PROFESSIONAL INFORMATION FOR

SILDENAFIL CIPLA

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

SILDENAFIL CIPLA, 50 mg film-coated tablets

SILDENAFIL 100 CIPLA, 100 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SILDENAFIL CIPLA 50 mg: each film-coated tablet contains sildenafil citrate equivalent to 50 mg sildenafil.

Contains sugar: lactose monohydrate 51,76 mg per film-coated tablet.

SILDENAFIL 100 CIPLA 100 mg: each film-coated tablet contains sildenafil citrate equivalent to 100 mg sildenafil.

Contains sugar: lactose monohydrate 59,52 mg per film-coated tablet.

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

Film-coated tablets.

SILDENAFIL CIPLA 50 mg film-coated tablets:

Violet coloured, oval shaped, biconvex, intact film-coated tablets with deep score on one side and plain on other side. It has a length of 10 mm.

SILDENAFIL 100 CIPLA 100 mg film-coated tablets:

Violet coloured, oval shaped, biconvex, intact film-coated tablets with deep score on one side and plain on other side. It has a length of 12 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

- SILDENAFIL CIPLA is indicated only for the treatment of erectile dysfunction.
- THIS PRODUCT IS NOT AN APHRODISIAC.

4.2. Posology and method of administration

Posology

Use in adults

The recommended dose is 50 mg, taken as needed approximately one hour before sexual activity. Based on efficacy and toleration, the dose may be increased to 100 mg or decreased to 25 mg. The maximum recommended dose is 100 mg. The maximum recommended dosing frequency is once per day.

The following factors are associated with increased plasma levels of SILDENAFIL CIPLA: Age > 65 (40 % increase in AUC), hepatic impairment (e.g. cirrhosis, 80 %), severe renal impairment (creatinine clearance < 30 mL/min, 100 %), and concomitant use of potent cytochrome P450 3A4 inhibitors (erythromycin 182 %, saquinavir 210 %, ketoconazole, itraconazole 200 %, ritonavir 1 000 %).

Special populations

Use in patients with mild to moderately impaired renal function

A starting dose of 25 mg should not be exceeded.

Use in patients with mild to moderately impaired hepatic function

Since SILDENAFIL CIPLA clearance is reduced in patients with hepatic impairment (e.g. cirrhosis), a starting dose of 25 mg should not be exceeded.

Use in elderly patients

Healthy elderly volunteers (65 years or over) had a reduced clearance of SILDENAFIL CIPLA. A starting dose of 25 mg should be considered in patients older than 65 years of age.

Use in patients using potent CYP 3A4 inhibitors

Given the extent of the interaction with patients receiving concomitant therapy with cytochrome P450 3A4 inhibitors (e.g. ritonavir, erythromycin, saquinavir, ketoconazole, itraconazole), SILDENAFIL CIPLA should not be used concomitantly with these medicines (see **section 4.3**).

SILDENAFIL CIPLA was shown to potentiate the hypotensive effects of nitrates and its administration in patients who use nitric oxide donors or nitrates in any form is therefore contraindicated.

Use in children

SILDENAFIL CIPLA is not indicated for use in children.

Method of administration

SILDENAFIL CIPLA tablets are for oral administration.

4.3. Contraindications

- Hypersensitivity to sildenafil or to any of the excipients (see **section 6.1**).

- Consistent with its known effects on the nitric oxide/cGMP pathway (see **section 5.1**), SILDENAFIL CIPLA was shown to potentiate the hypotensive effects of acute and chronic nitrates, and its administration to patients who are concurrently using nitric oxide donors, organic nitrates or organic nitrites in any form either regularly or intermittently is therefore contraindicated.
- The co-administration of PDE5 inhibitors, including sildenafil, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension (see **section 4.5**).
- Concomitant use of SILDENAFIL CIPLA with potent cytochrome P450 3A4 inhibitors e.g. ritonavir, erythromycin, saquinavir, ketoconazole and itraconazole is contraindicated.
- Medicines for the treatment of erectile dysfunction, including SILDENAFIL CIPLA, should not be used in men for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders such as unstable angina or severe cardiac failure).
- SILDENAFIL CIPLA is contraindicated in patients who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure (see **section 4.4**).
- The use of SILDENAFIL CIPLA is contraindicated in patients with severe hepatic impairment and patients with severe impairment of renal function (creatinine clearance < 30 mL/min) not on haemodialysis or continuous ambulatory peritoneal dialysis.
- The safety of sildenafil has not been studied in the following sub-groups of patients and its use is therefore contraindicated: hypotension (blood pressure < 90/50 mmHg), recent history of stroke or myocardial infarction and known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterases).

