NEW ZEALAND DATA SHEET

SOLIFENACIN VIATRIS

1. Product Name

Solifenacin Viatris 5 mg and 10 mg, film coated tablet.

2. Qualitative and Quantitative Composition

Each film coated tablet contains 5 mg or 10 mg of solifenacin succinate.

Excipients of known effect: Contains sugars as lactose.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Solifenacin Viatris 5 mg tablets: yellow film-coated, round, biconvex tablet debossed with M on one side of the tablet and SF over 5 on the other side.

Solifenacin Viatris 10 mg tablets: pink film-coated, round, biconvex tablet debossed with M on one side of the tablet and SF over 10 on the other side.

4. Clinical Particulars

4.1 Therapeutic indications

Solifenacin Viatris is indicated for the treatment of unstable bladder with symptoms of increased urinary urgency, frequent micturition, and/or urge incontinence.

4.2 Dose and method of administration

Dose

Adults

The recommended dose is 5 mg solifenacin succinate once daily. If needed, the dose may be increased to a maximum of 10 mg solifenacin succinate once daily.

Special populations

Children

Safety and effectiveness in children has not yet been established. Solifenacin Viatris is not recommended for use 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 not more than 5 mg once daily. Pharmacokinetics in patients undergoing haemodialysis has not been studied.

Patients with hepatic impairment

No dose adjustment is necessary for patients with mild hepatic impairment. Patients with moderate hepatic impairment (Child-Pugh B) should be treated with caution and receive not more than 5 mg once daily. Solifenacin Viatris is contraindicated in patients with severe hepatic impairment (Child-Pugh C).

Strong inhibitors of cytochrome P450 3A4

The maximum dose of Solifenacin Viatris should be limited to 5 mg when treated simultaneously with ketoconazole or therapeutic doses of other strong CYP3A4-inhibitors e.g. ritonavir, nelfinavir, itraconazole, cyclosporin, macrolide antibiotics (see section 4.5).

Method of administration

Solifenacin Viatris should be taken orally and should be swallowed whole with liquids. It can be taken with or without food, as is convenient.

4.3 Contraindications

Solifenacin Viatris is contraindicated in:

- patients with hypersensitivity to solifenacin or to any of the excipients
- patients with urinary retention
- patients with uncontrolled narrow angle glaucoma
- myasthenia gravis
- severe gastro-intestinal condition (including toxic megacolon and gastric retention)
- patients undergoing haemodialysis (see section 4.2)
- patients with severe hepatic impairment (see sections 4.2)
- patients with severe renal impairment or moderate hepatic impairment and on treatment with a strong CYP3A4 inhibitor e.g. ketoconazole (see section 4.5)

4.4 Special warnings and precautions for use

Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment with solifenacin. If urinary tract infection is present, an appropriate antibacterial therapy should be started.

Solifenacin Viatris 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
- in patients being treated for narrow-angle glaucoma
- hiatus/hernia/gastro-oesophagal reflux and/or who are concurrently taking medicinal products that can cause or exacerbate oesophagitis
- Autonomic neuropathy
- Known risk factors for QT prolongation, such as pre-existing long QT syndrome and hypokalaemia.
- concomitant use of a strong CYP3A4 inhibitor, e.g. ketoconazole (see sections 4.2 and 4.5)

Angioedema

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

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.

QT prolongation and Torsade de pointes

QT prolongation and Torsade de pointes have been observed in patients with known risk factors for these conditions.

As with other drugs in this class, caution is advised in patients with known risk factors for QT-prolongation (i.e. history of QT prolongation, long QT syndrome, hypokalaemia, bradycardia, coadministration of drugs known to prolong the QT interval) and relevant pre-existing cardiac diseases (i.e. myocardial ischaemia, arrhythmia, congestive heart failure) (see section 5.1, section 4.5 and section 4.8).

Appropriate investigations (e.g. ECG) should be considered in patients with risk factors for QTc prolongation.

Use in hepatic impairment

Doses of Solifenacin Viatris greater than 5 mg are not recommended in patients with moderate hepatic impairment (Child-Pugh B). Solifenacin Viatris is contraindicated in patients with severe hepatic impairment (Child-Pugh C) (see Section 4.3).

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.

Use in renal impairment

Solifenacin Viatris should be used with caution in patients with reduced renal function. Solifenacin Viatris should be used with caution in patients with severe renal impairment (creatinine clearance < 30 mL/min), and doses should not exceed 5 mg for these patients.

