For the use of a Registered Medical Practitioner only

PRESCRIBING INFORMATION

CAVERTA

(Sildenafil 100 mg Tablets)

COMPOSITION

Each film-coated tablet contains:
Sildenafil Citrate 140.48 mg equivalent to
Sildenafil..... 100 mg.

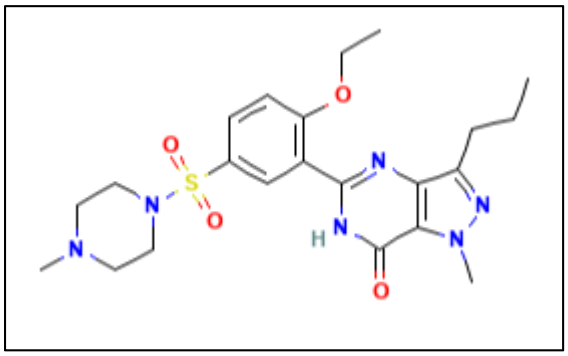
***Excipients**:* Anhydrous calcium hydrogen phosphate, croscarmellose sodium, opadry red 06855000, microcrystalline cellulose, magnesium stearate, purified water.

PRODUCT DESCRIPTION

Red coloured, rounded triangular shaped, film-coated tablet, with 'S23' engraved on one side and break line on the other side

DESCRIPTION

CAVERTA contains active substance sildenafil. Sildenafil functions as a selective and competitive inhibitor of type 5 phosphodiesterases (PDE5) on smooth muscle cells in the penis and pulmonary vasculature, and is used extensively for erectile dysfunction and less commonly for pulmonary hypertension. It is described chemically as 5-[2-ethoxy-5-(4-methylpiperazin-1-yl)sulfonylphenyl]-1-methyl-3-propyl-6H-pyrazolo[4,3-d]pyrimidin-7-one. Sildenafil has molecular formulae $C_{22}H_{30}N_6O_4S$ and molecular weight is 474.6. Sildenafil has the following structural formula:



STRUCTURAL FORMULAE OF SILDENAFIL

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

- **Pharmacodynamics**

Sildenafil, an oral therapy for erectile dysfunction, is the citrate salt of sildenafil, a selective inhibitor of cyclic guanosine monophosphate (cGMP) -specific phosphodiesterase type 5 (PDE5).

Mechanism of Action: The physiologic mechanism of erection of the penis involves release of nitric oxide (NO) in the corpus cavernosum during sexual stimulation.

NO then activates the enzyme guanylate cyclase, which results in increased levels of cyclic guanosine monophosphate (cGMP), producing smooth muscle relaxation in the corpus cavernosum and allowing inflow of blood.

Sildenafil has no direct relaxant effect on isolated human corpus cavernosum, but enhances the effect of NO by inhibiting of phosphodiesterase type 5 (PDE5), which is responsible for degradation of cGMP in the corpus cavernosum.

When sexual stimulation causes local release of NO, inhibition of PDE5 by sildenafil causes increased levels of cGMP in the corpus cavernosum, resulting in smooth muscle relaxation and inflow of blood to the corpus cavernosum.

Sildenafil at recommended doses has no effect in the absence of sexual stimulation.

As per the reported *in vitro* studies, sildenafil is selective for PDE5.

Its effect is more potent on PDE5 than on other known phosphodiesterases (10-fold for PDE6, >80-fold for PDE1, >700-fold for PDE2, PDE3, and PDE4, PDE7 - PDE11).

The approximately 4,000-fold selectivity for PDE5 versus PDE3 is important because PDE3 is involved in the control of cardiac contractility.

- **Pharmacokinetics**

Sildenafil pharmacokinetics are dose-proportional over the recommended dose range.

It is eliminated predominantly by hepatic metabolism (mainly cytochrome P450 3A4) and is converted to an active metabolite with properties similar to the parent, sildenafil.

Absorption
Sildenafil is rapidly absorbed after oral administration, with mean absolute bioavailability of 41% (range 25%-63%).

Sildenafil inhibits the human PDE5 enzyme *in vitro* by 50% at a concentration of 3.5 nM. In man, the mean maximum free plasma concentration of sildenafil following a single oral dose of 100 mg is approximately 18 ng/mL, or 38 nM.

Maximum observed plasma concentrations are reached within 30 to 120 minutes (median 60 minutes) of oral dosing in the fasted state.

When sildenafil film-coated tablets are taken with a high fat meal, the rate of absorption of sildenafil is reduced, with a mean delay in T_{max} of 60 minutes and a mean reduction in C_{max} of 29%, however, the extent of absorption has not been significantly affected (AUC decreased by 11%).

