26 cm.

19 cm.

SOFCARE 5 mg Tablet
SOFCARE 10 mg Tablet

Each film coated tablet contains:
Solifenacin succinate 5 mg
Solifenacin succinate 10 mg

PRODUCT DESCRIPTION:
5 mg: Light yellow, round, biconvex, film coated tablet with engraved 5 on one side and plain on the other side
10 mg: Light pink, oblong, biconvex, film coated tablet with engraved 10 on one side and plain on the other side

MECHANISM OF ACTION:
Pharmacology
Solifenacin is a competitive, specific cholinergic-receptor antagonist.
The urinary bladder is innervated by parasympathetic cholinergic nerves. Acetylcholine contracts the detrusor smooth muscle through muscarinic receptors of which the M3 subtype is predominantly involved. Solifenacin is a competitive inhibitor of the muscarinic M3 subtype receptor. In addition, Solifenacin showed to be a specific antagonist for muscarinic receptors by displaying low or no affinity for various other receptors and ion channels tested.
Pharmacokinetics
Absorption
After intake of Solifenacin, maximum Solifenacin plasma concentrations (C_{max}) are reached after 3 to 8 hours. The t_{max} is independent of the dose. The C_{max} and area under the curve (AUC) increase in proportion to the dose between 5 to 40 mg. Absolute bioavailability is approximately 90%.
Food intake does not affect the C_{max} and AUC of Solifenacin.
Distribution
The apparent volume of distribution of Solifenacin following intravenous administration is about 600 L. Solifenacin is to a great extent (approximately 98%) bound to plasma proteins, primarily α_1-acid glycoprotein.
Biotransformation
Solifenacin is extensively metabolized by the liver, primarily by cytochrome P450 3A4 (CYP3A4). However, alternative metabolic pathways exist, that can contribute to the metabolism of Solifenacin. The systemic clearance of Solifenacin is about 9.5 L/h and the terminal half life of Solifenacin is 45-68 hours. After oral dosing, one pharmacologically active (4*R*-hydroxy Solifenacin) and three inactive metabolites (*N*-glucuronide, *N*-oxide and 4*R*-hydroxy-*N*-oxide of Solifenacin) have been identified in plasma in addition to Solifenacin.
Elimination
After a single administration of 10 mg [14C-labelled]-Solifenacin, about 70% of the radioactivity was detected in urine and 23% in feces over 26 days. In urine, approximately 11% of the radioactivity is recovered as unchanged active substance; about 18% as the *N*-oxide metabolite, 9% as the 4*R*-hydroxy-*N*-oxide metabolite and 8% as the 4*R*-hydroxy metabolite (active metabolite).
Linearity/ non-linearity
Pharmacokinetics are linear in the therapeutic dose range.
Other special populations
Elderly
No dosage adjustment based on patient age is required. It have been shown that the exposure to Solifenacin, expressed as the AUC, after administration of Solifenacin succinate (5 mg and 10 mg once daily) was similar in healthy elderly subjects (aged 65 through 80 years) and healthy young subjects (aged less than 55 years). The mean rate of absorption expressed as t_{max} was slightly slower in the elderly and the terminal half-life was approximately 20% longer in elderly subjects. These modest differences were considered not clinically significant.
Children and adolescents
The pharmacokinetics of Solifenacin have not been established on children and adolescents.
Gender
The pharmacokinetics of Solifenacin are not influence by gender.
Race
The pharmacokinetics of Solifenacin are not influence by race.
Renal impairment
The AUC and C_{max} of Solifenacin in mild and moderate renally impaired patients, was not significantly different from that found in healthy volunteers. In patients with severe renal impairment (creatinine clearance ≤ 30 mL/min) exposure to Solifenacin was significantly greater than in the controls, with increases in C_{max} of about 30%, AUC of more than 100% and $t_{½}$ of more than 60%. A statistically significant relationship was observed between creatinine clearance and Solifenacin clearance.
Pharmacokinetics in patients undergoing hemodialysis have not been studied.
Hepatic impairment
In patients with moderate hepatic impairment (Child-Pugh score of 7 to 9) the C_{max} is not affected, AUC increased with 60% and $t_{½}$ doubled. Pharmacokinetics of Solifenacin in patients with severe hepatic impairment have not been studied.

INDICATION:
Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome.

DOSAGE AND ADMINISTRATION:
Oral
Posology
Adults, including the elderly
The recommended dose is 5 mg Solifenacin succinate once daily. If needed, the dose may be increased to 10 mg Solifenacin succinate once daily.
Pediatric population
The safety and efficacy of Solifenacin succinate in children have not yet been established. Therefore, Solifenacin succinate should not be used in children.
Patients with renal impairment
No dose adjustment is necessary for patients with mild to moderate renal impairment (creatinine clearance > 30 mL/min). Patients with severe renal impairment (creatinine clearance ≤ 30 mL/min) should be treated with caution and receive no more than 5 mg 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 5 mg once daily.
Potent inhibitors of cytochrome P450 3A4
The maximum dose of Solifenacin succinate should be limited to 5 mg when treated simultaneously with Ketoconazole or therapeutic doses of other potent CYP3A4-inhibitors e.g. Ritonavir, Nelfinavir, Itraconazole.
Method of administration
Solifenacin succinate should be taken orally and should be swallowed whole with liquids. It can be taken with or without food.