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 haemodialysis have not been studied.

Use in the elderly

No dosage adjustment based on patient age is required. Studies in the elderly have shown that C_{max}, AUC and $t_{1/2}$ values were 20-25% higher as compared to the younger volunteers (18-55 years). No overall differences were observed in the safety of solifenacin between older and younger patients treated for 4 to 12 weeks with 5 to 10 mg solifenacin succinate.

Paediatric use

Safety and effectiveness in children have not yet been established. Therefore, Solifenacin Viatris should not be used in children.

Effects on laboratory tests

No data available.

4.5 Interaction with other medicines and other forms of interaction

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 not likely to interact with the CYP mediated metabolism of co-administered drugs.

Effects of other drugs on the pharmacokinetics of solifenacin

In vitro drug metabolism studies have shown that solifenacin is a substrate of CYP3A4. Inducers or inhibitors of CYP3A4 may alter solifenacin pharmacokinetics. 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 Viatris should be restricted to 5 mg, when used simultaneously with ketoconazole or therapeutic doses of other potent CYP3A4 inhibitors (e.g. ritonavir, nelfinavir, itraconazole, cyclosporin, macrolide antibiotics).

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 metabolised 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).

Concomitant medication with other drugs with anticholinergic properties may result in more pronounced therapeutic effects and side effects. An interval of approximately one week should be allowed after stopping treatment with solifenacin, 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 drugs that stimulate the motility of the gastro-intestinal tract, such as metoclopramide and cisapride.

Effects of solifenacin on the pharmacokinetics of other medications

Oral Contraceptives:
Intake of solifenacin showed no pharmacokinetic interaction of solifenacin on combined oral contraceptives (ethinyl oestradiol/levonorgestrel, both CYP3A4 substrates).

Warfarin:
Intake of solifenacin did not alter the pharmacokinetics of *R*-warfarin (substrate for CYP3A4) or *S*-warfarin (substrate for CYP2C9) or their effect on prothrombin time.

Digoxin:
Intake of solifenacin showed no effects on the pharmacokinetics of digoxin.

Medicines which prolong the QT/QTc interval
There is no satisfactory information on the concurrent use of solifenacin succinate with medicines known to prolong the QT/QTc interval. In the absence of such information on these combinations the potential risk of pathological QT/QTc prolongation resulting in arrhythmias cannot be ruled out.

Medicines known to prolong the QT/QTc interval include: erythromycin, quinidine, procainamide, disopyramide, sotalol, amiodarone, cisapride, fluconazole, amitriptyline, haloperidol, chlorpromazine, thioridazine, pimozide and droperidol.

4.6 Fertility, pregnancy and lactation

Pregnancy (category B3)

Solifenacin (and/or its metabolites) has been shown to cross the placenta in pregnant mice. No embryotoxicity or teratogenicity was observed in mice treated with 1.2 times exposure at the maximum recommended human dose (MRHD). In one of two studies, higher doses (3.6 times exposure at the MRHD) resulted in maternal toxicity and reduced fetal body weight. No embryotoxic effects were observed in rabbits at up to 1.8 times exposure at the MRHD.

In utero and lactational exposures to maternal doses of solifenacin 3.6 times exposures at the MRHD resulted in reduced peripartum and postnatal survival, reductions in body weight gain, and delayed physical development (e.g. eye opening).

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

Lactation

Solifenacin is excreted into the breast milk of mice. There were no significant adverse effects at 1.2 times exposure at the maximum recommended human dose (MRHD) in a pre- and postnatal study in mice. Pups of female mice treated at 3.6 times exposure at the MRHD showed reduced body weights, postpartum pup mortality or delays in the onset of reflex and physical development during the lactation period. It is expected that solifenacin is excreted in human milk and solifenacin should not be administered during breast-feeding.

Fertility

Solifenacin had no effect on reproductive function, fertility or early embryonic development after oral treatment of male and female mice, which resulted in 13 times exposure at the maximum recommended human dose (MRHD).

4.7 Effects on ability to drive and use machines

Solifenacin, like other anticholinergics may cause blurred vision, and, uncommonly, somnolence and fatigue (see section 4.8), the ability to drive and use machines may be negatively affected.

