BACK

activity, to the patient's underlying cardiovascular disease, to a combination of these factors, or to other factors.

Hemic and Lymphatic:
Vaso-occlusive crisis: In a small, prematurely terminated study of sildenafil in patients with pulmonary arterial hypertension (PAH) secondary to sickle cell disease, vaso-occlusive crises requiring hospitalization were more commonly reported in patients who received sildenafil than in those randomized to placebo. The clinical relevance of this finding to men treated with sildenafil for ED is not known.

Nervous: seizure, seizure recurrence, anxiety, and transient global amnesia.

Respiratory: epistaxis

Special senses:

Hearing: Cases of sudden decrease or loss of hearing have been reported postmarketing in temporal association with the use of PDE5 inhibitors, including sildenafil. In some of the cases, medical conditions and other factors were reported that may have also played a role in the otologic adverse events. In many cases, medical follow-up information was limited. It is not possible to determine whether these reported events are related directly to the use of sildenafil, to the patient's underlying risk factors for hearing loss, a combination of these factors, or to other factors.

***Ocular*:** diplopia, temporary vision loss/decreased vision, ocular redness or bloodshot appearance, ocular burning, ocular swelling/pressure, increased intraocular pressure, retinal edema, retinal vascular disease or bleeding, and vitreous traction /detachment.

Non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, has been reported rarely post-marketing in temporal association with the use of phosphodiesterase type 5 (PDE5) inhibitors, including sildenafil.

Most, but not all, of these patients had underlying anatomic or vascular risk factors for developing NAION, including but not necessarily limited to: low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking.

Urogenital:
Prolonged erection, priapism

OVERDOSE
In published studies with healthy volunteers of single doses up to 800 mg, adverse reactions were similar to those seen at lower doses but incidence rates and severities were 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.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC

Pharmacotherapeutic group: Genito Urinary System and Sex Hormones, Urologicals; Drugs used in erectile dysfunction, ATC Code: G04B E03.

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 enhances the effect of NO by inhibiting 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. 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.

In addition to human corpus cavernosum smooth muscle, PDE5 is also found in other tissues including platelets, vascular and visceral smooth muscle, and skeletal muscle, brain, heart, liver, kidney, lung, pancreas, prostate, bladder, testis, and seminal vesicle. The inhibition of PDE5 in some of these tissues by sildenafil may be the basis for the enhanced platelet antiaggregatory activity of NO observed *in vitro*, an inhibition of platelet thrombus formation *in vivo* and peripheral arterial-venous dilatation *in vivo*.

PHARMACOKINETIC
Sildenafil is rapidly absorbed after oral administration, with a mean absolute bioavailability of 41% (range 25- 63%). The pharmacokinetics of sildenafil are dose-proportional over the recommended dose range. It is eliminated predominantly by hepatic metabolism (mainly CYP3A4) and is converted to an active metabolite with properties similar to the parent, sildenafil. Both sildenafil and the metabolite have terminal half-lives of about 4 hours.

Absorption & Distribution
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. When Sildenafil is taken with a high fat meal, the rate of absorption is reduced, with a mean delay in Tmax of 60 minutes and a mean reduction in Cmax of 29%. 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 drug concentrations.

Based upon measurements of sildenafil in semen of healthy volunteers 90 minutes after dosing, less than 0.001% of the administered dose may appear in the semen of patients.

Metabolism & Excretion
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. Plasma concentrations of this metabolite are approximately 40% of those seen for sildenafil, so that the metabolite accounts for about 20% of sildenafil's pharmacologic effects.

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). Similar values for pharmacokinetic parameters were seen in normal volunteers and in the patient population, using a population pharmacokinetic approach.

PRECLINICAL SAFETY DATA

Carcinogenesis
Sildenafil was not carcinogenic when administered to rats for 24 months at a dose resulting in total systemic drug exposure (AUCs) for unbound sildenafil and its major metabolite of 20- and 38-times, for male and female rats, respectively, the exposures observed in human males given the Maximum Recommended Human Dose (MRHD) of 100 mg. Sildenafil was not carcinogenic when administered to mice for 18-21 months at dosages up to the Maximum Tolerated Dose (MTD) of 10 mg/kg/day, approximately 0.4 times the MRHD on a mg/m^2 basis in a 50 kg subject.

Mutagenesis
Sildenafil was negative in in vitro bacterial and Chinese hamster ovary cell assays to detect mutagenicity, and in vitro human lymphocytes and in vivo mouse micronucleus assays to detect clastogenicity.

Impairment of Fertility
There was no impairment of fertility in rats given sildenafil up to 60 mg/kg/day for 36 days to females and 102 days to males, a dose producing an AUC value of more than 25 times the human male AUC.

PHARMACEUTICAL PARTICULARS
INCOMPATIBILITY
Not applicable.

SHELF LIFE
36 months

STORAGE CONDITION
Store at a temperature below 30°C. Protect from light.

NATURE AND CONTENTS OF CONTAINER
4 Tablets in a Blister Pack in a Printed Carton along with Package Insert.

MANUFACTURING AUTHORISATON HOLDER AND MANUFACTURER

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : 022-6913 2111/2112 Fax : 022-6913 2070 Email : info@ajantapharma.com	Ajanta Pharma Limited B-4-5-6, MIDC Industrial Area Paithan, Aurangabad, 431148 Dist: Aurangabad Maharashtra, India. Tel : +91-2431-664000 Fax : +91-2431-664100

Last Revision Date: Aug 18, 2023

KAMAGRA

Sildenafil Citrate Tablets

Patient Information Leaflet

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

1. What KAMAGRA is and what it is used for
KAMAGRA is a prescription medicine used to treat erectile dysfunction (ED). You will not get an erection just by taking this medicine. KAMAGRA helps a man with erectile dysfunction get and keep an erection only when he is sexually excited (stimulated).

KAMAGRA is not for use in women or children.

It is not known if KAMAGRA is safe and effective in women or children under 18 years of age.

2. What you need to know before you use Kamagra
KAMAGRA can cause your blood pressure to drop suddenly to an unsafe level if it is taken with certain other medicines. Do not take KAMAGRA if you take any other medicines called "nitrates." Nitrates are used to treat chest pain (angina). A sudden drop in blood pressure can cause you to feel dizzy, faint, or have a heart attack or stroke.