Distribution
The mean steady-state volume of distribution (V_{ss}) for sildenafil is reported to be 105 L, indicating distribution into the tissues.

Sildenafil and its major circulating N-desmethyl metabolite are both reported as approximately 96% bound to plasma proteins.

Protein binding is independent of total drug concentrations.

Based upon measurements of sildenafil in semen of healthy volunteers 90 minutes after dosing, less than 0.0002% (average 188 ng) of the administered dose may appear in the semen of patients.

Metabolism
Sildenafil is cleared predominantly by the CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes.

The major circulating metabolite results from N-desmethylation of sildenafil, and is itself further metabolized.

This metabolite has a PDE selectivity profile similar to sildenafil and an *in vitro* potency for PDE5 approximately 50% of the parent drug.

In healthy volunteers, plasma concentrations of this metabolite are reported as approximately 40% of those seen for sildenafil.

The N-desmethyl metabolite is further metabolized, with a terminal half-life of approximately 4 hours.

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

Pharmacokinetics in special patient groups:

Elderly
Reduced clearance of sildenafil has been reported in healthy elderly volunteers (65 years or over), resulting in approximately 90% higher plasma concentrations of sildenafil and the active N-desmethyl metabolite compared to those seen in healthy younger volunteers (18-45 years). Due to age-differences in plasma protein binding, the corresponding increase in free sildenafil plasma concentration has been reported to be approximately 40%.

Renal Insufficiency
In volunteers with mild (creatinine clearance = 50-80 mL/min) and moderate (creatinine clearance = 30-49 mL/min) renal impairment, the pharmacokinetics of a single oral dose of sildenafil (50 mg) have not been altered.

In volunteers with severe (creatinine clearance = <30 mL/min) renal impairment, sildenafil clearance has been reduced, resulting in approximately doubling of AUC (100%) and C_{max} (88%) compared to age-matched volunteers with no renal impairment (see **DOSE AND METHOD OF ADMINISTRATION**).

In addition, N-desmethyl metabolite AUC and C_{max} values have been reported to be significantly increased by 200% and 79% respectively in subjects with severe renal impairment compared to subjects with normal renal function.

Hepatic Insufficiency
In volunteers with hepatic cirrhosis (Child-Pugh A and B), sildenafil clearance has been reduced, resulting in increases in AUC (85%) and C_{max} (47%) compared to age-matched volunteers with no hepatic impairment (see **DOSE AND METHOD OF ADMINISTRATION**). The pharmacokinetics of

sildenafil in patients with severely impaired hepatic function (Child-Pugh class C) have not been reported.

INDICATIONS

CAVERTA TABLETS is indicated for the treatment of erectile dysfunction, which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance.

In order for sildenafil to be effective, sexual stimulation is required.

DOSE AND METHOD OF ADMINISTRATION

CAVERTA is available in the strengths of 100 mg only and may not be suitable for all dosage recommendations given below. Therefore, other suitable available strengths and dosage forms of sildenafil should be used in such cases**.**

Sildenafil tablets are for oral administration.

Use in adults

For most patients, the recommended dose is 50 mg taken, as needed, approximately 1 hour before sexual activity. Based on effectiveness and toleration, the dose may be increased to a maximum recommended dose of 100 mg or decreased to 25 mg. The maximum recommended daily dose is 100 mg. The maximum recommended dosing frequency is once per day.

Use in patients with impaired renal function

Dosage adjustments are not required in patients with mild to moderate renal impairment (creatinine clearance = 30 - 80 mL/min). Since sildenafil clearance is reduced in patients with severe renal impairment (creatinine clearance <30 mL/min), a 25 mg dose should be considered.

Use in patients with impaired hepatic function

Since sildenafil clearance is reduced in patients with hepatic impairment (e.g., cirrhosis), a 25 mg dose should be considered.

Use in patients using other medications

Given the extent of the interaction with patients receiving concomitant therapy with ritonavir (see **DRUG INTERACTIONS**), it is recommended not to exceed a maximum single dose of 25 mg of sildenafil in a 48-hour period.

A starting dose of 25 mg should be considered in patients receiving concomitant treatment with the CYP3A4 inhibitors (e.g., erythromycin, saquinavir, ketoconazole, itraconazole) see **DRUG INTERACTIONS**.

In order to minimize the potential for developing postural hypotension, patients should be stable on alpha-blocker therapy prior to initiating sildenafil treatment. In addition, initiation of sildenafil at lower doses should be considered (see **WARNINGS AND PRECAUTIONS** and **DRUG INTERACTIONS**).