4.4. Special warnings and precautions for use

A thorough medical history and physical examination should be undertaken to diagnose erectile dysfunction, determine potential underlying causes, and identify appropriate treatment.

Cardiovascular risk factors

There is a potential for cardiac risk of sexual activity in patients with pre-existing cardiovascular disease. Therefore, treatment for erectile dysfunction, including SILDENAFIL CIPLA should not be generally used in men for whom sexual activity is inadvisable because of their underlying cardiovascular status.

SILDENAFIL CIPLA has systemic vasodilatory properties that resulted in transient decreases in supine blood pressure in healthy volunteers. Medical practitioners should carefully consider whether their patients with underlying cardiovascular disease could be affected adversely by such vasodilatory effects, especially in combination with sexual activity. Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction (e.g. aortic stenosis, hypertrophic obstructive cardiomyopathy), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure.
SILDENAFIL CIPLA potentiates the hypotensive effect of nitrates (see **section 4.3**).

Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular dysrhythmia, cerebrovascular haemorrhage, transient ischaemic attack, hypertension and hypotension have been reported post-marketing in temporal association with the use of SILDENAFIL CIPLA. Most, but not all, of these patients had pre-

existing cardiovascular risk factors. Many events were reported to occur during or shortly after sexual intercourse and a few were reported to occur shortly after the use of SILDENAFIL CIPLA without sexual activity. It is not possible to determine whether these events are related directly to these factors or to other factors.

Priapism

Medicines for the treatment of erectile dysfunction, including SILDENAFIL CIPLA, should be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease), or in patients who have conditions which may predispose them to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia).

Prolonged erections and priapism have been reported with sildenafil in post-marketing experience. In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency could result.

Concomitant use with other PDE5 inhibitors or other treatments for erectile dysfunction

The safety and efficacy of combinations of sildenafil with other PDE5 inhibitors, or other pulmonary arterial hypertension (PAH) treatments containing sildenafil or other treatments for erectile dysfunction have not been studied. Therefore, the use of such combinations is not recommended.

Effects on vision

Cases of visual defects have been reported spontaneously in connection with the intake of sildenafil and other PDE5 inhibitors (see **section 4.8**). Cases of non-arteritic anterior ischaemic optic neuropathy (NAION) have been reported spontaneously and in an

observational study in connection with the intake of sildenafil and other PDE5 inhibitors (see **section 4.8**). Patients should be advised that in the event of any sudden visual defect, they should stop taking SILDENAFIL CIPLA and consult a medical practitioner immediately (see **section 4.3**).

Retinal detachment

There have been reports indicating that regular use of phosphodiesterase 5 inhibitors (PDE5Is), such as sildenafil, may increase the risk of reversible serous retinal detachment (SRD). Although no clinical trials have established a causal relationship, it is imperative that regular users of PDE5Is remain vigilant for ocular adverse events associated with these medicines and report any visual deficits to their doctors. It is also essential for prescribing doctors to be aware of this association and consider the potential risks before prescribing PDE5Is to their patients.

Concomitant use with ritonavir

Co-administration of SILDENAFIL CIPLA with ritonavir is contraindicated (see **section 4.5**).

Concomitant use with alpha-blockers

Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the co-administration may lead to symptomatic hypotension in a few susceptible individuals (see **section 4.5**). To minimize the potential for developing postural hypotension, patients should be haemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Initiation of sildenafil at a dose of 25 mg should be considered (see **section 4.2**). In addition, medical practitioners should advise patients what to do in the event of postural hypotensive symptoms.

Effect on bleeding

Studies with human platelets indicate that sildenafil potentiates the anti-aggregatory effect of sodium nitroprusside *in vitro*. There is no safety information on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration. Therefore, SILDENAFIL CIPLA should be administered with caution to these patients.