Do not take KAMAGRA if you take medicines called guanylate cyclase stimulators which include:

Riociguat a medicine that treats pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

Tell all your healthcare providers that you take KAMAGRA.

If you need emergency medical care for a heart problem, it will be important for your healthcare provider to know when you last took KAMAGRA.

Stop sexual activity and get medical help right away if you get symptoms such as chest pain, dizziness, or nausea during sex.

Sexual activity can put an extra strain on your heart, especially if your heart is already weak from a heart attack or heart disease. Ask your doctor if your heart is healthy enough to handle the extra strain of having sex.

KAMAGRA does not protect you or your partner from getting sexually transmitted diseases, including HIV—the virus that causes AIDS.

Do not take KAMAGRA if you:
- take medicines called nitrates (such as nitroglycerin)
- use street drugs called "poppers" such as amyl nitrate or amyl nitrite, and butyl nitrate
- take any medicines called guanylate cyclase stimulators such as riociguat.
- are allergic to sildenafil, as contained in KAMAGRA and REVATIO, or any of the ingredients in KAMAGRA. See the end of this leaflet for a complete list of ingredients in KAMAGRA.

Before you take KAMAGRA, tell your healthcare provider if you:
- have or have had heart problems such as a heart attack, irregular heartbeat, angina, chest pain, narrowing of the aortic valve or heart failure
- have had heart surgery within the last 6 months
- have pulmonary hypertension
- have had a stroke
- have low blood pressure, or high blood pressure that is not controlled
- have a deformed penis shape
- have had an erection that lasted for more than 4 hours
- have problems with your blood cells such as sickle cell anemia, multiple myeloma, or leukemia
- have retinitis pigmentosa, a rare genetic (runs in families) eye disease
- have ever had severe vision loss, including an eye problem called non-arteritic anterior ischemic optic neuropathy (NAION)
- have bleeding problems
- have or have had stomach ulcers
- have liver problems
- have kidney problems or are having kidney dialysis
- have any other medical conditions

Tell your healthcare provider about all the medicines you take*,
Including prescription and over-the-counter medicines, vitamins, and herbal supplements.
KAMAGRA may affect the way other medicines work, and other medicines may affect the way KAMAGRA works causing side effects. Especially tell your healthcare provider if you take any of the following:
- Medicines called nitrates (see "What is the most important information I should know about KAMAGRA?")
- medicines called guanylate cyclase stimulators, such as riociguat.
- Medicines called alpha blockers such as terazosin, tamsulosin, doxazosin, prazosin, alfuzosin, dutasteride and tamsulosin, or silodosin. Alpha-blockers are sometimes prescribed for prostate problems or high blood pressure. In some patients, the use of KAMAGRA with alpha-blockers can lead to a drop in blood pressure or to fainting.
- medicines called HIV protease inhibitors, such as ritonavir, indinavir sulfate, saquinavir or atazanavir sulfate.
- some types of oral antifungal medicines, such as ketoconazole, and itraconazole.
- some types of antibiotics, such as clarithromycin, telithromycin, or erythromycin
- other medicines that treat high blood pressure
- other medicines or treatments for ED
- KAMAGRA contains sildenafil, KAMAGRA should not be used with other pulmonary arterial hypertension (PAH) treatments containing sildenafil or any other PDE5 inhibitors (such as tadalafil).

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.
Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

3. How to use KAMAGRA
- Take KAMAGRA exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much KAMAGRA to take and when to take it.
- Your healthcare provider may change your dose if needed.
- Take KAMAGRA about 1 hour before sexual activity. You may take KAMAGRA between 30 minutes to 4 hours before sexual activity if needed.
- KAMAGRA can be taken with or without food. If you take KAMAGRA after a high fat meal (such as a cheeseburger and french fries), KAMAGRA may take a little longer to start working
- **Do not** take KAMAGRA more than 1 time a day.

If you accidentally take too much KAMAGRA, call your doctor or go to the nearest hospital emergency room right away

4. Possible side effects
KAMAGRA can cause serious side effects. Rarely reported side effects include:
- **An erection that will not go away (priapism).** If you have an erection that lasts more than 4 hours, get medical help right away. If it is not treated right away, priapism can permanently damage your penis.
- **Sudden vision loss in one or both eyes.** Sudden vision loss in one or both eyes can be a sign of a serious eye problem called non-arteritic anterior ischemic optic neuropathy (NAION). It is uncertain whether PDE5 inhibitors directly cause the vision loss. Stop taking KAMAGRA and call your healthcare provider right away if you have sudden vision loss in one or both eyes.
- **Sudden hearing decrease or hearing loss.** Some people may also have ringing in their ears (tinnitus) or dizziness. If you have these symptoms, stop taking KAMAGRA and contact a doctor right away.

The most common side effects of KAMAGRA are:
- headache
- flushing
- upset stomach
- abnormal vision, such as changes in color vision (such as having a blue color tinge) and blurred vision
- stuffy or runny nose
- back pain
- muscle pain
- nausea
- dizziness
- rash

In addition, heart attack, stroke, irregular heartbeats and death have happened rarely in men taking KAMAGRA. Most, but not all, of these men had heart problems before taking KAMAGRA. It is not known if KAMAGRA caused these problems.

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all the possible side effects of KAMAGRA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects.

5. How to store KAMAGRA

Keep this medicine out of the sight and reach of children.

Store at a temperature below 30°C. Protect from light.

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

6. Contents of the pack and other information
What KAMAGRA contains:

Kamagra 50 (Sildenafil Citrate Tablets 50 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil 50 mg

Kamagra 100 (Sildenafil Citrate Tablets 100 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil 100 mg

List of Excipients:
Sodium Starch Glycolate (Type A), Povidone, Isopropyl Alcohol, Microcrystalline Cellulose, Purified Talc, Magnesium Stearate, Insta Moistshield Aqua II A22D20470 Green and Purified Water.

What KAMAGRA looks like and contents of the pack
4 Tablets in a Blister Pack in a Printed Carton along with Package Insert.

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : 022-6913 2111/2112 Fax : 022-6913 2070 Email : info@ajantapharma.com	Ajanta Pharma Limited B-4-5-6, MIDC Industrial Area Paithan, Aurangabad, 431148 Dist: Aurangabad Maharashtra, India. Tel : +91-2431-664000 Fax : +91-2431-664100

For any information about this medicinal product, please contact Manufacturing Authorization Holder.

