Front

VEZITIC®

(SOLIFENACIN SUCCINATE)

TABLET

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COMPOSITION:
Vezitic Tablet 5 mg:
Each film coated tablet contains:
Solifenacin Succinate ..... 5 mg.

Product Specs.: CCL Pharmaceuticals

Vezitic Tablet 10 mg:
Each film coated tablet contains:
Solifenacin Succinate ..... 10 mg.

Product Specs.: CCL Pharmaceuticals

DESCRIPTION:
Solifenacin succinate is a muscarinic receptor antagonist.

CLINICAL PHARMACOLOGY:
Solifenacin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of urinary bladder smooth muscle and stimulation of salivary secretion.
Pharmacokinetics:
Absorption: After oral administration of Solifenacin tablet, peak plasma levels (C_{max}) of solifenacin are reached within 3 to 8 hours after administration, and at steady state ranged from 32.3 to 62.9 ng/mL for the 5 and 10 mg solifenacin tablets, respectively. The absolute bioavailability of solifenacin is approximately 90%, and plasma concentrations of solifenacin are proportional to the dose administered.
Effect of food: There is no significant effect of food on the pharmacokinetics of solifenacin.
Distribution: Solifenacin is approximately 98% (in vivo) bound to human plasma proteins, principally to α1-acid glycoprotein. Solifenacin is highly distributed to non-CNS tissues, having a mean steady-state volume of distribution of 600L.
Metabolism: Solifenacin is extensively metabolized in the liver. The primary pathway for elimination is by way of CYP3A4; however, alternate metabolic pathways exist. The primary metabolic routes of solifenacin are through N-oxidation of the quinuclidin ring and 4R-hydroxylation of tetrahydroisoquinoline ring.
Excretion: Approximately 69.2% of the administered (10mg) dose was excreted in the urine (in the form of metabolites) and 22.5% in the feces over 26 days. Less than 15% (as mean value) of the dose was excreted in the urine as intact solifenacin. The elimination half-life of solifenacin following chronic dosing is approximately 45-68 hours.
Pharmacokinetics In Special Populations:
Age: Multiple dose studies of solifenacin in elderly volunteers (65 to 80 years) showed that C_{max}, AUC and t1/2 values were 20-25% higher as compared to the younger volunteers (18 to 55 years).
Pediatric: The pharmacokinetics of solifenacin has not been established in pediatric patients.
Renal impairment: Solifenacin should be used with caution in patients with renal impairment.
Severe renal impairment. There is a 2.1-fold increase in AUC and 1.6-fold increase in t1/2 of solifenacin in patients with severe renal impairment. Doses of solifenacin greater than 5 mg are not recommended in patients with severe renal impairment (CLcr < 30 mL/min).
Hepatic impairment: Solifenacin should be used with caution in patients with reduced hepatic function.
Moderate hepatic impairment: There is a 2 -fold increase in the t1/2 and 35% increase in AUC of solifenacin in patients with moderate hepatic impairment. Doses of solifenacin greater than 5 mg are not recommended in patients with moderate hepatic impairment (Child-Pugh B).
Severe hepatic impairment: Solifenacin is not recommended for patients with severe hepatic impairment (Child-Pugh C) .

DRUG-DRUG INTERACTIONS:
Drugs metabolized by cytochrome P450: At therapeutic concentrations, solifenacin does not inhibit CYP1A1/2, 2C9, 2C19, 2D6, or 3A4 derived from human liver microsomes.
CYP3A4 inhibitors: In vitro drug metabolism studies have shown that solifenacin is a substrate of CYP3A4. Inducers or inhibitors of CYP3A4 may alter solifenacin pharmacokinetics.
Ketoconazole interaction: When ketoconazole, a potent inhibitor of CYP3A4, administerd with Solifencacin 10 mg, the mean C_{max} and AUC of solifenacin increased by 1.5 and 2.7 fold, respectively. Therefore, it is recommended not to exceed a 5 mg daily dose of Solifenacin when administered with therapeutic doses of ketoconazole or other potent CYP3A4 inhibitors.
Warfarin, oral contraceptives and digoxin: Solifenacin has no significant effect on the pharmacokinetics of R-warfarin or S-warfarin and digoxin (0.125 mg/day) in healthy subjects.

INDICATIONS AND USAGE:
Solifenacin is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency.

CONTRAINDICATIONS:
Solifenacin is contraindicated in patients with urinary retention, gastric retention, uncontrolled narrow-angle glaucoma, and in patients who have demonstrated hypersensitivity to the drug substance or other components of the product.

