SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG PRODUCT

SOLIFEN 5 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:
Solifenacin succinate.....5 mg

3. PHARMACEUTICAL FORM

White, oblong, biconvex shaped film coated tablet plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and Method of Administration

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

Adults:
The recommended dose of SOLIFEN (Solifenacin Succinate) 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 (CLcr >30mL/min). Patients with severe renal impairment (CLcr<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.

4.3 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.

4.4 Special warnings and special precautions for use

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 (CL_{cr} <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 hernia/ 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.

4.5 Interaction with other medicaments

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).

4.6 Uses in Pregnancy and Lactation

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.

4.7 Effects on ability to drive and operate 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.

4.8 Undesirable effects

Very common: Dry mouth

Common: Constipation, nausea, dyspepsia, abdominal pain, blurred vision.

Uncommon: Gastroesophageal reflux diseases, dry throat, urinary tract infection, cystitis, somnolence, dysgeusia, dry eyes, fatigue, peripheral edema, nasal dryness, dry skin, difficulty in micturation.

Rare: Colonic obstruction, fecal impaction, urinary retention.

4.9 Overdosage

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacokinetic Properties

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.

5.2 Pharmacodynamic properties

Mechanism of Action:
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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Pharmatose DCL 11 (Anhydrous Lactose), Avicel PH-102 (Microcrystalline Cellulose), Pregelatinized Starch, Magnesium Stearate, Opadry White YS-1-7027.

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

2 years
The expiration dates refers to the product correctly stored in the required conditions.

6.4 Special precautions for storage

- Store below 30°C.
- Protect from sunlight & moisture.

6.5 Nature and contents of container

SOLIFEN 5 mg Tablets are available in Alu-Alu blister pack of 3 x 10's tablets in a unit carton along with the patient information leaflet.

6.6 Instructions for use/handling

Keep out of reach of children.
To be dispensed on prescription only.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

Getz Pharma (Private) Limited
29-30/27, Korangi Industrial Area Karachi-74900, Pakistan
Tel: (92-21) 111-111-511
Fax: (92-21) 5057592

8. DRUG PRODUCT MANUFACTURER

Getz Pharma (Private) Limited
29-30/27, Korangi Industrial Area Karachi-74900, Pakistan
Tel: (92-21) 111-111-511
Fax: (92-21) 5057592

9. NAFDAC REGISTRATION NUMBER

B4-9699.