WARNING AND PRECAUTION:
Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment with Solifenacin succinate. If urinary tract infection is present, an appropriate antibacterial therapy should be started.
Solifenacin succinate should be used with caution in patients with:
- clinically significant bladder outflow obstruction at risk of urinary retention
- gastrointestinal obstructive disorders
- risk of decreased gastrointestinal motility
- severe renal impairment (creatinine clearance ≤ 30 mL/min), and doses should not exceed 5 mg for these patients
- moderate hepatic impairment (Child-Pugh score of 7 to 9), and doses should not exceed 5 mg for these patients
- concomitant use of a potent CYP3A4 inhibitor, e.g. Ketoconazole
- hiatus hernia/gastroesophageal reflux and/or who are concurrently taking medicinal products (such as Bisphosphonates) that can cause or exacerbate esophagitis
- autonomic neuropathy

Safety and efficacy have not yet been established in patients with a neurogenic cause for detrusor overactivity.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.
Angioedema with airway obstruction has been reported in some patients on Solifenacin succinate. If angioedema occurs, Solifenacin succinate should be discontinued and appropriate therapy and/or measures should be taken.
Anaphylactic reaction has been reported in some patients treated with Solifenacin succinate. In patients who develop anaphylactic reactions, Solifenacin should be discontinued and appropriate therapy and/or measures should be taken.
The maximum effect of Solifenacin succinate can be determined after 4 weeks at the earliest.

Warning^:
This preparation contains Sodium metabisulfite that may cause serious allergic type reactions in certain susceptible patients. Do not use if known to be hypersensitive to bisulfites.

PREGNANCY AND LACTATION:
Pregnancy
No clinical data are available from women who became pregnant while taking Solifenacin. The potential risk for humans is unknown. Caution should be exercised when prescribing to pregnant women.
Breastfeeding
No data on the excretion of Solifenacin in human milk are available. The use of Solifenacin should therefore be avoided during breastfeeding.

SIDE EFFECT:
Summary of the safety profile
Due to the pharmacological effect of Solifenacin, Sofcare may cause anticholinergic undesirable effects of (in general) mild or moderate severity. The frequency of anticholinergics undesirable effects is dose related. The most common adverse reaction with Sofcare is dry mouth.

Tabulated list of adverse reactions

MeDdra System Organ Class	Very common	Common	Uncommon	Rare	Very rare	Not known
Infections and infestations			Urinary tract infection, Cystitis			
Immune system disorders						Anaphylactic reaction*
Metabolism and nutrition disorders						Decreased appetite* Hyperkalemia
Psychiatric disorders					Hallucinations* Confusional state*	Delirium*
Nervous system disorders			Somnolence Dysgeusia	Dizziness* Headache*		
Eye disorders		Blurred vision	Dry eyes			Glaucoma*
Cardiac disorders						Torsade de Pointes* Electrocardiogram QT prolonged* Atrial fibrillation* Palpitations* Tachycardia*
Respiratory, thoracic and mediastinal disorders			Nasal dryness			Dysphonia*
Gastrointestinal disorders	Dry mouth	Constipation Nausea Dyspepsia Abdominal pain	Gastroesophageal reflux diseases Dry throat	Colonic obstruction Fecal impaction, Vomiting*		Ileus* Abdominal discomfort*
Hepatobiliary disorders						Liver disorder* Liver function test abnormal*
Skin and subcutaneous tissue disorders			Dry skin	Pruritus*, Rash*	Eythema multiforme*, Urticaria*, Angioedema*	Exfoliative dermatitis*
Musculoskeletal and connective tissue disorders						Muscular weakness*
Renal and urinary disorders			Difficulty in micturition	Urinary retention		Renal impairment*
General disorders and administration site conditions			Fatigue Peripheral edema			

*observed post-marketing

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Since Solifenacin, like other anticholinergics may cause blurred vision, and, uncommonly, somnolence and fatigue, the ability to drive and use machines may be negatively affected.

