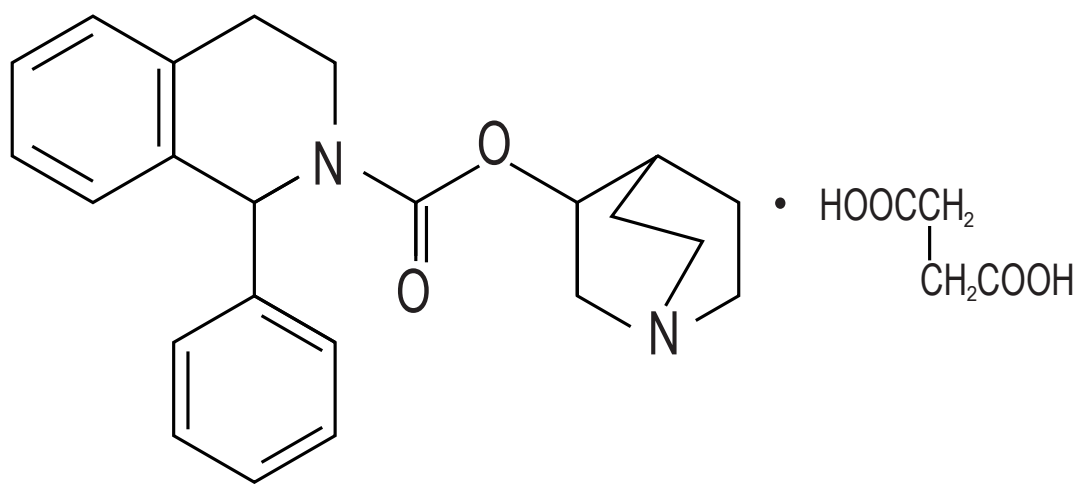
Solif®
(Solifenacin Succinate)
Tablets B.P.

سولِف ۵ ملی گرام ۱۰ ملی گرام
(سولیفیناسِن سکسینیٹ) ٹیبلٹس بی۔پی۔

DRUG DESCRIPTION
SOLIF (Solifenacin Succinate) is a muscarinic receptor antagonist and is available as SOLIF Tablets for oral administration. Chemically solifenacin succinate is (1S)-(3R)-1-azabicyclo [2.2.2] oct-3-yl3,4- dihydro-1 -phenyl -2 (1H) -iso-quinolinecarboxylate(1:1) having an empirical formulaa $C_{23}H_{26}N_2O_2.C_4H_6O_4$.

Structure:



COMPOSITION
Solif 5mg Tablets:
Each film-coated tablet contains:
Solifenacin Succinate B.P. 5mg

Solif 10mg Tablets:
Each film-coated tablet contains:
Solifenacin Succinate B.P. 10mg

INDICATIONS
SOLIF (solifenacin succinate) is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency.

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 succinate to healthy volunteers, peak plasma levels (Cmax) 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 succinate tablets, respectively. The absolute bioavailability of solifenacin is approximately 90%, and plasma concentrations of solifenacin are proportional to the dose administered.
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 mean steady-state distribution volume 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. One pharmacologically active metabolite (4R-hydroxy solifenacin), occurring at low concentrations and unlikely to contribute significantly to clinical activity, and three pharmacologically inactive metabolites (N-glucuronide and the N-oxide and 4R-hydroxy-N-oxide of solifenacin) have been found in human plasma after oral dosing.
Excretion: Following the administration of 10 mg of 14C-solifenacin succinate to healthy volunteers, 69.2% of the radioactivity was recovered in the urine and 22.5% in the feces over 26 days. Less than 15% (as mean value) of the dose was recovered in the urine as intact solifenacin. The major metabolites identi-

fied in urine were N-oxide of solifenacin, 4R-hydroxy solifenacin and 4R-hydroxy-N-oxide of solifenacin and in feces 4R-hydroxy solifenacin. The elimination half-life of solifenacin following chronic dosing is approximately 45-68 hours.