DATE OF PUBLICATION OR REVISION
Aug 18, 2023

KAMAGRA
(Sildenafil Citrate Tablets)

Patient Information Leaflet

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

1. What KAMAGRA is and what it is used for

KAMAGRA is a prescription medicine used to treat erectile dysfunction (ED). You will not get an erection just by taking this medicine. KAMAGRA helps a man with erectile dysfunction get and keep an erection only when he is sexually excited (stimulated).

KAMAGRA is not for use in women or children.

It is not known if KAMAGRA is safe and effective in women or children under 18 years of age.

2. What you need to know before you use Kamagra

KAMAGRA can cause your blood pressure to drop suddenly to an unsafe level if it is taken with certain other medicines. Do not take KAMAGRA if you take any other medicines called “nitrates.” Nitrates are used to treat chest pain (angina). A sudden drop in blood pressure can cause you to feel dizzy, faint, or have a heart attack or stroke.

Do not take KAMAGRA if you take medicines called guanylate cyclase stimulators which include:

Riociguat a medicine that treats pulmonary arterial hypertension and chronic-thromboembolic pulmonary hypertension.

Tell all your healthcare providers that you take KAMAGRA.

If you need emergency medical care for a heart problem, it will be important for your healthcare provider to know when you last took KAMAGRA.

Stop sexual activity and get medical help right away if you get symptoms such as chest pain, dizziness, or nausea during sex.

Sexual activity can put an extra strain on your heart, especially if your heart is already weak from a heart attack or heart disease. Ask your doctor if your heart is healthy enough to handle the extra strain of having sex.

KAMAGRA does not protect you or your partner from getting sexually transmitted diseases, including HIV—the virus that causes AIDS.

Do not take KAMAGRA if you:

• take medicines called nitrates (such as nitroglycerin)

• use street drugs called "poppers" such as amyl nitrate or amyl nitrite, and butyl nitrate

• take any medicines called guanylate cyclase stimulators such as riociguat.

• are allergic to sildenafil, as contained in KAMAGRA and REVATIO, or any of the ingredients in KAMAGRA. See the end of this leaflet for a complete list of ingredients in KAMAGRA.

Before you take KAMAGRA, tell your healthcare provider if you:

• have or have had heart problems such as a heart attack, irregular heartbeat, angina, chest pain, narrowing of the aortic valve or heart failure

• have had heart surgery within the last 6 months

• have pulmonary hypertension

• have had a stroke

• have low blood pressure, or high blood pressure that is not controlled

• have a deformed penis shape

• have had an erection that lasted for more than 4 hours

• have problems with your blood cells such as sickle cell anemia, multiple myeloma, or leukemia

• have retinitis pigmentosa, a rare genetic (runs in families) eye disease

• have ever had severe vision loss, including an eye problem called non-arteritic anterior ischemic optic neuropathy (NAION)

• have bleeding problems

• have or have had stomach ulcers

• have liver problems

• have kidney problems or are having kidney dialysis

• have any other medical conditions

Tell your healthcare provider about all the medicines you take*,

Including prescription and over-the-counter medicines, vitamins, and herbal supplements.

KAMAGRA may affect the way other medicines work, and other medicines may affect the way KAMAGRA works causing side effects. Especially tell your healthcare provider if you take any of the following:

• Medicines called nitrates (see "What is the most important information I should know about KAMAGRA?")

• medicines called guanylate cyclase stimulators, such as riociguat.

• Medicines called alpha blockers such as terazosin, tamsulosin, doxazosin, prazosin, alfuzosin, dutasteride and tamsulosin, or silodosin. Alpha-blockers are sometimes prescribed for prostate problems or high blood pressure. In some patients, the use of KAMAGRA with alpha-blockers can lead to a drop in blood pressure or to fainting.

• medicines called HIV protease inhibitors, such as ritonavir, indinavir sulfate, saquinavir or atazanavir sulfate.

• some types of oral antifungal medicines, such as ketoconazole, and itraconazole.

• some types of antibiotics, such as clarithromycin, telithromycin, or erythromycin

• other medicines that treat high blood pressure

• other medicines or treatments for ED

•KAMAGRA contains sildenafil, KAMAGRA should not be used with other pulmonary arterial hypertension (PAH) treatments containing sildenafil or any other PDE5 inhibitors (such as tadalafil).

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

3. How to use KAMAGRA

- Take KAMAGRA exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much KAMAGRA to take and when to take it.
- Your healthcare provider may change your dose if needed.
- Take KAMAGRA about 1 hour before sexual activity. You may take KAMAGRA between 30 minutes to 4 hours before sexual activity if needed.
- KAMAGRA can be taken with or without food. If you take KAMAGRA after a high fat meal (such as a cheeseburger and french fries), KAMAGRA may take a little longer to start working
- **Do not** take KAMAGRA more than 1 time a day.

If you accidentally take too much KAMAGRA, call your doctor or go to the nearest hospital emergency room right away

4. Possible side effects

KAMAGRA can cause serious side effects. Rarely reported side effects include:

- **An erection that will not go away (priapism).** If you have an erection that lastsmore than 4 hours, get medical help right away. If it is not treated right away, priapism can permanently damage your penis.
- **Sudden vision loss in one or both eyes.** Sudden vision loss in one or both eyes can be a sign of a serious eye problem called non-arteritic anterior ischemic optic neuropathy (NAION). It is uncertain whether PDE5 inhibitors directly cause the vision loss. Stop taking KAMAGRA and call your healthcare provider right away if you have sudden vision loss in one or both eyes.
- **Sudden hearing decrease or hearing loss.** Some people may also have ringing in their ears (tinnitus) or dizziness. If you have these symptoms, stop taking KAMAGRA and contacta doctor right away.

The most common side effects of KAMAGRA are:

- headache
- flushing
- upset stomach
- abnormal vision, such as changes in color vision (such as having a blue color tinge) and blurred vision
- stuffy or runny nose
- back pain
- muscle pain
- nausea
- dizziness
- rash

In addition, heart attack, stroke, irregular heartbeats and death have happened rarely in men taking KAMAGRA. Most, but not all, of these men had heart problems before taking KAMAGRA. It is not known if KAMAGRA caused these problems.

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all the possible side effects of KAMAGRA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects.

5. How to store KAMAGRA

Keep this medicine out of the sight and reach of children.

Store at a temperature below 30°C. Protect from light.