Hearing loss

A sudden unilateral or bilateral decrease or loss of hearing (sensorineural deafness) with or without associated vestibular symptoms has been reported with the use of PDE5 inhibitors, including SILDENAFIL CIPLA. There is insufficient information regarding the reversibility of hearing loss and the role of underlying risk factors for hearing loss in individual subjects.

Women

SILDENAFIL CIPLA is not indicated for use by women.

SILDENAFIL CIPLA contains lactose, which may have an effect on the glycaemic control of patients with diabetes mellitus. 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 medicines and other forms of interaction

Effects of other medicines on sildenafil

In vitro studies

Sildenafil metabolism is principally mediated by the cytochrome P450 (CYP) isoforms 3A4 (major route) and 2C9 (minor route). Therefore, inhibitors of these isoenzymes may reduce sildenafil clearance and inducers of these isoenzymes may increase sildenafil clearance.

In vivo studies

Population pharmacokinetic analysis of clinical trial data indicated a reduction in sildenafil clearance when co-administered with CYP3A4 inhibitors (such as ketoconazole, erythromycin, and cimetidine). Although no increased incidence of adverse events was observed in these patients, when sildenafil is administered concomitantly with CYP3A4 inhibitors, a starting dose of 25 mg should be considered.

Co-administration of the HIV protease inhibitor ritonavir, which is a highly potent P450 inhibitor, at steady state (500 mg twice daily) with sildenafil (100 mg single dose) resulted in a 300 % (4-fold) increase in sildenafil C_{max} and a 1 000 % (11-fold) increase in sildenafil plasma AUC. At 24 hours, the plasma levels of sildenafil were still approximately 200 ng/mL, compared to approximately 5 ng/mL when sildenafil was administered alone. This is consistent with ritonavir's marked effects on a broad range of P450 substrates. Sildenafil had no effect on ritonavir pharmacokinetics. Based on these pharmacokinetic results co-administration of sildenafil with ritonavir is contraindicated (see **section 4.3**).

Co-administration of the HIV protease inhibitor saquinavir, also a CYP3A4 inhibitor, at steady state (1 200 mg three times daily) with sildenafil (100 mg single dose) resulted in a 140 % increase in sildenafil C_{max} and a 210 % increase in sildenafil AUC. Sildenafil had no effect on saquinavir pharmacokinetics (see **section 4.2**). Stronger CYP3A4 inhibitors such as ketoconazole and itraconazole would be expected to have greater effects.

When a single 100 mg dose of sildenafil was administered with erythromycin, a moderate CYP3A4 inhibitor, at steady state (500 mg twice daily for 5 days), there was a 182 % increase in sildenafil systemic exposure (AUC). In normal healthy male volunteers, there was no evidence of an effect of azithromycin (500 mg daily for 3 days) on the AUC, C_{max}, t_{max},

elimination rate constant, or subsequent half-life of sildenafil or its principal circulating metabolite.

Cimetidine (800 mg), a cytochrome P450 inhibitor and non-specific CYP3A4 inhibitor, caused a 56 % increase in plasma sildenafil concentrations when co-administered with sildenafil (50 mg) to healthy volunteers.

Grapefruit juice is a weak inhibitor of CYP3A4 gut wall metabolism and may give rise to modest increases in plasma levels of sildenafil.

Single doses of antacid (magnesium hydroxide/aluminium hydroxide) did not affect the bioavailability of sildenafil.

Although specific interaction studies were not conducted for all medicines, population pharmacokinetic analysis showed no effect of concomitant treatment on sildenafil pharmacokinetics when grouped as CYP2C9 inhibitors (such as tolbutamide, warfarin, phenytoin), CYP2D6 inhibitors (such as selective serotonin reuptake inhibitors, tricyclic antidepressants), thiazide and related diuretics, loop and potassium sparing diuretics, angiotensin converting enzyme inhibitors, calcium channel blockers, beta-adrenoreceptor antagonists or inducers of CYP450 metabolism (such as rifampicin, barbiturates).

In a study of healthy male volunteers, co-administration of the endothelin antagonist, bosentan, (an inducer of CYP3A4 [moderate], CYP2C9 and possibly of CYP2C19) at steady state (125 mg twice a day) with sildenafil at steady state (80 mg three times a day) resulted in 62,6 % and 55,4 % decrease in sildenafil AUC and C_{max}, respectively. Therefore, concomitant administration of strong CYP3A4 inducers, such as rifampin, is expected to cause greater decreases in plasma concentrations of sildenafil.