Use in children
Sildenafil is not indicated for use in children (<18 years old).

Use in elderly men
Dosage adjustments are not required in elderly patients.

CONTRAINDICATIONS

Use of sildenafil is contraindicated in patients with a known hypersensitivity to any component of the tablet.

Agents for the treatment of erectile dysfunction, including sildenafil, 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).

Consistent with its known effects on the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway, Sildenafil has been reported 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 (see **DRUG INTERACTIONS**).

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.

Sildenafil 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 has a connection or not with previous PDE5 inhibitor exposure.

The safety of sildenafil has not been reported in the following sub-groups of patients and its use is therefore contraindicated: severe hepatic impairment, 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).

WARNINGS AND PRECAUTIONS

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

There is a degree of cardiac risk associated with sexual activity; therefore, physicians may wish to consider the cardiovascular status of their patients prior to initiating any treatment for erectile dysfunction.

Sildenafil potentiates the hypotensive effect of nitrates.

Agents for the treatment of erectile dysfunction should not be used in men for whom sexual activity is inadvisable.

Serious cardiovascular events, including myocardial infarction, sudden cardiac death, ventricular arrhythmia, cerebrovascular hemorrhage and transient ischemic attack have been reported post-marketing in temporal association with the use of sildenafil for erectile dysfunction. Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many of these events have been reported to occur during or shortly after sexual activity, and a few have been reported to occur shortly after the use of sildenafil without sexual activity. Others have been reported to have occurred hours to days after the use of sildenafil and sexual activity. It is not possible to determine whether these events are related directly to sildenafil, to sexual activity, to the patient's underlying cardiovascular disease, to a combination of these factors, or to other factors.

Sildenafil has been reported to have systemic vasodilatory properties that result in transient decreases in blood pressure. This is of little or no consequence in most patients. However, prior to prescribing sildenafil, physicians should carefully consider whether their patients with certain underlying conditions could be adversely affected 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.

Non-arteritic anterior ischemic optic neuropathy (NAION), a rare condition and a cause of decreased vision or loss of vision, has been reported rarely post-marketing with the use of all

PDE5 inhibitors, including sildenafil. Most of these patients had risk factors such as low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking.

Individuals who have already experienced NAION are at increased risk of NAION recurrence. Therefore physicians should discuss this risk with these patients and whether they could be adversely affected by use of PDE5 inhibitors. PDE5 inhibitors, including sildenafil, should be used with caution in these patients and only when the anticipated benefits outweigh the risks.

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 **DRUG INTERACTIONS**). In order to minimize the potential for developing postural hypotension, patients should be hemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Initiation of sildenafil at lower doses should be considered (see **DOSE AND METHOD OF ADMINISTRATION**). In addition, physicians should advise patients what to do in the event of postural hypotensive symptoms.

A minority of patients with the inherited condition retinitis pigmentosa have genetic disorders of retinal phosphodiesterases. There is no safety information has been reported on the administration of sildenafil to patients with retinitis pigmentosa, therefore, sildenafil should be administered with caution to these patients.

Reported In vitro studies with human platelets indicate that sildenafil potentiates the anti-aggregatory effect of sodium nitroprusside (a nitric oxide donor). There is no safety information has been reported on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration, therefore sildenafil should be administered with caution to these patients.

Agents for the treatment of erectile dysfunction 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 anemia, multiple myeloma or leukemia).

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.

The safety and efficacy of combinations of sildenafil with other PDE5 inhibitors, or other pulmonary arterial hypertension (PAH) treatments containing sildenafil (REVATIO), or other

treatments for erectile dysfunction have not been reported, and the use of such combinations is not recommended.

Sudden decrease or loss of hearing has been reported with the use of all PDE5 inhibitors, including sildenafil. Most of these patients had risk factors for sudden decrease or loss of hearing. No causal relationship has been reported to be made between the use of PDE5 inhibitors and sudden decrease or loss of hearing. In case of sudden decrease or loss of hearing patients should be advised to stop taking sildenafil and consult a physician promptly.

Concomitant use with ritonavir
Co-administration of sildenafil with ritonavir is not advised.

Women
Sildenafil is not indicated for use by women.

Effects on ability to drive and use machines
As dizziness and altered vision were reported with sildenafil, patients should be aware of how they react to sildenafil, before driving or operating machinery. The effect of sildenafil on the ability to drive and use machinery has not been reported.

DRUG INTERACTIONS

Reported 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.