WARNINGS & PRECAUTIONS:
Angioedema of the face, lips, tongue, and/or larynx have been reported with solifenacin. In some cases angioedema occurred after the first dose. Angioedema associated with upper airway swelling may be life threatening. If involvement of the tongue, hypopharynx, or larynx occurs, solifenacin should be promptly discontinued and appropriate therapy and/or measures necessary to ensure a patent airway should be promptly provided.
Bladder outflow obstruction:
Solifenacin, like other anticholinergic drugs, should be administered with caution to patients with clinically significant bladder outflow obstruction because of the risk of urinary retention.
Gastrointestinal obstructive disorders and decreased gi motility: Solifenacin, like other anticholinergics, should be used with caution in patients with decreased gastrointestinal motility.
Controlled narrow-angle glaucoma: Solifenacin should be used with caution in patients being treated for narrow-angle glaucoma.
Reduced renal function: Solifenacin should be used with caution in patients with reduced renal function. Doses of Solifenacin greater than 5 mg are not recommended in patients with severe renal impairment (CLcr <30 mL/min).
Reduced hepatic function: Solifenacin should be used with caution in patients with reduced hepatic function. Doses of Solifenacin greater than 5 mg are not recommended in patients with moderate hepatic impairment (Child-Pugh B). Solifenacin is not recommended for patients with severe hepatic impairment (Child-Pugh C).
Drug-drug interactions: Do not exceed a 5 mg daily dose of Solifenacin when administered with therapeutic doses of ketoconazole or other potent CYP3A4 inhibitors.
Patients with congenital or acquired qt prolongation: In a study of the effect of solifenacin on the QT interval in 76 healthy women , the QT prolonging effect appeared less with solifenacin 10 mg than with 30 mg (three times the maximum recommended dose), and the effect of solifenacin 30 mg did not appear as large as that of the positive control moxifloxacin at its therapeutic dose. This observation should be considered in clinical decisions to prescribe Solifenacin for patients with a known history of QT prolongation or patients who are taking medications known to prolong the QT interval.
Pregnancy: Teratogenic Effects, Pregnancy Category
Pregnancy category C: There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Solifenacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Labor and delivery: The effect of Solifenacin on labor and delivery in humans has not been studied.
Nursing mothers: It is not known whether solifenacin is excreted in human milk. Because many drugs are excreted in human milk, Solifenacin should not be administered during nursing. A decision should be made whether to discontinue nursing or to discontinue Solifenacin in nursing mothers.
Pediatric use: The safety and effectiveness of Solifenacin in pediatric patients have not been established.
Geriatric use: In placebo controlled clinical studies, similar safety and effectiveness were observed between older and younger patients treated with Solifenacin.

ADVERSE REACTIONS:
Expected side effects of antimuscarinic agents are dry mouth, constipation, blurred vision (accommodation abnormalities), urinary retention, and dry eyes. The most common adverse events reported in patients treated with Solifenacin were dry mouth and constipation and the incidence of these side effects was higher in the 10 mg compared to the 5 mg dose group. The incidence and severity of adverse events were similar in patients who remained on drug for up to 12 months. Adverse events that were reported in randomized, placebo-controlled trials at an incidence greater than placebo and in 1% or more of patients treated with Solifenacin 5 or 10 mg once daily for up to 12 weeks are as follows.
Gastrointestinal disorders: Dry Mouth, Constipation, Nausea, Dyspepsia, Abdominal Pain Upper, Vomiting
Infections and infestations: Urinary Tract Infection , Influenza, Pharyngitis
Nervous system disorders: Dizziness
Eye disorders: Blurred Vision, Dry Eyes
Renal and urinary disorders: Urinary Retention
General disorders: Edema of Lower Limb, Fatigue, Hypertension and Cough
Psychiatric disorders: Depression

OVERDOSAGE:
Acute: Over dosage with Solifenacin can potentially result in severe anticholinergic effects and should be treated accordingly. The highest dose ingested in an accidental overdose of solifenacin succinate was 280 mg in a 5-hour period. This case was associated with mental status changes. Some cases reported a decrease in the level of consciousness.
Chronic: Intolerable anticholinergic side effects (fixed and dilated pupils, blurred vision, failure of heel-to toe exam, tremors and dry skin) occurred on day 3 in normal volunteers taking 50 mg daily (5 times the maximum recommended therapeutic dose) and resolved within 7 days following discontinuation of drug.
Treatment of over dosage: In the event of overdose with Solifenacin, treat with gastric lavage and appropriate supportive measures. ECG monitoring is also recommended.

DOSAGE AND ADMINISTRATION:
The recommended dose of Solifenacin is 5 mg once daily. If the 5 mg dose is well tolerated, the dose may be increased to 10 mg once daily. Solifenacin should be taken with liquids and swallowed whole. Solifenacin can be administered with or without food.
Dose adjustment in renal impairment: For patients with severe renal impairment (CLcr <30 mL/min), a daily dose of Solifenacin greater than 5 mg is not recommended.
Dose adjustment in hepatic impairment: For patients with moderate hepatic impairment (Child-Pugh B), a daily dose of Solifenacin greater than 5 mg is not recommended. Use of Solifenacin in patients with severe hepatic impairment (Child-Pugh C) is not recommended.
Dose Adjustment CYP3A4 Inhibitors: When administered with therapeutic doses of ketoconazole or other potent CYP3A4 inhibitors, a daily dose of Solifenacin greater than 5 mg is not recommended.

INSTRUCTIONS:
- Store below 30ºC.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Vezitic Tablet 5 mg	:	Pack of 1 x 10 tablets.
Vezitic Tablet 10 mg	:	Pack of 1 x 10 tablets.

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT:

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