Nicorandil is a hybrid of potassium channel activator and nitrate. Due to the nitrate component it has the potential to result in a serious interaction with sildenafil.

Effects of sildenafil on other medicines

In vitro studies

Sildenafil is a weak inhibitor of the cytochrome P450 isoforms 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 (IC50 > 150 µM). Given sildenafil peak plasma concentrations of approximately 1 µM after recommended doses, it is unlikely that SILDENAFIL CIPLA will alter the clearance of substrates of these isoenzymes. There is no data on the interaction of sildenafil and non-specific phosphodiesterase inhibitors such as theophylline or dipyridamole.

In vivo studies

Consistent with its known effects on the nitric oxide/cGMP pathway (see **section 5.1**), sildenafil was shown to potentiate the hypotensive effects of nitrates, and its co-administration with nitric oxide donors or nitrates in any form is therefore contraindicated (see **section 4.3**).

Riociguat: Preclinical studies showed additive systemic blood pressure lowering effect when PDE5 inhibitors were combined with riociguat. In clinical studies, riociguat has been shown to augment the hypotensive effects of PDE5 inhibitors. There was no evidence of favourable clinical effect of the combination in the population studied. Concomitant use of riociguat with PDE5 inhibitors, including sildenafil, is contraindicated (see **section 4.3**).

Concomitant administration of sildenafil to patients taking alpha-blocker therapy may lead to symptomatic hypotension in a few susceptible individuals. This is most likely to occur within 4 hours post sildenafil dosing (see **sections 4.2** and **4.4**). In three specific interaction studies, the alpha-blocker doxazosin (4 mg and 8 mg) and sildenafil (25 mg, 50 mg, or 100 mg) were administered simultaneously to patients with benign prostatic hyperplasia (BPH) stabilized on doxazosin therapy. In these study populations, mean additional reductions of

supine blood pressure of 7/7 mmHg, 9/5 mmHg, and 8/4 mmHg, and mean additional reductions of standing blood pressure of 6/6 mmHg, 11/4 mmHg, and 4/5 mmHg, respectively, were observed. When sildenafil and doxazosin were administered simultaneously to patients stabilized on doxazosin therapy, there were infrequent reports of patients who experienced symptomatic postural hypotension. These reports included dizziness and light-headedness, but not syncope.

No significant interactions were shown when sildenafil (50 mg) was co-administered with tolbutamide (250 mg) or warfarin (40 mg), both of which are metabolised by CYP2C9. Sildenafil (50 mg) did not potentiate the increase in bleeding time caused by acetyl salicylic acid (150 mg).

Sildenafil (50 mg) did not potentiate the hypotensive effects of alcohol in healthy volunteers with mean maximum blood alcohol levels of 80 mg/dL.

Pooling of the following classes of antihypertensive medication; diuretics, beta-blockers, ACE inhibitors, angiotensin II antagonists, antihypertensive medicines (vasodilator and centrally acting), adrenergic neuron blockers, calcium channel blockers and alpha-adrenoceptor blockers, showed no difference in the side effect profile in patients taking sildenafil compared to placebo treatment.

In a specific interaction study, where sildenafil (100 mg) was co-administered with amlodipine in hypertensive patients, there was an additional reduction on supine systolic blood pressure of 8 mmHg. The corresponding additional reduction in supine diastolic blood pressure was 7 mmHg. These additional blood pressure reductions were of a similar magnitude to those seen when sildenafil was administered alone to healthy volunteers.

Sildenafil (100 mg) did not affect the steady state pharmacokinetics of the HIV protease inhibitors, saquinavir and ritonavir, both of which are CYP3A4 substrates.

In healthy male volunteers, sildenafil at steady state (80 mg three times a day.) resulted in a 49,8 % increase in bosentan AUC and a 42 % increase in bosentan C_{max} (125 mg twice a day).

4.6. Fertility, pregnancy and lactation

SILDENAFIL CIPLA is not indicated for use in women.

There are no adequate and well-controlled studies in pregnant or breast-feeding women.

No relevant adverse effects were found in reproduction studies in rats and rabbits following oral administration of sildenafil.

There was no effect on sperm motility or morphology after single 100 mg oral doses of sildenafil in healthy volunteers.

