

Solifenacin succinate

R_x

Solifen[®]

5mg and 10mg Film-Coated Tablets
Urological (Drugs for urinary frequency and incontinence)

PRODUCT DESCRIPTION

Solifenacin succinate (Solifen) 5mg film-coated tablet is available as white oblong, biconvex shaped film-coated tablet plain on both sides.

Solifenacin succinate (Solifen) 10mg film-coated tablet is available as white, oval biconvex shaped, film-coated tablet, bisect line on one side & embossed "GETZ" on other side.

FORMULATION

Solifenacin succinate (Solifen) 5mg Film-Coated Tablet

Each film-coated tablet contains:

Solifenacin succinate... 5mg

Solifenacin succinate (Solifen) 10mg Film-Coated Tablet

Each film-coated tablet contains:

Solifenacin succinate...10mg

CLINICAL PHARMACOLOGY

Pharmacodynamics

Solifenacin is a competitive, muscarinic acetylcholine receptor antagonist. The binding of acetylcholine to these receptors, particularly the M₃ receptor subtype, plays a critical role in the contraction of smooth muscles. By preventing the binding of acetylcholine to these receptors, solifenacin reduces smooth muscle tone in the bladder, allowing the bladder to retain larger volumes of urine and reducing the number of micturation, urgency and incontinence episodes.

Pharmacokinetics

After oral administration of solifenacin succinate, it is absorbed from the gastrointestinal tract, with the peak plasma concentrations reaching after 3 to 8 hours and a bioavailability of about 90%. There is no effect of food on the pharmacokinetics of solifenacin. Solifenacin succinate is about 98% bound to plasma proteins principally to (alpha1)-acid glycoprotein. It is highly distributed to non-CNS tissues, having a mean steady-state volume of distribution of 600L. Solifenacin succinate is extensively metabolised in the liver mainly by the cytochrome P450 isoenzyme CYP3A4, and has a terminal half-life of 45-68 hours. Solifenacin succinate is excreted mainly as metabolites in urine and feces.

THERAPEUTIC INDICATIONS

Solifenacin Succinate (Solifen) is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and urinary frequency or frequent micturation.

DOSAGE AND ADMINISTRATION

Solifenacin Succinate (Solifen) should be taken with liquids and swallowed whole. Solifenacin Succinate (Solifen) can be administered with or without food.

Adults

The recommended dose of Solifenacin Succinate (Solifen) is 5mg once daily. If needed, the dose may be increased to 10mg once daily.

Patients with renal impairment

No dose adjustment is necessary for patients with mild to moderate renal impairment (CL_{cr} >30mL/min). Patients with severe renal impairment (CL_{cr} <30mL/min) should be treated with caution and receive no more than 5mg once daily.

Patients with hepatic impairment

No dose adjustment is necessary for patients with mild

hepatic impairment. Patients with moderate hepatic impairment (Child-Pugh score of 7 to 9) should be treated with caution and receive no more than 5mg once daily.

Potent Inhibitors of Cytochrome P4503A4:

Maximum dose of 5mg is recommended in the patients receiving drugs such as ketoconazole or ritonavir that are strong inhibitors of the cytochrome P450 isoenzyme CYP3A4.

ADVERSE DRUG REACTIONS

Gastrointestinal disorders:

dry mouth, constipation, nausea, vomiting, dyspepsia, gastroesophageal reflux disease, ileus

Infections and infestations:

urinary tract infection NOS

Eye disorders:

vision blurred, dry eye NOS, glaucoma

General disorders and administration site conditions:

fatigue, oedema peripheral

Nervous system disorders:

dizziness, headache, somnolence

Psychiatric disorders:

hallucination, delirium

Skin and subcutaneous tissue disorders:

pruritus, rash, urticaria, angioedema, erythema multiforme, exfoliative dermatitis

Renal and urinary disorders:

urinary retention, renal impairment

Cardiac disorders:

atrial fibrillation, palpitations, tachycardia, Torsade de Pointes

Hepatobiliary disorders:

liver disorders, mostly characterized by abnormal liver function tests (AST, ALT, GGT)

Immune system disorders:

anaphylactic reaction

Investigations:

electrocardiogram QT prolonged

Metabolism and nutrition disorders:

decreased appetite, hyperkalemia

Musculoskeletal and connective tissue disorders:

muscular weakness

Respiratory, thoracic and mediastinal disorders:

dysphonia

CONTRAINDICATIONS

Solifenacin succinate is contraindicated in patients with:

- Hypersensitivity to the active substance or to any of the excipients.
- Urinary retention.
- Gastric retention.
- Uncontrolled narrow-angle glaucoma.
- Myasthenia gravis.
- Patients undergoing hemodialysis.
- Patients with severe hepatic impairment and renal impairment.