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What KAMAGRA contains:

Kamagra 50 (Sildenafil Citrate Tablets 50 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil ..... 50 mg

Kamagra 100 (Sildenafil Citrate Tablets 100 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil ..... 100 mg

List of Excipients:
Sodium Starch Glycolate (Type A), Povidone, Isopropyl Alcohol, Microcrystalline Cellulose, Purified Talc, Magnesium Stearate, Insta Moistshield Aqua II A22D20470 Green and Purified Water.

What KAMAGRA looks like and contents of the pack
4 Tablets in a Blister Pack in a Printed Carton along with Package Insert.

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : 022-6913 2111/2112 Fax : 022-6913 2070 Email : info@ajantapharma.com	Ajanta Pharma Limited B-4-5-6, MIDC Industrial Area Paithan, Aurangabad, 431 148 Maharashtra, India Tel : +91-2431-664000 Fax : +91-2431-664100

For any information about this medicinal product, please contact Manufacturing Authorization Holder.

DATE OF PUBLICATION OR REVISION
Aug 18, 2023

Serving global healthcare needs with empathy, innovation and technology

Kamagra 50
(Location: Dahej)

ajanta pharma limited

FRONT

TN62941

KAMAGRA

Sildenafil Citrate Tablets

COMPOSITION

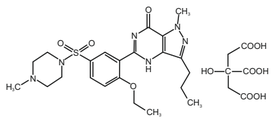
Kamagra 50 (Sildenafil Citrate Tablets 50 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil 50 mg

Kamagra 100 (Sildenafil Citrate Tablets 100 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil 100 mg

DOSAGE FORM
Tablets

Distribution Category: Prescription Only Medicine or POM

DESCRIPTION
Sildenafil Citrate is Phosphodiesterase type 5 (PDE5) inhibitor. The IUPAC name is {1-[[3-(6,7-Dihydro-1-Methyl-7-Oxo-3-Propyl-1HPyrazolo-[4,3-D]-Pyrimidine-5-yl)-4-Ethoxy-Phenyl]Sulfonyl]-4-Methyl Piperazine Citrate}with an empirical formula of C28H38N6O11S and molecular weight is 666.71 g/mol. The structural formula of Sildenafil Citrate is:



EXCIPIENT LIST
Sodium Starch Glycolate (Type A), Povidone, Isopropyl Alcohol, Microcrystalline Cellulose, Purified Talc, Magnesium Stearate, Insta Moistshield Aqua II A22D20470 Green and Purified Water.

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS
KAMAGRA tablet is indicated for the treatment of erectile dysfunction.

POSOLOGY & METHOD OF ADMINISTRATION

Posology
For most patients, the recommended dose is 50 mg taken, as needed, approximately 1 hour before sexual activity. However, KAMAGRA tablets may be taken anywhere from 30 minutes to 4 hours before sexual activity.

The maximum recommended dosing frequency is once per day.

Based on effectiveness and toleration, the dose may be increased to a maximum recommended dose of 100 mg or decreased to 25 mg.

Use with food
KAMAGRA tablets may be taken with or without food.

Dosage Adjustments in Specific Situations
KAMAGRA tablets was shown to potentiate the hypotensive effects of nitrates and its administration in patients who use nitric oxide donors such as organic nitrates or organic nitrites in any form is therefore contraindicated.

When KAMAGRA tablets is co-administered with an alpha-blocker, patients should be stable on alpha-blocker therapy prior to initiating KAMAGRA tablets treatment and KAMAGRA tablets should be initiated at 25 mg.

Dosage Adjustments Due to Drug Interactions
Ritonavir
The recommended dose for ritonavir-treated patients is 25 mg prior to sexual activity and the recommended maximum dose is 25 mg within a 48 hour period because concomitant administration increased the blood levels of sildenafil by 11-fold.

CYP3A4 Inhibitors
Consider a starting dose of 25 mg in patients treated with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or saquinavir) or erythromycin. Clinical data have shown that co-administration with saquinavir or erythromycin increased plasma levels of sildenafil by about 3 fold.

Dosage Adjustments in Special Populations
Consider a starting dose of 25 mg in patients > 65 years, patients with hepatic impairment (e.g., cirrhosis), and patients with severe renal impairment (creatinine clearance <30 mL/minute) because administration of KAMAGRA tablets in these patients resulted in higher plasma levels of sildenafil

Method of administration

For oral use.

The tablets should be chewed before swallowed.

SPECIAL WARNINGS & PRECAUTIONS FOR USE

Cardiovascular
There is a potential for cardiac risk of sexual activity in patients with pre-existing cardiovascular disease. Therefore, treatments for erectile dysfunction, including Sildenafil, should not be generally used in men for whom sexual activity is inadvisable because of their underlying cardiovascular status. The evaluation of erectile dysfunction should include a determination of potential underlying causes and the identification of appropriate treatment following a complete medical assessment.

Sildenafil has systemic vasodilatory properties that resulted in transient decreases in supine blood pressure in healthy volunteers (mean maximum decrease of 8.4/5.5 mmHg). While this normally would be expected to be of little consequence in most patients, prior to prescribing Sildenafil, physicians should carefully consider whether their patients with underlying cardiovascular disease could be affected adversely by such vasodilatory effects, especially in combination with sexual activity.

Use with caution in patients with the following underlying conditions which can be particularly sensitive to the actions of vasodilators including Sildenafil – those with left ventricular outflow obstruction (e.g., aortic stenosis, idiopathic hypertrophic subaortic stenosis) and those with severely impaired autonomic control of blood pressure.

There are no controlled clinical data on the safety or efficacy of Sildenafil in the following groups; if prescribed, this should be done with caution.

- Patients who have suffered a myocardial infarction, stroke, or life-threatening arrhythmia within the last 6 months;
- Patients with resting hypotension (BP <90/50 mmHg) or hypertension (BP >170/110 mmHg);
- Patients with cardiac failure or coronary artery disease causing unstable angina.

Prolonged Erection and Priapism
Prolonged erection greater than 4 hours and priapism (painful erections greater than 6 hours in duration) have been reported infrequently since market approval of Sildenafil. 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.

Sildenafil 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). However, there are no controlled clinical data on the safety or efficacy of Sildenafil in patients with sickle cell or related anemias.