DRUG INTERACTIONS

Drug-Drug Interactions: Do not exceed a 5 mg daily dose of Solifenacin succinate when administered with therapeutic doses of ketoconazole or other potent CYP3A4 inhibitors

PRECAUTIONS

Bladder Outflow Obstruction: SOLIF (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: SOLIF (solifenacin succinate), like other anticholinergics, should be used with caution in patients with decreased gastrointestinal motility. Controlled Narrow-Angle Glaucoma: SOLIF (solifenacin succinate) should be used with caution in patients being treated for narrow-angle glaucoma. Reduced Renal Function: SOLIF (solifenacin succinate) should be used with caution in patients with reduced renal function. Doses of SOLIF greater than 5 mg are not recommended in patients with severe renal impairment (CLcr < 30 mL/min).

SIDE EFFECTS

Percentages of Patients with Treatment-emergent Adverse Events Exceeding Placebo Rate and Reported by 1% or More Patients for Combined Pivotal Studies

SYSTEM ORGAN CLASS MedDRA Preferred Term	Placebo (%)	Solefinacin 5mg (%)	Solefinacin 10mg (%)
Number of Patients	1216	578	1233
Number of Patients with Treatment emergent AE	634	265	773
GASTROINTESTINAL DISORDERS			
Dry Mouth	4.2	10.9	27.6
Constipation	2.9	5.4	13.4
Nausea	2.0	1.7	3.3
Dyspepsia	1.0	1.4	3.9
Abdominal Pain Upper	1.0	1.9	1.2
Vomiting NOS	0.9	0.2	1.1
INFECTIONS AND INFESTATIONS			
Dizziness	1.8	1.9	1.8
EYE DISORDERS			
Vision Blurred	1.8	3.8	4.8
Dry Eyes NOS	0.6	0.3	1.6
RENAL AND URINARY DISORDERS			
Urinary Retention	0.6	0	1.4
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS			
Edema Lower Limb	0.7	0.3	1.1
Fatigue	1.1	1.0	2.1
PSYCHIATRIC DISORDERS			
Depression NOS	0.8	1.2	0.8
RESPIRATORY, THORACIC AND MEDIA STINAL DISORDERS			
Cough	0.2	0.2	1.1
VASCULAR DISORDERS			
Hypertension NOS	0.6	1.4	0.5

USE IN SPECIAL POPULATION

Pregnancy: Pregnancy Category-C: Nursing Mothers: It is not known wheth-

er solifenacin is excreted in human milk. Because many drugs are excreted in human milk, solifenacin succinate should not be administered during nursing. Pediatric Use: The safety and effectiveness of solifenacin succinate in pediatric patients have not been established. Geriatric Use: In placebo controlled clinical studies, similar safety and effectiveness were observed between older (623 patients ≥ 65 years and 189 patients ≥ 75 years) and younger patients (1188 patients < 65 years).

OVERDOSE

In the event of overdose with solifenacin succinate treat with gastric lavage and appropriate supportive measures. ECG monitoring is also recommended.

CONTRAINDICATIONS

Solifenacin succinate 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.

DOSAGE AND ADMINISTRATION

The recommended dose of SOLIF (solifenacin succinate) is 5mg once daily. If the 5 mg dose is well tolerated, the dose may be increased to 10 mg once daily. SOLIF (solifenacin succinate) should be taken with liquids and swallowed whole. SOLIF (solifenacin succinate) can be administered with or without food.

PRESENTATION

SOLIF 5mg tablets are available in Alu-Alu blister pack of 1x10's. SOLIF 10mg tablets are available in Alu-Alu blister pack of 2x15's.

INSTRUCTIONS

Dosage as directed by the physician. Store below 30°C.Protect from heat,light and moisture. For oral use only. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم پر رکھیں۔

روشنی، گرمی اور نمی سے محفوظ رکھیں۔ صرف کھانے کے استعمال کیلئے۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں۔

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ISO 9001:2015 ISO 14001:2015 ISO 45001:2018

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