catarrhalis, S. pneumoniae
- **Acute bacterial sinusitis** caused by S. pneumoniae, H. influenzae, M. catarrhalis, S. aureus

Urinary Tract Infections:
- **Acute uncomplicated pyelonephritis** caused by E. coli, K. pneumoniae
- **Uncomplicated urinary tract infections (uUTI)** in females caused by E. coli, K. pneumoniae

CONTRA-INDICATIONS:
- Known hypersensitivity to gemifloxacin, any of its excipients or other quinolones
- Patients who have previously suffered tendon damage with fluoroquinolones
- Gemifloxacin should not be used in children and adolescents under 18 years of age
- Gemifloxacin should not be used in pregnant or lactating woman

WARNINGS:

Fluoroquinolones, including **Renova**, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants

Safety and efficacy in children and adolescents ≤18 years have not been studied. Quinolones as a class have been shown to cause arthropathy in immature animals
Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics. Hence it is important to consider this diagnosis in patients who develop diarrhoea during or after treatment with antibiotics, including gemifloxacin, particularly if the diarrhoea is severe

Tendinitis and tendon ruptures may occur in any age group during treatment with quinolones, including gemifloxacin, but particularly in elderly patients or when corticosteroids are being co-administered. Gemifloxacin should be discontinued if tendinitis is suspected or at the first sign of pain or inflammation and the affected limb should be rested
Gemifloxacin should be used with caution in patients predisposed to QT interval prolongation or in patients taking other medications that are known to prolong the QT interval
Gemifloxacin should be used with caution in patients with epilepsy or with other factors that predispose for seizures. Quinolones should be used with caution in patients with existing or family history of glucose-6-phosphate dehydrogenase deficiency as hemolytic reactions may develop during therapy
Photosensitization has been reported with the use of quinolones. Patients taking gemifloxacin should avoid unnecessary exposure to strong sunlight or artificial UV rays e.g. sunray lamp, solarium

DOSAGE AND DIRECTIONS FOR USE:
Gemifloxacin can be taken with or without food and should be swallowed with a tolerant amount of liquid

The recommended dose of gemifloxacin is 320mg daily, according to the following table:

INDICATION	DOSE	DURATION
Acute bacterial exacerbations of chronic bronchitis	One 320mg tablet daily	5 days
Acute sinusitis	One 320mg tablet daily	5 days
Community-acquired pneumonia	One 320mg tablet daily	7 days*
Uncomplicated urinary tract infections	One 320mg tablet daily	3 days
Acute pyelonephritis	One 320mg tablet daily	10 days

* Therapy may be extended to 14 days of therapy in cases of serious pneumonia

OR
As directed by the physician

Renally Impaired Patients:
Dose adjustment in patients with mild/moderate renal impairment is not required. Some modification of dosage is recommended for patients with severe renal dysfunction. The following table provides dosage guidelines for use in patients with renal impairment:

Creatinine Clearance (mL/min)	**Dose**
≥ 40	See Usual Dosage
≤ 40	160mg q24h

Patients on haemodialysis or continuous ambulatory peritoneal dialysis therapy should receive 160mg q24h

OR
As directed by the physician

SIDE EFFECTS:
The most frequently reported adverse events include abdominal pain, diarrhoea, headache, nausea, rash and vomiting. The following side effects have been infrequently reported:

- **Body as a whole**: Fungal overgrowth
- **Central nervous system/Psychiatric:** Dizziness and insomnia
- **Laboratory abnormalities:** Asymptomatic transient elevation in liver enzymes
- **Skin:** Urticaria, pruritis and a maculopapular erythematous skin rash. A diffuse maculopapular or erythematous skin rash was reported in some patients. The rash that occurs after one week is generally mild to moderate and appeared to be a type IV hypersensitivity reaction. It is recommended that treatment with gemifloxacin should be discontinued if a patient experiences rash
  Elevated bilirubin was reported in <0.3% of patients and tendinitis, thrombocytopenia and photosensitivity reactions were reported in <0.1%

Peripheral neuropathy: This serious nerve damage potentially caused by fluoroquinolones may occur soon after these drugs are taken and may be permanent
If a patient develops symptoms of peripheral neuropathy, the fluoroquinolone should be stopped, and the patient should be switched to another, non-fluoroquinolones antibacterial drug, unless the benefit of continued treatement with a fluoroquinolone outweighs the risk

SPECIAL PRECAUTIONS:
For patients with severe impairment of renal function, alteration of the dosage regimen to 160mg q24h is necessary (See DOSAGE AND DIRECTIONS FOR USE)
Patients receiving gemifloxacin should be adequately hydrated to prevent the formation of a highly concentrated urine and crystalluria. The photosensitivity potential of gemifloxacin is low, with <0.1%. However, it is recommended that patients should avoid unnecessary exposure to strong sunlight or to artificial UV rays (e.g. Sunlamps, solariums), and should be advised of the appropriate use of broad-spectrum sunblock if in bright sunlight. Treatment should be discontinued if a photosensitivity reaction is suspected. Gemifloxacin may cause dizziness; if this occurs, patients should not operate an automobile or machinery or engage in activities requiring mental alertness or co-ordination

INTERACTIONS:
Gemifloxacin absorption is significantly reduced when aluminium or magnesium-containing antacids and iron salts are concomitantly administered. Gemifloxacin should be taken at least 2 hrs. before or 3 hrs. after these agents. Gemifloxacin should be taken at least 2 hrs. before sucralfate administration
Gemifloxacin do not cause drug interactions with compounds mediated by CYP450 enzymes
Gemifloxacin AUC increased (Average 45%) when co-administered with probenecid

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
No specific antidote is known. Dialysis does not remove gemifloxacin sufficiently. 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, treated symptomatically and adequate hydration should be maintained

PRESENTATION:
Renova 320mg tablets are available in blister pack of 7's

STABILITY:
See expiry on the pack

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity
Store at 25°C or below
Improper storage may deteriorate the medicine

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

رینووا ۳۲۰ ملی گرام
(جیمی فلاکسا سن) ٹیبلٹ

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں
ہدایات: بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ
یا اس سے کم درجہ حرارت پر رکھیں ورنہ دوا خراب ہو جائیگی