SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product:

Solimax-Q (Solifenacin Succinate) film coated Tablet 5mg.

2. Qualitative and Quantitative Composition

Each film coated tablet contains:
Solifenacin Succinate 5mg e.q. Solifenacin 3.8mg

Excipient(s) with known effect: lactose monohydrate

For a full list of excipients, see section 6.1.

3. Pharmaceutical form:

Film coated tablets
Yellow round biconvex film coated tablet plain from both sides.

4. Clinical particulars

4.1. Therapeutic indications:

Indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency.

4.2. Posology and method of Administration

4.2.1. Posology

Adults and Elderly.
The recommended dose is 5mg once daily for adults including the elderly.
If needed, the dose may be increased to 10mg solifenacin succinate once daily

Paediatric population
The safety and efficacy of Vesicare in children have not yet been established Therefore, Vesicare 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

The maximum dose of Vesicare should be limited to 5 mg when treated simultaneously with ketoconazole or therapeutic doses of other potent CYP3A4- inhibitors e.g. ritonavir, nelfinavir,itraconazole

4.2.2. Method of administration:

Solimax-Q should be taken with liquids and swallowed whole.
Solimax-Q can be administered with or without food.

4.3. Contraindications:

Solifenacin is contraindicated in patients with urinary retention, severe gastro-intestinal condition (including toxic megacolon) uncontrolled narrow-angle glaucoma, myasthenia gravis and in patients who have demonstrated hypersensitivity to the drug substance or other components of the product

4.4. Special warnings and Precautions for Use

Bladder Outflow Obstruction:
Solimax-Q, 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:
Solimax-Q, like other anticholinergics, should be used with caution in patients with decreased gastrointestinal motility.

Controlled Narrow-Angle Glaucoma:
Solimax-Q should be used with caution in patients being treated for narrow-angle glaucoma.

Reduced Renal Function:
Solimax-Q should be used with caution in patients with reduced renal function. Doses of Solimax-Q greater than 5 mg are not recommended in patients with severe renal impairment
(CLcr < 30 mL/min).

Reduced Hepatic Function:
Solimax-Q should be used with caution in patients with reduced hepatic function. Doses of Solimax-Q greater than 5 mg are not recommended in patients with moderate hepatic impairment. Solimax-Q is not recommended for patients with severe hepatic impairment.

Drug-Drug Interaction:
Do not exceed a 5 mg daily dose of Solimax-Q 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 Solimax-Q for patients with a known history of QT prolongation or patients who are taking medications known to prolong the QT interval.
Anaphylactic reaction has been reported in some patients treated with solifenacin succinate. In patients who develop anaphylactic reactions, solifenacin succinate should be discontinued and appropriate therapy and/or measures should be taken.
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5. Interaction with other medicinal products and other forms of interaction:

Drugs Metabolized by Cytochrome P450:
At therapeutic concentrations, solifenacin does not inhibit CYP1A1/2, 2C9, 2C19, 2D6, or 3A4 derived from human liver microsomes.

CYP 3A4 Inhibitors:
In vitro studies have demonstrated that at therapeutic concentrations, solifenacin does not inhibit CYP1A1/2, 2C9, 2C19, 2D6, or 3A4 derived from human liver microsomes. Therefore, solifenacin is unlikely to alter the clearance of drugs metabolised by these CYP enzymes.

Ketoconazole Interaction Study:
Following the administration of 10 mg of Solifenacin in the presence of 400 mg of ketoconazole, a potent inhibitor of CYP3A4, the mean Cmax 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.

Oral Contraceptives:
In the presence of solifenacin there are no significant changes in the plasma concentrations of combined oral contraceptives (ethinyl estradiol/levogestrel).

Warfarin:
Solifenacin has no significant effect on the pharmacokinetics of *R*-warfarin or *S*-warfarin.