Reported in vivo studies:
It has been reported that a reduction in sildenafil clearance when co-administered with CYP3A4 inhibitors (such as ketoconazole, erythromycin, and cimetidine). Although no increased incidence of adverse events has been reported in these patients, when sildenafil is administered concomitantly with CYP3A4 inhibitors, a starting dose of 25 mg should be considered.

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

It has been reported that when a single 100 mg dose of sildenafil is administered with erythromycin, a moderate CYP3A4 inhibitor, at steady-state (500 mg twice daily for 5 days), there

is a 182% increase in sildenafil systemic exposure (AUC). In addition, co-administration of the HIV protease inhibitor saquinavir, also a CYP3A4 inhibitor, at steady-state (1200 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 has no effect on saquinavir pharmacokinetics (see **DOSE AND METHOD OF ADMINISTRATION**). Stronger CYP3A4 inhibitors such as ketoconazole and itraconazole would be expected to have greater effects.

Co-administration with 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 1000% (11-fold) increase in sildenafil plasma AUC. At 24 hours, the plasma levels of sildenafil have been reported to be approximately 200 ng/mL, compared to approximately 5 ng/mL when sildenafil was dosed alone. This is consistent with ritonavir's marked effects on a broad range of P450 substrates. Sildenafil has no effect on ritonavir pharmacokinetics see **DOSE AND METHOD OF ADMINISTRATION**.

As per the reported study, when the dose of sildenafil for subjects receiving potent CYP3A4 inhibitors was administered as recommended, the maximum free plasma sildenafil concentration did not exceed 200 nM for any individual and was consistently well tolerated.

Single doses of antacid (magnesium hydroxide/aluminium hydroxide) has no effect on the bioavailability of sildenafil.

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. Sildenafil increased bosentan AUC and C_{max} by 49.8% and 42%, respectively. Concomitant administration of strong CYP3A4 inducers, such as rifampin, is expected to cause greater decreases in plasma concentrations of sildenafil.

It has been reported that no effect on sildenafil pharmacokinetics of CYP2C9 inhibitors (such as tolbutamide, warfarin), CYP2D6 inhibitors (such as selective serotonin reuptake inhibitors, tricyclic antidepressants), thiazide and related diuretics, angiotensin converting enzyme (ACE) inhibitors, and calcium channel blockers.

There is no evidence of an effect of azithromycin (500 mg daily for 3 days) in healthy male volunteers on the AUC, C_{max}, T_{max}, elimination rate constant, or subsequent half-life of sildenafil or its major circulating metabolite.

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

Reported 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 will alter the clearance of substrates of these isoenzymes.

No study has been reported on the interaction of sildenafil and non-specific phosphodiesterase inhibitors such as theophylline or dipyridamole.

Reported in vivo studies:
Consistent with its known effects on the nitric oxide/cGMP pathway, Sildenafil has been reported to potentiate the hypotensive effect of acute and chronic nitrates. Therefore, use of nitric oxide donors, organic nitrates, or organic nitrites in any form either regularly or intermittently with sildenafil is contraindicated (see **CONTRAINDICATIONS**).

Riociguat: It has been reported that additive systemic blood pressure lowering effect when PDE5 inhibitors were combined with riociguat. riociguat has been reported to augment the hypotensive effects of PDE5 inhibitors. There is no evidence of favourable clinical effect of the combination. Concomitant use of riociguat with PDE5 inhibitors, including sildenafil, is contraindicated.

The alpha-blocker doxazosin (4 mg and 8 mg) and sildenafil (25 mg, 50 mg, or 100 mg) have been reported to be 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, have been reported. When sildenafil and doxazosin have been reported to be 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. Concomitant administration of sildenafil to patients taking alpha-blocker therapy may lead to symptomatic hypotension in a few susceptible individuals (see **DOSE AND METHOD OF ADMINISTRATION** and **WARNINGS AND PRECAUTIONS**).

No significant interactions have been reported when sildenafil (50 mg) was co-administered with tolbutamide (250 mg) or warfarin (40 mg), both of which are metabolized by CYP2C9.

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

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).

Sildenafil (50 mg) did not potentiate the increase in bleeding time caused by aspirin (150 mg). Sildenafil (50 mg) did not potentiate the hypotensive effect of alcohol in healthy volunteers with mean maximum blood alcohol levels of 0.08% (80 mg/dL).

No interaction has been reported when sildenafil (100 mg) was co-administered with amlodipine in hypertensive patients. The mean additional reduction on supine systolic blood pressure was 8 mmHg systolic and 7 mmHg diastolic.