4.7. Effects on ability to drive and use machines

SILDENAFIL CIPLA may have a minor influence on the ability to drive and use machines.

As dizziness and altered vision were reported in clinical trials with sildenafil, patients should be aware how they react to SILDENAFIL CIPLA before driving or operating machinery.

4.8. Undesirable effects

MedDRA system organ class	**Frequency**	**Adverse reactions**
Infections and infestations	Less frequent	Rhinitis
Immune system disorders	Less frequent	Hypersensitivity

MedDRA system organ class	**Frequency**	**Adverse reactions**
Nervous system disorders	Frequent	Headache, dizziness
	Less frequent	Somnolence, hypoaesthesia, cerebrovascular accident, transient ischaemic attack, syncope
	Frequency unknown	Seizure, seizure recurrence
Eye disorders	Frequent	Visual colour distortions, visual disturbance, blurred vision
	Less frequent	Lacrimation disorders, eye pain, photophobia, photopsia, ocular hyperaemia, visual brightness, conjunctivitis, retinal haemorrhage, arteriosclerotic retinopathy, retinal disorder, glaucoma, visual field defect, diplopia, visual acuity reduced, myopia, asthenopia, vitreous floaters, iris disorder, mydriasis, halo vision, eye oedema, eye swelling, eye disorder, conjunctival hyperaemia, eye

MedDRA system organ class	Frequency	Adverse reactions
		irritation, abnormal sensation in eye, eyelid oedema, scleral discoloration
	Frequency unknown	Non-arteritic anterior ischaemic optic neuropathy (NAION), retinal vascular occlusion, serious retinal detachment (SRD)
Ear and labyrinth disorders	Less frequent	Vertigo, tinnitus, deafness
Cardiac disorders	Less frequent	Tachycardia, palpitations, myocardial infarction, atrial fibrillation, unstable angina
	Frequency unknown	Sudden cardiac death, ventricular dysrhythmia
Vascular disorders	Frequent	Flushing, hot flush
	Less frequent	Hypertension, hypotension
Respiratory, thoracic and mediastinal disorders	Frequent	Nasal congestion
	Less frequent	Epistaxis, sinus congestion, throat tightness, nasal oedema, nasal dryness
Gastrointestinal disorders	Frequent	Nausea, dyspepsia
	Less frequent	Gastro oesophageal reflux disease, vomiting, abdominal

MedDRA system organ class	Frequency	Adverse reactions
		pain upper, dry mouth, oral hypoaesthesia
Skin and subcutaneous tissue disorders	Less frequent	Rash
	Frequency unknown	Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN)
Musculoskeletal and connective tissue disorders	Less frequent	Myalgia, pain in extremity
Renal and urinary disorders	Less frequent	Haematuria
Reproductive system and breast disorders	Less frequent	Penile haemorrhage, haematospermia, increased erection
	Frequency unknown	Priapism
General disorders and administration site conditions	Less frequent	Chest pain, fatigue, feeling hot, irritability
Investigations	Less frequent	Increased heart rate

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. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website or to Cipla Medpro (Pty) Ltd. by e-mail to drugsafetysa@cipla.com or telephone to 080 222 6662 (toll free).

4.9. Overdose

In single dose volunteer studies of doses up to 800 mg, adverse reactions were similar to those seen at lower doses, but the incidence rates and severities were increased. Doses of 200 mg did not result in increased efficacy but the incidence of adverse reactions (headache, flushing, dizziness, dyspepsia, nasal congestion, altered vision) was increased. In cases of overdose, standard supportive measures should be adopted as required. Renal dialysis is not expected to accelerate clearance as sildenafil is highly bound to plasma proteins and not eliminated in the urine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals; Drugs used in erectile dysfunction

ATC code: G04B E03

Pharmacological classification: A 7.1.5 Vasodilators – peripheral

Sildenafil restores impaired erectile function by increasing blood flow to the penis in response to sexual stimulation.

Sildenafil is a selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5), which is responsible for degradation of cGMP in the corpus cavernosum. Sildenafil has no direct

relaxant effect on isolated human corpus cavernosum but enhances the relaxant effect of nitric oxide (NO) on this tissue. When the NO/cGMP pathway is activated during sexual stimulation, inhibition of PDE5 by sildenafil results in increased corpus cavernosum levels of cGMP, producing smooth muscle relaxation in the corpus cavernosum allowing the inflow of blood.