Digoxin:

Solifenacin had no significant effect on the pharmacokinetics of digoxin

4.6. Fertility, pregnancy and breastfeeding:

Pregnancy:
Pregnancy Category C.

Breastfeeding:
It is not known whether solifenacin is excreted in human milk. In mice, solifenacin and/or its metabolites was excreted in milk, and caused a dose dependent failure to thrive in neonatal mice Because many drugs are excreted in human milk, Solimax-Q should not be administered during nursing.

Fertility:
There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Solimax-Q should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

4.7. Effects on ability to drive and use machines:

Patients should be informed that antimuscarinic agents such as Solimax-Q have been associated with blurred vision and uncommonly, somnolence and fatigue . Because Patients should be advised that their ability to drive and use machines may be negatively affected.

4.8. Undesirable effects:

Solimax-Q has been evaluated for safety in 1811 patients in randomized, placebo-controlled trials. 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 Solimax-Q 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 overall rate of serious adverse events in the double -blind trials was 2%.

4.9. Overdose

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 catheterisation.
- 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. hypokalaemia, bradycardia and concurrent administration of medicinal products known to prolong QT-interval) and relevant pre-existing cardiac diseases (i.e. myocardial ischaemia, arrhythmia, congestive heart failure).

5.0. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Urological, ATC code: G04B D08.

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.

5.2. Pharmacokinetic properties

Absorption	
Oral bioavailability	approximately 90%
Food effect	There is no significant effect of food on the pharmacokinetics of solifenacin.
Distribution	
Volume of distribution (mean)	is about 600L
Plasma protein binding	Solifenacin is approximately 98% (in vivo) bound to human plasma proteins, principally to a_1-acid glycoprotein.
Tissue distribution	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 metabolic routes of solifenacin are through N oxidation of the quinuclidin ring and 4R hydroxylation of tetrahydroisoquinoline ring.

Elimination	
General note	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.
Elimination half life	45 - 68 hours
Mean systemic clearance (Cl/F)	Less than 15% (as mean value) of the dose was recovered in the urine as intact solifenacin.
% of dose excreted in urine	69.2 %
% of dose excreted in faeces	22.5 %

5.3. Preclinical safety data

Non-clinical data have not revealed significant hazards for humans, based on standard studies of safety pharmacology, repeated-dose toxicity, Geno toxicity, carcinogenic potential and reproductive toxicity. Effects in non-clinical studies were observed only at exposures sufficiently in excess of the maximum human exposure to be of little clinical relevance.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Lactose Monohydrate HMS ,Maize Starch ,Hydroxy Propyl methy cellulose (HPMC 2910 ES) ,Magnesium stearate ,Vivacoat (Vivacoat PM-1P-0000 White) ,Iron oxide yellow (Sicovit Yellow) and Polyethylene Glycol 6000

6.2. Incompatibilities:

Not applicable.

6.3. Shelf life:

24 months

6.4. Special precautions for storage:

Store below 30°C. Protect from heat, light and moisture.

6.5. Nature and contents ofcontainer:

The product is packed in ALU/ALU blister. Each blister contains ten tablets and each unit carton contains two blisters (10's, 30's, 90's & 100's tablets/pack).

6.6. Special precautions for disposal:

No special requirements.

7. Marketing Authorisation Holder and manufacturing site addresses

Marketing authorization holder:
Q PHARMA DMCC ,ADDRESS: Unit No: 2681 DMCC Business Centre Level No. 1 Dubai P.O BOX 119023, UAE COUNTRY> UAE

Manufacturing site address:
Dynatis Pakistan (Pvt) Ltd Address: Plot no. 710, Sunder Industrial Estate, Lahore. Country:. Pakistan

Marketing Authorization Number(s):
CTD 10050

8. Date of first registration
26/05/2023

9. Date of revision of the text:
13/09/2023

10. Dosimetry:
Not Applicable

11. Instructions for Preparation of Radiopharmaceuticals:
Not Applicable