4.8 Undesirable effects

In a four 12-week double-blind clinical trials 3027 patients were involved (1811 on solifenacin succinate and 1216 on placebo), and approximately 90% of these patients completed the 12-week studies. The most frequent reason for discontinuation due to an adverse event was dry mouth, 1.5%. There were three intestinal serious adverse events in patients all treated with solifenacin succinate 10 mg (one faecal impaction, one colonic obstruction, and one intestinal obstruction).

The table below lists the adverse events reported in ≥1.0% of the patients in the 12 week studies. The relationship to study medication for most of these events is uncertain; many are thought to represent spontaneous events reported by patients with bladder dysfunction (and other concomitant diseases) and are not necessarily causally related to solifenacin succinate.

Numbers (%) of patients with treatment-emergent adverse events reported by 1% or more patients:controlled phase 3 studies (all combined)			
SYSTEM ORGAN CLASS **MedDRA Preferred Term**	**Placebo (%)**	**Solifenacin succinate 5 mg (%)**	**Solifenacin succinate 10 mg (%)**
Number of patients	1216	578	1233
Number of patients with treatment-emergent AE	634	265	773
GASTRO-INTESTINAL 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
Diarrhoea NOS	2.1	0.7	1.9
Vomiting NOS	0.9	0.2	1.1
Abdominal pain upper	1.0	1.9	1.2
Abdominal pain NOS	1.2	0.2	0.6
INFECTIONS AND INFESTATIONS			
Urinary tract infection NOS	2.8	2.8	4.8
Upper respiratory tract infection NOS	2.0	0.9	1.5
Influenza	1.3	2.2	0.9
Sinusitis NOS	1.2	0.9	1.0
Nasopharyngitis	2.7	0.9	1.0
Pharyngitis NOS	1.0	0.3	1.1
Bronchitis	1.1	0.7	0.7
NERVOUS SYSTEM DISORDERS			
Headache	4.5	1.9	1.8
Dizziness	1.8	1.9	1.8
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS			
Arthralgia	2.2	0.7	1.2
Back pain	1.8	0.5	1.5

Neck pain	0.5	0.3	0.1
GENERAL DISORDERS AND ADMINISTRATION SITE DISORDERS			
Fatigue	1.1	1.0	2.1
Oedema lower limb	0.7	0.3	1.1
Influenza like illness	0.5	0.3	0.3
EYE DISORDERS			
Vision blurred	1.8	3.8	4.8
Dry Eye NOS	0.6	0.3	1.6
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS			
Cough	0.2	0.2	1.1
SKIN AND SUBCUTANEOUS TISSUE DISORDERS			
Rash	1.0	0	0.6
RENAL AND URINARY DISORDERS			
Urinary retention	0.6	0	1.4
Dysuria	0.4	0.3	0.7
PSYCHIATRIC DISORDERS			
Insomnia	1.2	0.3	1.1
Depression NOS	0.8	1.2	0.8
VASCULAR DISORDERS			
Hypertension NOS	0.6	1.4	0.5

Adverse reactions reported in the clinical trials with a frequency of occurrence less than 1% are:

Gastrointestinal disorders: flatulence, gastro-oesophageal reflux diseases, throat irritation, eructation, dry throat

Infections and infestations: cystitis

Nervous system disorders: somnolence, dysgeusia, syncope

General disorders and administration site disorders: thirst, suprapubic pain, chest tightness

Renal and urinary disorders: difficulty in micturition, bladder pain, micturition urgency

Respiratory, thoracic and mediastinal disorders: nasal dryness

Investigations: abnormal liver function tests (AST, ALT, GGT), electrocardiogram QT prolonged

Musculoskeletal and connective tissue disorders: peripheral swelling

Skin and subcutaneous tissue disorders: dry skin

Post Marketing Experience:

The following adverse reactions have been spontaneously reported during worldwide post-approval use of solifenacin succinate. The adverse reactions reported are presented below according to System Organ Class and frequency.

Adverse event frequencies are defined as follows: Very common (>10%), common (>1%, < 10%), uncommon (>0.1%, <1%), rare (>0.01%, <0.1%) and very rare (<0.01%), not known (cannot be estimated from the available data).