Effects on the Eye
Physicians should advise patients to stop use of all phosphodiesterase type 5 (PDE5) inhibitors, including Sildenafil, and seek medical attention in the event of a sudden loss of vision in one or both eyes. Such an event may be a sign of non-arteritic anterior ischemic optic neuropathy (NAION), a rare condition and a cause of decreased vision including permanent loss of vision, that has been reported rarely post-marketing in temporal association with the use of all PDE5 inhibitors. Based on published literature, the annual incidence of NAION is 2.5-11.8 cases per 100,000 in males aged ≥ 50. An observational case-crossover study evaluated the risk of NAION when PDE5 inhibitor use, as a class, occurred immediately before NAION onset (within 5 half-lives), compared to PDE5 inhibitor use in a prior time period. The results suggest an approximate 2-fold increase in the risk of NAION, with a risk estimate of 2.15 (95% CI 1.06, 4.34). A similar study reported a consistent result, with a risk estimate of 2.27 (95% CI 0.99, 5.20). Other risk factors for NAION, such as the presence of "crowded" optic disc, may have contributed to the occurrence of NAION in these studies. Neither the rare post-marketing reports, nor the association of PDE5 inhibitor use and NAION in the observational studies, substantiate a causal relationship between PDE5 inhibitor use and NAION.

Physicians should consider whether their patients with underlying NAION risk factors could be adversely affected by use of PDE5 inhibitors. Individuals who have already experienced NAION are at increased risk of NAION recurrence. Therefore, PDE5 inhibitors, including Sildenafil, should be used with caution in these patients and only when the anticipated benefits outweigh the risks. Individuals with "crowded" optic disc are also considered at greater risk for NAION compared to the general population, however, evidence is insufficient to support screening of prospective users of PDE5 inhibitors, including Sildenafil, for this uncommon condition.

There are no controlled clinical data on the safety or efficacy of Sildenafil in patients with retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterases); if prescribed, this should be done with caution.

Hearing Loss
Physicians should advise patients to stop taking PDE5 inhibitors, including Sildenafil, and seek prompt medical attention in the event of sudden decrease or loss of hearing. These events, which may be accompanied by tinnitus and dizziness, have been reported in temporal association to the intake of PDE5 inhibitors, including Sildenafil. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors.

Hypotension when Co-administered with Alpha-blockers or Anti-hypertensives
Alpha-blockers
Caution is advised when PDE5 inhibitors are co-administered with alpha-blockers. PDE5 inhibitors, including Sildenafil, and alpha-adrenergic blocking agents are both vasodilators with blood pressure lowering effects. When vasodilators are used in combination, an additive effect on blood pressure may occur. In some patients, concomitant use of these two drug classes can lower blood pressure significantly leading to symptomatic hypotension (e.g.,dizziness, lightheadedness, fainting).
Consideration should be given to the following:

- Patients who demonstrate hemodynamic instability on alpha-blocker therapy alone are at increased risk of symptomatic hypotension with concomitant use of PDE5 inhibitors. Patients should be stable on alpha-blocker therapy prior to initiating a PDE5 inhibitor.
- In those patients who are stable on alpha-blocker therapy, PDE5 inhibitors should be initiated at the lowest dose.
- In those patients already taking an optimized dose of a PDE5 inhibitor, alpha-blocker therapy should be initiated at the lowest dose. Stepwise increase in alpha-blocker dose may be associated with further lowering of blood pressure when taking a PDE5 inhibitor.
- Safety of combined use of PDE5 inhibitors and alpha-blockers may be affected by other variables, including intravascular volume depletion and other anti-hypertensive drugs.

Anti-hypertensives
Sildenafil has systemic vasodilatory properties and may further lower blood pressure in patients taking anti- hypertensive medications.

In a separate drug interaction study, when amlodipine, 5 mg or 10 mg, and Sildenafil, 100 mg were orally administered concomitantly to hypertensive patients mean additional blood pressure reduction of 8 mmHg systolic and 7 mmHg diastolic were noted.

Adverse Reactions with the Concomitant Use of Ritonavir.
The concomitant administration of the protease inhibitor ritonavir substantially increases serum concentrations of sildenafil (11-fold increase in AUC). If Sildenafil is prescribed to patients taking ritonavir, caution should be used. Data from subjects exposed to high systemic levels of sildenafil are limited. Decreased blood pressure, syncope, and prolonged erection were reported in some healthy volunteers exposed to high doses of sildenafil (200-800 mg). To decrease the chance of adverse reactions in patients taking ritonavir, a decrease in sildenafil dosage is recommended.

Combination with other PDE5 Inhibitors or Other Erectile Dysfunction Therapies
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. Such combinations may further lower blood pressure. Therefore, the use of such combinations is not recommended.

Effects on Bleeding
There have been postmarketing reports of bleeding events in patients who have taken sildenafil. A causal relationship between sildenafil and these events has not been established. In humans, sildenafil has no effect on bleeding time when taken alone or with aspirin. However, *in vitro* studies with human platelets indicate that sildenafil potentiates the antiaggregatory effect of sodium nitroprusside (a nitric oxide donor). In addition, the combination of heparin and sildenafil had an additive effect on bleeding time in the anesthetized rabbit, but this interaction has not been studied in humans.

The safety of sildenafil is unknown in patients with bleeding disorders and patients with active peptic ulceration.

Counselling Patients about Sexually Transmitted Diseases
The use of sildenafil offers no protection against sexually transmitted diseases. Counseling of patients about the protective measures necessary to guard against sexually transmitted diseases, including the Human Immunodeficiency Virus (HIV), may be considered.

INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Nitrates
Administration of sildenafil with nitric oxide donors such as organic nitrates or organic nitrites in any form is contraindicated. Consistent with its known effects on the nitric oxide/cGMP pathway, sildenafil was shown to potentiate the hypotensive effects of nitrates.

Alpha-blockers
Use caution when co-administering alpha-blockers with sildenafil because of potential additive blood pressure- lowering effects. When sildenafil is co-administered with an alpha-blocker, patients should be stable on alpha- blocker therapy prior to initiating sildenafil treatment and sildenafil should be initiated at the lowest dose.

Amlodipine
When sildenafil 100 mg was co-administered with amlodipine (5 mg or 10 mg) to hypertensive patients, the mean additional reduction on supine blood pressure was 8 mmHg systolic and 7 mmHg diastolic.

Ritonavir and other CYP3A4 inhibitors
Co-administration of ritonavir, a strong CYP3A4 inhibitor, greatly increased the systemic exposure of sildenafil (11-fold increase in AUC). It is therefore recommended not to exceed a maximum single dose of 25 mg of sildenafil in a 48 hour period.