No difference has been reported in the side effect profile in patients taking sildenafil with and without antihypertensive medication.

Pooling of the following classes of antihypertensive medication: diuretics, beta-blockers, ACE inhibitors, angiotensin II antagonists, antihypertensive medicinal products (vasodilator and centrally-acting), adrenergic neurone blockers, calcium channel blockers and alpha-adrenoceptor blockers, reported no difference in the side effect profile in patients taking sildenafil compared to placebo treatment. In a reported 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 reported when sildenafil was administered alone to healthy volunteers.

SIDE EFFECTS/UNDESIRABLE EFFECTS

Summary of the safety profile

The adverse events were generally transient and mild to moderate in nature. The most commonly reported adverse reactions in sildenafil treated patients were headache, flushing, dyspepsia, nasal congestion, dizziness, nausea, hot flush, visual disturbance, cyanopsia and vision blurred.

In reported studies, the incidence of some adverse events increased with dose.

Tabulated list of adverse reactions

In the table below all medically important adverse reactions, have been reported by system organ class and frequency (very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1: Medically important adverse reactions reported at an incidence greater than placebo in controlled clinical studies and medically important adverse reactions reported through post-marketing surveillance

System Organ Class	**Very common** ***(≥ 1/10)***	**Common** ***(≥ 1/100 and <1/10)***	**Uncommon** ***(≥ 1/1,000 and <1/100)***	**Rare** ***(≥ 1/10,000 and <1/1,000)***
Infections and infestations			Rhinitis	
Immune system disorders			Hypersensitivity	
Nervous system disorders	Headache	Dizziness	Somnolence, Hypoaesthesia	Cerebrovascular accident, Transient ischaemic attack, Seizure,* Seizure recurrence,* Syncope
Eye disorders		Visual colour distortions**, Visual disturbance, Vision blurred, Cyanopsia	Lacrimation disorders***, Eye pain, Photophobia, Photopsia, Ocular hyperaemia, Visual brightness, Conjunctivitis	Non-arteritic anterior ischaemic optic neuropathy (NAION)*, Retinal vascular occlusion*, 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 irritation, Abnormal sensation in eye, Eyelid oedema, Scleral discoloration

Ear and labyrinth disorders			Vertigo, Tinnitus	Deafness
Cardiac disorders			Tachycardia, Palpitations	Sudden cardiac death*, Myocardial infarction, Ventricular arrhythmia*, Atrial fibrillation, Unstable angina
Vascular disorders		Flushing, Hot flush	Hypertension, Hypotension	
Respiratory, thoracic and mediastinal disorders		Nasal congestion	Epistaxis, Sinus congestion	Throat tightness, Nasal oedema, Nasal dryness
Gastrointestinal disorders		Nausea, Dyspepsia	Gastro oesophagael reflux disease, Vomiting, Abdominal pain upper, Dry mouth	Hypoaesthesia oral
Skin and subcutaneous tissue disorders			Rash	Stevens-Johnson Syndrome (SJS)*, Toxic Epidermal Necrolysis (TEN)*
Musculoskeletal and connective tissue disorders			Myalgia, Pain in extremity	
Renal and urinary disorders			Haematuria	
Reproductive system and breast disorders				Penile haemorrhage, Priapism*, Haematospermia, Erection increased
General disorders and administration site conditions			Chest pain, Fatigue, Feeling hot	Irritability
Investigations			Heart rate increased	

*****Reported during post-marketing surveillance only

**Visual colour distortions: Chloropsia, Chromatopsia, Cyanopsia, Erythropsia and Xanthopsia

***Lacrimation disorders: Dry eye, Lacrimal disorder and Lacrimation increased

USE IN SPECIAL POPULATIONS

Sildenafil is not indicated for use in women.

No teratogenic effects, impairment of fertility or adverse effects on peri-/post-natal development have been reported in reproduction studies in rats and rabbits following oral administration of sildenafil.

There are no reported studies in pregnant or lactating women.
There was no effect on sperm motility or morphology after single 100 mg oral doses of sildenafil in healthy volunteers.

OVERDOSE

In reported studies with healthy volunteers of single doses up to 800 mg, adverse events have been reported to be similar to those reported at lower doses but incidence rates and severities have been 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) has been reported to be 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 it is not eliminated in the urine.

STORAGE
Store below 30°C, protect from moisture.
Keep all medicines out of the reach of children.

PACKING
Blister pack of 1 x10's, 3 x 10's, 6 x 10's and 10 x 10's.

Date of Revision: July 2022

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