Cardiac disorders

Very Rare: Torsade de pointes, atrial fibrillation, palpitations, tachycardia

Eye disorders

Very rare: glaucoma

Gastrointestinal disorders

Very rare: Gastro-oesophageal reflux disease, vomiting, ileus

General disorders and administration site conditions

Very rare: Peripheral oedema

Hepatobiliary disorders

Very rare: Liver disorders mostly characterised by abnormal liver function tests (AST, ALT, GGT)

Immune System Disorders

Very rare: Anaphylactic reaction

Investigations

Very rare: Electrocardiogram QT prolonged

Metabolism and nutrition disorders

Very rare: Decreased appetite, hyperkalaemia

Musculoskeletal and connective tissue disorders

Very rare: Muscular weakness

Nervous system disorders

Very rare: Dizziness, headache, somnolence

Psychiatric disorders

Very rare: Hallucinations, delirium, confusion state

Renal and urinary disorders

Very rare: Renal impairment, urinary retention

Respiratory, thoracic and mediastinal disorders

Very rare: dysphonia, nasal dryness

Skin and subcutaneous tissue disorders

Very rare: Pruritus, rash, urticaria, angioedema, erythema multiforme, exfoliative dermatitis

Postmarketing pharmacovigilance data confirmed QT prolongation associated with therapeutic doses of solifenacin succinate in cases with known risk factors (see Section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Overdosage with solifenacin succinate can potentially result in severe anticholinergic effects (headache, dry mouth, dizziness, drowsiness and blurred vision) and should be treated accordingly. 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.

Overdosage with solifenacin succinate may prolong the QTc interval, therefore, in the event of overdosage, ECG monitoring is recommended and standard supportive measures for managing QT prolongation should be adopted.

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), to patients who are concurrently using medicinal products known to prolong QT-interval as no data is available on potential interaction between solifenacin and drugs prone to cause QT-prolongation and to patients with relevant pre-existing cardiac diseases (i.e. myocardial ischaemia, arrhythmia, congestive heart failure).

In the event of overdosage with solifenacin the patient should be treated with activated charcoal. Gastric lavage may be performed, 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.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urinary antispasmodics, ATC code: G04BD08

Mechanism of action

Solifenacin is a competitive, specific cholinergic-receptor antagonist with selectivity for the urinary bladder over salivary glands *in vivo.*

Pharmacodynamic effects

Treatment with solifenacin in doses of 5 mg and 10 mg daily was studied in several double blind, randomised, controlled clinical trials in men and women with overactive bladder. As shown in Table 2 (European studies) and 3 (US studies) below, both the 5 mg and 10 mg doses of solifenacin produced statistically significant improvements in the primary and secondary endpoints compared with placebo. Efficacy was observed within one week of starting treatment and stabilises over a period of 12 weeks. A long-term open label study demonstrated that efficacy was maintained for at least 12 months. After 12 weeks of treatment approximately 50% of patients suffering from incontinence before treatment were free of incontinence episodes, and in addition 35% of patients achieved a micturition frequency of less than 8 micturitions per day. Treatment with solifenacin also showed benefit on a number of Quality of Life measures, such as general limitations, emotions, symptom severity, severity measures and sleep/energy.

Table 2: Results (pooled data) of two controlled Phase 3 European studies with a treatment duration of 12 weeks

	Placebo	**Solifenacin succinate 5 mg o.d.**	**Solifenacin Succinate 10 mg o.d.**
No. of micturitions/24 hr			
Mean reduction from baseline % change from baseline n p-value*	1.4 (11%) 534	2.3 (19%) 552 <0.001	2.8 (23%) 554 <0.001
No. of urgency episodes/24 hr			
Mean reduction from baseline % change from baseline n p-value*	1.7 (31%) 526	2.9 (49%) 548 <0.001	3.0 (53%) 550 <0.001
No. of incontinence episodes/24 hr			
Mean reduction from baseline % change from baseline n p-value*	1.0 (33%) 306	1.5 (58%) 314 <0.001	1.5 (56%) 323 <0.001
No. of nocturia episodes/24 hr			
Mean reduction from baseline % change from baseline n p-value*	0.5 (25%) 459	0.6 (30%) 494 0.033	0.6 (30%) 494 0.006
Volume voided/micturition			
Mean increase from baseline % change from baseline n p-value*	10 mL (7%) 534	32 mL (21%) 552 <0.001	38 mL (26%) 554 <0.001
No. of pads/24 hr			
Mean reduction from baseline % change from baseline n p-value*	0.8 (27%) 238	1.3 (46%) 236 <0.001	1.3 (48%) 242 <0.001

Note: Not all parameters and treatment groups were evaluated in each individual study. Therefore, the number of patients listed may deviate per parameter and treatment group.