Co-administration of erythromycin, a moderate CYP3A4 inhibitor, resulted in a 160% and 182% increases in sildenafil Cmax and AUC, respectively. Co-administration of saquinavir, a strong CYP3A4 inhibitor, resulted in 140% and 210% increases in sildenafil Cmax and AUC, respectively. Stronger CYP3A4 inhibitors such as ketoconazole or itraconazole could be expected to have greater effects than seen with saquinavir. A starting dose of 25 mg of sildenafil should be considered in patients taking erythromycin or strong CYP3A4 inhibitors (such as saquinavir, ketoconazole, itraconazole).

Alcohol
In a drug-drug interaction study sildenafil 50 mg given with alcohol 0.5 g/kg in which mean maximum blood alcohol levels of 0.08% was achieved, sildenafil did not potentiate the hypotensive effect of alcohol in healthy volunteers

USE IN SPECIFIC POPULATIONS

Pediatric Use
Sildenafil is not indicated for use in pediatric patients. Safety and effectiveness have not been established in pediatric patients.

Geriatric Use
Healthy elderly volunteers (65 years or over) had a reduced clearance of sildenafil resulting in approximately 84% and 107% higher plasma AUC values of sildenafil and its active N-desmethyl metabolite, respectively, compared to those seen in healthy young volunteers (18-45 years). Due to age-differences in plasma protein binding, the corresponding increase in the AUC of free (unbound) sildenafil and its active N-desmethyl metabolite were 45% and 57%, respectively.

However, since higher plasma levels may increase the incidence of adverse reactions, a starting dose of 25 mg should be considered in older subjects due to the higher systemic exposure.

Renal Impairment
No dose adjustment is required for mild (CLcr=50-80 mL/min) and moderate (CLcr=30-49 mL/min) renal impairment. In volunteers with severe renal impairment (Clcr<30 mL/min), sildenafil clearance was reduced, resulting in higher plasma exposure of sildenafil (~2 fold), approximately doubling of Cmax and AUC. A starting dose of 25 mg should be considered in patients with severe renal impairment.

Hepatic Impairment
In volunteers with hepatic impairment (Child-Pugh Class A and B), sildenafil clearance was reduced, resulting in higher plasma exposure of sildenafil (47% for Cmax and 85% for AUC). The pharmacokinetics of sildenafil in patients with severely impaired hepatic function (Child-Pugh Class C) have not been studied. A starting dose of 25 mg should be considered in patients with any degree of hepatic impairment.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Sildenafil 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 of how they react to Sildenafil, before driving or operating machinery

UNDESIRABLE EFFECTS

The following are discussed in more detail in other sections of the labeling:

- Cardiovascular
- Prolonged Erection and Priapism
- Effects on the Eye
- Hearing Loss
- Hypotension when Co-administered with Alpha-blockers or Anti-hypertensives
- Adverse Reactions with the Concomitant Use of Ritonavir
- Combination with other PDE5 Inhibitors or Other Erectile Dysfunction Therapies
- Effects on Bleeding
- Counseling Patients About Sexually Transmitted Diseases

The most common adverse reactions reported in clinical trials (≥ 2%) are headache, flushing, dyspepsia, abnormal vision, nasal congestion, back pain, myalgia, nausea, dizziness, and rash.

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Sildinafil was administered to over 3700 patients (aged 19-87 years) during pre-marketing clinical trials worldwide. Over 550 patients were treated for longer than one year.

In placebo-controlled clinical studies, the discontinuation rate due to adverse reactions for Sildinafil (2.5%) was not significantly different from placebo (2.3%).

In fixed-dose studies, the incidence of some adverse reactions increased with dose. The type of adverse reactions in flexible-dose studies, which reflect the recommended dosage regimen, was similar to that for fixed- dose studies. At doses above the recommended dose range, adverse reactions were similar to those detailed in Table 1 below but generally were reported more frequently.

Table: Adverse Reactions Reported by ≥2% of Patients Treated with sildenafil and More Frequent than Placebo in Fixed-Dose Phase II/III Studies

Adverse reaction	25mg (n=312)	50mg (n=511)	100mg (n=506)	Placebo (n=607)
Headache	16%	21%	28%	7%
Flushing	10%	19%	18%	2%
Dyspepsia	3%	9%	17%	2%
Abnormal Vision	1%	2%	11%	1%
Nasal Congestion	4%	4%	9%	2%
Back pain	3%	4%	4%	2%
Myalgia	2%	2%	4%	1%
Nausea	2%	3%	3%	1%
Dizziness	3%	4%	3%	2%
Rash	1%	2%	3%	1%

Abnormal Vision: Mild to moderate in severity and transient, predominantly color tinge to vision, but also increased sensitivity to light, or blurred vision.

The following events occurred in <2% of patients in controlled clinical trials; a causal relationship to sildenafil is uncertain. Reported events include those with a plausible relation to drug use; omitted are minor events and reports too imprecise to be meaningful:

Body as a Whole: face edema, photosensitivity reaction, shock, asthenia, pain, chills, accidental fall, abdominal pain, allergic reaction, chest pain, accidental injury.

Cardiovascular: angina pectoris, AV block, migraine, syncope, tachycardia, palpitation, hypotension, postural hypotension, myocardial ischemia, cerebral thrombosis, cardiac arrest, heart failure, abnormal electrocardiogram, and cardiomyopathy.

Digestive: vomiting, glossitis, colitis, dysphagia, gastritis, gastroenteritis, esophagitis, stomatitis, dry mouth, liver function tests abnormal, rectal hemorrhage, gingivitis.

Hemic and Lymphatic: anemia and leukopenia.

Metabolic and Nutritional: thirst, edema, gout, unstable diabetes, hyperglycemia, peripheral edema, hyperuricemia, hypoglycemic reaction, hypernatremia.

Musculoskeletal: arthritis, arthrosis, myalgia, tendon rupture, tenosynovitis, bone pain, myasthenia, synovitis.

Nervous: ataxia, hypertonia, neuralgia, neuropathy, paresthesia, tremor, vertigo, depression, insomnia, somnolence, abnormal dreams, reflexes decreased, hypesthesia.

Respiratory: asthma, dyspnea, laryngitis, pharyngitis, sinusitis, bronchitis, sputum increased, cough increased.