CONTRAINDICATION:
Solifenacin is contraindicated in patients with urinary retention, severe gastro-intestinal condition (including toxic megacolon), myasthenia gravis or narrow-angle glaucoma and in patients at risk for these conditions.
- Patients hypersensitive to the active substance or to any of the excipients
- Patients undergoing hemodialysis
- Patients with severe hepatic impairment
- Patients with severe renal impairment or moderate hepatic impairment and who are on treatment with a potent CYP3A4 inhibitor, e.g. Ketoconazole

DRUG INTERACTION:
Pharmacological interactions
Concomitant medication with other medicinal products with anticholinergic properties may result in more pronounced therapeutic effects and undesirable effects. An interval of approximately one week should be allowed after stopping treatment with Solifenacin succinate, before commencing other anticholinergic therapy. The therapeutic effect of Solifenacin may be reduced by concomitant administration of cholinergic receptor agonists.
Solifenacin can reduce the effect of medicinal products that stimulate the motility of the gastrointestinal tract, such as Metoclopramide and Cisapride.
Pharmacokinetic interactions
Solifenacin is unlikely to alter the clearance of drugs metabolized by CYP1A1/2, 2C9, 2C19, 2D6, or 3A4 enzymes.
Effect of other medicinal products on the pharmacokinetics of Solifenacin
Solifenacin is metabolized by CYP3A4. Simultaneous administration of Ketoconazole (200 mg/day), a potent CYP3A4 inhibitor, resulted in a two-fold increase of the AUC of Solifenacin, while Ketoconazole at a dose of 400 mg/day resulted in a three-fold increase of the AUC of Solifenacin. Therefore, the maximum dose of Solifenacin succinate should be restricted to 5 mg, when used simultaneously with Ketoconazole or therapeutic doses of other potent CYP3A4 inhibitors (e.g. Ritonavir, Nelfinavir, Itraconazole). Simultaneous treatment of Solifenacin and a potent CYP3A4 inhibitor is contraindicated in patients with severe renal impairment or moderate hepatic impairment.
The effects of enzyme induction on the pharmacokinetics of Solifenacin and its metabolites have not been studied as well as the effect of higher affinity CYP3A4 substrates on Solifenacin exposure. Since Solifenacin is metabolized by CYP3A4, pharmacokinetic interactions are possible with other CYP3A4 substrates with higher affinity (e.g. Verapamil, Diltiazem) and CYP3A4 inducers (e.g. Rifampicin, Phenytoin, Carbamazepine).
Effect of Solifenacin on the pharmacokinetics of other medicinal products
Oral Contraceptives
Intake of Solifenacin succinate showed no pharmacokinetic interaction of Solifenacin on combined oral contraceptives (Ethinylestradiol/Levonorgestrel).
Warfarin
Intake of Solifenacin succinate did not alter the pharmacokinetics of *R*-warfarin or *S* warfarin or their effect on prothrombin time.
Digoxin
Intake of Solifenacin succinate showed no effect on the pharmacokinetics of Digoxin.

OVERDOSE AND TREATMENT:
Symptoms
Overdosage with Solifenacin succinate can potentially result in severe anticholinergic effects. The highest dose of Solifenacin succinate accidentally given to a single patient was 280 mg in a 5 hour period, resulting in mental status changes not requiring hospitalization.
Treatment
In the event of overdose with Solifenacin succinate the patient should be treated with Activated charcoal. Gastric lavage is useful if performed within 1 hour, but vomiting should not be induced.
As for other anticholinergics, symptoms can be treated as follows:
- Severe central anticholinergic effects such as hallucinations or pronounced excitation: Treat with Physostigmine or Carbachol.
- Convulsions or pronounced excitation: Treat with benzodiazepines.
- Respiratory insufficiency: Treat with artificial respiration.
- Tachycardia: Treat with beta-blockers.
- Urinary retention: Treat with catheterization.
- Mydriasis: Treat with Pilocarpine eye drops and/or place patient in dark room.
- As with other antimuscarinics, in case of overdosing, specific attention should be paid to patients with known risk for QT-prolongation (i.e. hypokalemia, bradycardia and concurrent administration of medicinal products known to prolong QT-interval) and relevant pre-existing cardiac diseases (i.e. myocardial ischemia, arrhythmia, congestive heart failure).

STORAGE:
Store at temperature of not more than 30°C.

DOSAGE FORM AND PACKAGING AVAILABLE:
5 mg Tablet, Blister 3x10's
10 mg Tablet, Blister 3x10's

DATE OF REVISION:
March 19, 2024

Manufactured by:
UNISON LABORATORIES CO., LTD.
39 Moo 4, Klong Udomcholjorn, Muang Chachoengsao,
Chachoengsao 24000 Thailand

C-MY/190324-06 (AR).
(Vesicare Tab_MY, 8/16; ^NPRA_DRGD p. 500)
ISMY 0081

Print: Fit To Page

SOFCARE 5 mg_Insert_Front_ISMY 0081_By...DA 20/03/2024

PM Specification	Product	Code No.	Dimension	Packaging Type	Thickness
	SOFCARE 5/10 mg	ISMY 0081	W 26 x L 19 cm.	Wood Free Paper (กระดาษปอนด์)	60 g (0.08 mm.)

Designed by: (PDM, ASPD, PDC-M, PDC-A, PDO-M, PDO-A) | Checked by: (PDM/ASPD) | Approved by: (MD (Only Pattern and Colors))

Approved by: PLC: (Date) | LRA: (Date) | IRA: (Date) | QCC-PM: (Date) | CUSTOMER/SALES DEPT.: (Date)