Solifenacin succinate should not be used in children as safety and efficacy in children have not yet been established.

PRECAUTIONS

Bladder Outflow Obstruction

Solifenacin succinate 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 succinate, like other anticholinergics, should be used with caution in patients with decreased gastrointestinal motility.

Controlled Narrow-Angle Glaucoma

Solifenacin succinate should be used with caution in patients being treated for narrow-angle glaucoma.

Reduced Renal Function

Solifenacin succinate should be used with caution in patients with reduced renal function. Doses of solifenacin succinate greater than 5mg are not recommended in patients with severe renal impairment (CLcr <30 mL/min).

Reduced Hepatic Function

Solifenacin succinate should be used with caution in patients with reduced hepatic function. Doses of solifenacin succinate greater than 5mg are not recommended in patients with moderate hepatic impairment. Solifenacin succinate is not recommended for patients with severe hepatic impairment.

Hiatus Hernia

Solifenacin succinate should be used with caution in patients of hiatus hernial Gastroesophageal reflux who are concurrently taking medicinal products (such as bisphosphonates) that cause or exacerbate oesophagitis.

Hereditary problems

Patients with rare hereditary problems of galactose intolerance, the Lapp Lactase deficiency or glucose-glucose malabsorption should not take this medicinal product.

Congenital or Acquired QT prolongation

Caution should be taken for the patients with known history of QT prolongation or the patients who are taking the medications known to prolong the QT interval.

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Solifenacin succinate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether solifenacin succinate is excreted in human milk. Because many drugs are excreted in human milk, solifenacin succinate should not be administered during nursing. A decision should be made whether to discontinue nursing or to discontinue solifenacin succinate in nursing mothers.

DRUG INTERACTIONS*Pharmacological Interactions*

Concomitant administration with other drugs having anticholinergic properties may result in more pronounced therapeutic and side effects. An interval of approximately one week should be allowed after stopping the treatment with solifenacin succinate before commencing other cholinergic therapy.

The therapeutic effect of solifenacin succinate may be reduced by concomitant administration of cholinergic receptor agonists. Solifenacin succinate can reduce the effect of the drugs that stimulate the motility of gastrointestinal tract, such as metoclopramide and cisapride.

Ketoconazole and other CYP3A4 Inhibitors

Simultaneous administration of solifenacin succinate and ketoconazole (200mg/day) resulted in a two-fold increase of the AUC of solifenacin succinate while ketoconazole at a dose of 400mg/day resulted in a three-fold increase

of the AUC of solifenacin succinate. Therefore, the maximum dose of Solifenacin succinate should be restricted to 5mg, when used simultaneously with ketoconazole or therapeutic doses of other strong CYP3A4 inhibitors. Since Solifenacin succinate is metabolized by CYP3A4, pharmacokinetic interactions are possible with other CYP3A4 substrates with higher affinity (e.g., verapamil, diltiazem) and CYP3A4 inducers (e.g., rifampacin, phenytoin, carbamazepin).

OVERDOSE AND TREATMENT

Overdosage with solifenacin succinate can potentially result in severe anticholinergic effects and should be treated accordingly. The highest dose of solifenacin succinate accidentally given to a single patient was 280mg in a 5 hour period, resulting in mental status changes not requiring hospitalization.

In the event of overdosage with solifenacin succinate the patient should be treated with activated charcoal. Gastric lavage may be performed, but vomiting should not be induced.

AVAILABILITY

Solifenacin Succinate (Solifen) 5mg Film-Coated Tablet in Alu/Alu blister pack x 10's, box of 30's.

Solifenacin Succinate (Solifen) 10mg Film-Coated Tablet in Alu/Alu blister pack x 10's, box of 30's.

STORAGE CONDITIONS

Store at temperatures not exceeding 30°C.

Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

Keep out of reach of children.

CAUTION

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA at www.fda.gov.ph.

The patient is advised to seek immediate medical attention at the first sign of adverse drug reaction.

REGISTRATION NUMBER:

Solifenacin Succinate (Solifen) 5mg Tablet: DR-XY48356
Solifenacin Succinate (Solifen) 10mg Tablet: DR-XY48357

DATE OF FIRST AUTHORIZATION

Solifenacin Succinate (Solifen) 5mg Tablet:

Initial: 15 September 2022

Solifenacin Succinate (Solifen) 10mg Tablet:

Initial: 15 September 2022

DATE OF REVISION: 26 September 2022

Please read the contents carefully before use.
This package insert is continually updated from time to time.



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The Getz Group,
USA.
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PHP-200016215

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Imported by: Getz Pharma (Phils.) Inc., 2/F Tower 1, The Rockwell Business Center, Ortigas Ave., Pasig City, Philippines.