Skin and Appendages: urticaria, herpes simplex, pruritus, sweating, skin ulcer, contact dermatitis, exfoliative dermatitis.

Special Senses: sudden decrease or loss of hearing, mydriasis, conjunctivitis, photophobia, tinnitus, eye pain, ear pain, eye hemorrhage, cataract, dry eyes.

Urogenital: cystitis, nocturia, urinary frequency, breast enlargement, urinary incontinence, abnormal ejaculation, genital edema and anorgasmia.

Analysis of the safety database from controlled clinical trials showed no apparent difference in adverse reactions in patients taking sildenafil with and without anti-hypertensive medication. This analysis was performed retrospectively, and was not powered to detect any pre-specified difference in adverse reactions.

Postmarketing Experience
The following adverse reactions have been identified during post approval use of sildenafil. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events have been chosen for inclusion either due to their seriousness, reporting frequency, lack of clear alternative causation, or a combination of these factors.

Cardiovascular and cerebrovascular
Serious cardiovascular, cerebrovascular, and vascular events, including myocardial infarction, sudden cardiac death, ventricular arrhythmia, cerebrovascular hemorrhage, transient ischemic attack, hypertension, subarachnoid and intracerebral hemorrhages, and pulmonary hemorrhage have been reported post-marketing in temporal association with the use of sildenafil. Most, but not all, of these patients had preexisting cardiovascular risk factors. Many of these events were reported to occur during or shortly after sexual activity, and a few were reported to occur shortly after the use of sildenafil without sexual activity. Others were 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

Pharma Code : 100000 Standard

Direction for Travel

Date	: 23-08-2023
Artist	: SPG
Product	: Kamagra
Actual Size	: 420 x 210 mm
Ref artwork	: -
Colour	: Black
Country	: Tanzania

BACK

activity, to the patient's underlying cardiovascular disease, to a combination of these factors, or to other factors.

Hemic and Lymphatic:
Vaso-occlusive crisis: In a small, prematurely terminated study of sildenafil in patients with pulmonary arterial hypertension (PAH) secondary to sickle cell disease, vaso-occlusive crises requiring hospitalization were more commonly reported in patients who received sildenafil than in those randomized to placebo. The clinical relevance of this finding to men treated with sildenafil for ED is not known.

Nervous: seizure, seizure recurrence, anxiety, and transient global amnesia.

Respiratory: epistaxis

Special senses:

Hearing: Cases of sudden decrease or loss of hearing have been reported postmarketing in temporal association with the use of PDE5 inhibitors, including sildenafil. In some of the cases, medical conditions and other factors were reported that may have also played a role in the otologic adverse events. In many cases, medical follow-up information was limited. It is not possible to determine whether these reported events are related directly to the use of sildenafil, to the patient's underlying risk factors for hearing loss, a combination of these factors, or to other factors.

***Ocular*:** diplopia, temporary vision loss/decreased vision, ocular redness or bloodshot appearance, ocular burning, ocular swelling/pressure, increased intraocular pressure, retinal edema, retinal vascular disease or bleeding, and vitreous traction /detachment.

Non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, has been reported rarely post-marketing in temporal association with the use of phosphodiesterase type 5 (PDE5) inhibitors, including sildenafil.

Most, but not all, of these patients had underlying anatomic or vascular risk factors for developing NAION, including but not necessarily limited to: low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking.

Urogenital:
Prolonged erection, priapism

OVERDOSE
In published studies with healthy volunteers of single doses up to 800 mg, adverse reactions were similar to those seen at lower doses but incidence rates and severities were 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.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC

Pharmacotherapeutic group: Genito Urinary System and Sex Hormones, Urologicals; Drugs used in erectile dysfunction, ATC Code: G04B E03.

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 enhances the effect of NO by inhibiting 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. 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.

In addition to human corpus cavernosum smooth muscle, PDE5 is also found in other tissues including platelets, vascular and visceral smooth muscle, and skeletal muscle, brain, heart, liver, kidney, lung, pancreas, prostate, bladder, testis, and seminal vesicle. The inhibition of PDE5 in some of these tissues by sildenafil may be the basis for the enhanced platelet antiaggregatory activity of NO observed *in vitro*, an inhibition of platelet thrombus formation *in vivo* and peripheral arterial-venous dilatation *in vivo*.

PHARMACOKINETIC
Sildenafil is rapidly absorbed after oral administration, with a mean absolute bioavailability of 41% (range 25- 63%). The pharmacokinetics of sildenafil are dose-proportional over the recommended dose range. It is eliminated predominantly by hepatic metabolism (mainly CYP3A4) and is converted to an active metabolite with properties similar to the parent, sildenafil. Both sildenafil and the metabolite have terminal half-lives of about 4 hours.

Absorption & Distribution
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. When Sildenafil is taken with a high fat meal, the rate of absorption is reduced, with a mean delay in Tmax of 60 minutes and a mean reduction in Cmax of 29%. 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 drug concentrations.

Based upon measurements of sildenafil in semen of healthy volunteers 90 minutes after dosing, less than 0.001% of the administered dose may appear in the semen of patients.

Metabolism & Excretion
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. Plasma concentrations of this metabolite are approximately 40% of those seen for sildenafil, so that the metabolite accounts for about 20% of sildenafil's pharmacologic effects.

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). Similar values for pharmacokinetic parameters were seen in normal volunteers and in the patient population, using a population pharmacokinetic approach.

PRECLINICAL SAFETY DATA

Carcinogenesis
Sildenafil was not carcinogenic when administered to rats for 24 months at a dose resulting in total systemic drug exposure (AUCs) for unbound sildenafil and its major metabolite of 20- and 38-times, for male and female rats, respectively, the exposures observed in human males given the Maximum Recommended Human Dose (MRHD) of 100 mg. Sildenafil was not carcinogenic when administered to mice for 18-21 months at dosages up to the Maximum Tolerated Dose (MTD) of 10 mg/kg/day, approximately 0.4 times the MRHD on a mg/m^2 basis in a 50 kg subject.

Mutagenesis
Sildenafil was negative in in vitro bacterial and Chinese hamster ovary cell assays to detect mutagenicity, and in vitro human lymphocytes and in vivo mouse micronucleus assays to detect clastogenicity.

Impairment of Fertility
There was no impairment of fertility in rats given sildenafil up to 60 mg/kg/day for 36 days to females and 102 days to males, a dose producing an AUC value of more than 25 times the human male AUC.