5.2. Pharmacokinetic properties

Absorption

Sildenafil is rapidly absorbed. Maximum observed plasma concentrations are reached within 30 to 120 minutes (median 60 minutes) of oral dosing in the fasted state. The mean absolute oral bioavailability is approximately 40 % (range 25 to 63 %). The oral pharmacokinetics of sildenafil is proportional over the recommended dose range (25 to 100 mg). When sildenafil is taken with a high fat meal, the rate of absorption is reduced with a mean delay in T_{max} of 60 minutes and a mean reduction in Cmax of 29 %.

Distribution

The mean steady state volume of distribution (Vss) for sildenafil is 105 L, indicating distribution into the tissues. Sildenafil and its major circulating N-desmethyl metabolite are both approximately 96 % bound to plasma proteins. Protein binding is independent of total medicine concentrations. In healthy volunteers receiving sildenafil (100 mg single dose), less than 0,0002 % (average 188 ng) of the administered dose was present in ejaculate 90 minutes after dosing.

Biotransformation

Sildenafil is cleared predominantly by the CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes. The major circulating metabolite results from N-

demethylation of sildenafil. This metabolite has a PDE selectivity profile similar to sildenafil and an *in vitro* potency for PDE5 approximately 50 % that of the parent compound. Plasma concentrations of this metabolite are approximately 40 % of those seen for sildenafil. The N-desmethyl metabolite is further metabolised, with a terminal half-life of approximately 4 hours.

Elimination

The total body clearance of sildenafil is 41 L/h with a resultant terminal phase half-life of 3 to 5 hours. After either oral or intravenous administration, sildenafil is excreted as metabolites predominantly in the faeces (approximately 80 % of administered oral dose) and to a lesser extent in the urine (approximately 13 % of administered oral dose).

Special patient groups

Elderly

Healthy elderly volunteers (65 years or over) had a reduced clearance of sildenafil, with free plasma concentrations approximately 40 % greater than those seen in healthy younger volunteers (18 to 45 years).

Renal insufficiency

In volunteers with mild CrCl (creatinine clearance = 50 to 80 mL/min) and moderate CrCl (creatinine clearance = 30 to 49 mL/min) renal impairment, the pharmacokinetics of a single oral dose of sildenafil (50 mg) were not altered. In volunteers with severe CrCl ≤ 30 mL/min renal impairment, sildenafil clearance was reduced, resulting in increases in AUC (100 %) and C_{max} (88 %) compared to age-matched volunteers with no renal impairment.

Hepatic insufficiency

In volunteers with hepatic cirrhosis (Child-Pugh A and B) sildenafil clearance was reduced, resulting in increases in AUC (84 %) and C_{max} (47 %) compared to age-matched volunteers with no hepatic impairment.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Colloidal anhydrous silica (Aerosil)

Crospovidone

Lactose monohydrate

Magnesium stearate (vegetable grade)

Maize starch

Microcrystalline cellulose

Opadry Purple 04F50241

Purified talc

Opadry Purple 04F50241 composed of:

Carmoisine (Azorubine) aluminium lake

Hypromellose

Indigo carmine aluminium lake

Macrogol

Titanium dioxide

6.2. Incompatibilities

Not applicable.

6.3. Shelf Life

24 months.

6.4. Special precautions for storage

Store at or below 30 °C.

Keep blisters in the carton until required for use.

6.5. Nature and contents of container

SILDENAFIL CIPLA 50 mg film-coated tablets are packed in blister of 2 and 4 tablets composed of clear PVC film and plain blister foil, packed in an outer carton.

SILDENAFIL 100 CIPLA 100 mg film-coated tablets are packed in blister of 4 tablets composed of clear PVC film and plain blister foil, packed in an outer carton.

6.6. Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements**.**

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBERS

SILDENAFIL CIPLA: 45/7.1.5/0780

SILDENAFIL 100 CIPLA: 47/7.1.5/0216

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

SILDENAFIL CIPLA:

First authorisation: 27 November 2014

Latest renewal: Not applicable.

SILDENAFIL 100 CIPLA:

First authorisation: 29 March 2022

Latest renewal: Not applicable.

10. DATE OF REVISION OF THE TEXT

16 January 2026