*P-value for the pairwise comparison to placebo.

Table 3: Results (pooled data) of two controlled Phase 3 US studies with a treatment duration of 12 weeks.

	Placebo	Solifenacin succinate 10 mg o.d.
No. of micturitions/24 hr		
Mean reduction from baseline	1.4	2.7
% change from baseline	(12%)	(23%)
n	604	604
p-value*		<0.001
No. of urgency episodes/24 hr		
Mean reduction from baseline	2.2	3.7
% change from baseline	(31%)	(56%)
n	598	601
p-value*		<0.001
No. of incontinence episodes/24 hr		
Mean reduction from baseline	1.2	2.0
% change from baseline	(41%)	(67%)
n	475	455
p-value*		<0.001
No. of nocturia episodes/24 hr		
Mean reduction from baseline	0.4	0.5
% change from baseline	(24%)	(29%)
n	546	541
p-value*		0.012
Volume voided/micturition		
Mean increase from baseline	8 mL	47 mL
% change from baseline	(4%)	(26%)
n	601	602
p-value*		<0.001

Note: Not all parameters and treatment groups were evaluated in each individual study. Therefore, the number of patients listed may deviate per parameter and treatment group.

*P-value for the pairwise comparison to placebo.

5.2 Pharmacokinetic properties

Absorption

After intake of solifenacin tablets, maximum solifenacin plasma concentrations (C_{max}) are reached after 3 to 8 hours and at steady state ranged from 32.3 to 62.9 ng/mL for the 5 and 10 mg solifenacin tablets, respectively. The t_{max} is independent of the dose. The C_{max} and AUC increase in proportion to the dose between 5 to 40 mg. Absolute bioavailability is approximately 90%.

Food intake does not directly affect C_{max} and AUC of solifenacin.

Distribution

The apparent volume of distribution of solifenacin following intravenous administration is about 600 litres. Solifenacin is highly bound to plasma proteins (approximately 98%), primarily to α_1-acid glycoprotein.

Metabolism

Solifenacin is extensively metabolised 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

After a single administration of 10mg [^{14}C-labelled]-solifenacin, about 70% of the radioactivity was detected in urine and 23% in faeces over 26 days. In urine, approximately 11% of the radioactivity is recovered as unchanged drug; 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). The systemic clearance of solifenacin following chronic dosing is about 9.5 L/hour and the terminal half-life of solifenacin is 45 – 68 hours.

Dose Proportionality

Solifenacin pharmacokinetics are linear in the therapeutic dose range.

Characteristics in specific groups of subjects or patients

Elderly

No dosage adjustment based on patient age is required. Studies in elderly have 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 tmax 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 in children and adolescents.

Gender

The pharmacokinetics of solifenacin are not influenced by gender.

Race

The pharmacokinetics of solifenacin are not influenced 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 haemodialysis 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.

5.3 Preclinical safety data

Genotoxicity

Solifenacin was not mutagenic in the in vitro Salmonella typhimurium or Escherichia coli microbial mutagenicity test or chromosomal aberration test in human peripheral blood lymphocytes, with or without metabolic activation, or in the in vivo micronucleus test in rats.

Carcinogenicity

No significant increase in tumors was found following the administration of solifenacin to male and female mice for 104 weeks up to 5 and 9 times exposure at the maximum recommended human dose (MRHD), respectively, and male and female rats for 104 weeks at doses that resulted in <1 times exposure at the MRHD.

6. Pharmaceutical Particulars

6.1 List of excipients

Solifenacin Viatris also contains:

Core tablet:

- lactose
- maize starch
- Hypromellose
- purified talc
- magnesium stearate.

Film Coating:

- Hypromellose
- titanium dioxide
- propylene glycol
- iron oxide yellow
- iron oxide red (10 mg).

Contains sulfites and sugars as lactose.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25°C, protect from light.

6.5 Nature and contents of container

Solifenacin Viatris film coated tablets are available in blister packs of 30 tablets and bottles of 500 tablets.

Not all pack types and sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Viatris Ltd
PO Box 11-183
Ellerslie
AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

23 October 2017

10. Date of Revision of the Text

15 September 2022

Section	Summary of new information
All	Name change from Solifenacin Mylan to Solifenacin Viatris.
2	Added statement contains sugars as lactose.
6.1	Added statement contains sulfites and sugars as lactose.