PHARMACEUTICAL PARTICULARS
INCOMPATIBILITY
Not applicable.

SHELF LIFE
36 months

STORAGE CONDITION
Store at a temperature below 30°C. Protect from light.

NATURE AND CONTENTS OF CONTAINER
4 Tablets in a Blister Pack in a Printed Carton along with Package Insert.

MANUFACTURING AUTHORISATON HOLDER AND MANUFACTURER

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : 022-6913 2111/2112 Fax : 022-6913 2070 Email : info@ajantapharma.com	Ajanta Pharma Limited Z/103/A, Dahej SEZ II, Bharuch-392 130, Dist. Bharuch, Gujarat State. Tel : 91-0361-7188500/ +91-0361-7188511

Last Revision Date: Aug 18, 2023

KAMAGRA

Sildenafil Citrate Tablets

Patient Information Leaflet

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

1. What KAMAGRA is and what it is used for
KAMAGRA is a prescription medicine used to treat erectile dysfunction (ED). You will not get an erection just by taking this medicine. KAMAGRA helps a man with erectile dysfunction get and keep an erection only when he is sexually excited (stimulated).

KAMAGRA is not for use in women or children.

It is not known if KAMAGRA is safe and effective in women or children under 18 years of age.

2. What you need to know before you use Kamagra
KAMAGRA can cause your blood pressure to drop suddenly to an unsafe level if it is taken with certain other medicines. Do not take KAMAGRA if you take any other medicines called "nitrates." Nitrates are used to treat chest pain (angina). A sudden drop in blood pressure can cause you to feel dizzy, faint, or have a heart attack or stroke.

Do not take KAMAGRA if you take medicines called guanylate cyclase stimulators which include:

Riociguat a medicine that treats pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

Tell all your healthcare providers that you take KAMAGRA.

If you need emergency medical care for a heart problem, it will be important for your healthcare provider to know when you last took KAMAGRA.

Stop sexual activity and get medical help right away if you get symptoms such as chest pain, dizziness, or nausea during sex.

Sexual activity can put an extra strain on your heart, especially if your heart is already weak from a heart attack or heart disease. Ask your doctor if your heart is healthy enough to handle the extra strain of having sex.

KAMAGRA does not protect you or your partner from getting sexually transmitted diseases, including HIV—the virus that causes AIDS.

Do not take KAMAGRA if you:
- take medicines called nitrates (such as nitroglycerin)
- use street drugs called "poppers" such as amyl nitrate or amyl nitrite, and butyl nitrate
- take any medicines called guanylate cyclase stimulators such as riociguat.
- are allergic to sildenafil, as contained in KAMAGRA and REVATIO, or any of the ingredients in KAMAGRA. See the end of this leaflet for a complete list of ingredients in KAMAGRA.

Before you take KAMAGRA, tell your healthcare provider if you:
- have or have had heart problems such as a heart attack, irregular heartbeat, angina, chest pain, narrowing of the aortic valve or heart failure
- have had heart surgery within the last 6 months
- have pulmonary hypertension
- have had a stroke
- have low blood pressure, or high blood pressure that is not controlled
- have a deformed penis shape
- have had an erection that lasted for more than 4 hours
- have problems with your blood cells such as sickle cell anemia, multiple myeloma, or leukemia
- have retinitis pigmentosa, a rare genetic (runs in families) eye disease
- have ever had severe vision loss, including an eye problem called non-arteritic anterior ischemic optic neuropathy (NAION)
- have bleeding problems
- have or have had stomach ulcers
- have liver problems
- have kidney problems or are having kidney dialysis
- have any other medical conditions

Tell your healthcare provider about all the medicines you take*,
Including prescription and over-the-counter medicines, vitamins, and herbal supplements.
KAMAGRA may affect the way other medicines work, and other medicines may affect the way KAMAGRA works causing side effects. Especially tell your healthcare provider if you take any of the following:
- Medicines called nitrates (see "What is the most important information I should know about KAMAGRA?")
- medicines called guanylate cyclase stimulators, such as riociguat.
- Medicines called alpha blockers such as terazosin, tamsulosin, doxazosin, prazosin, alfuzosin, dutasteride and tamsulosin, or silodosin. Alpha-blockers are sometimes prescribed for prostate problems or high blood pressure. In some patients, the use of KAMAGRA with alpha-blockers can lead to a drop in blood pressure or to fainting.
- medicines called HIV protease inhibitors, such as ritonavir, indinavir sulfate, saquinavir or atazanavir sulfate.
- some types of oral antifungal medicines, such as ketoconazole, and itraconazole.
- some types of antibiotics, such as clarithromycin, telithromycin, or erythromycin
- other medicines that treat high blood pressure
- other medicines or treatments for ED
- KAMAGRA contains sildenafil, KAMAGRA should not be used with other pulmonary arterial hypertension (PAH) treatments containing sildenafil or any other PDE5 inhibitors (such as tadalafil).

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.
Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

3. How to use KAMAGRA
- Take KAMAGRA exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much KAMAGRA to take and when to take it.
- Your healthcare provider may change your dose if needed.
- Take KAMAGRA about 1 hour before sexual activity. You may take KAMAGRA between 30 minutes to 4 hours before sexual activity if needed.
- KAMAGRA can be taken with or without food. If you take KAMAGRA after a high fat meal (such as a cheeseburger and french fries), KAMAGRA may take a little longer to start working
- **Do not** take KAMAGRA more than 1 time a day.

If you accidentally take too much KAMAGRA, call your doctor or go to the nearest hospital emergency room right away

4. Possible side effects
KAMAGRA can cause serious side effects. Rarely reported side effects include:
- **An erection that will not go away (priapism).** If you have an erection that lasts more than 4 hours, get medical help right away. If it is not treated right away, priapism can permanently damage your penis.
- **Sudden vision loss in one or both eyes.** Sudden vision loss in one or both eyes can be a sign of a serious eye problem called non-arteritic anterior ischemic optic neuropathy (NAION). It is uncertain whether PDE5 inhibitors directly cause the vision loss. Stop taking KAMAGRA and call your healthcare provider right away if you have sudden vision loss in one or both eyes.
- **Sudden hearing decrease or hearing loss.** Some people may also have ringing in their ears (tinnitus) or dizziness. If you have these symptoms, stop taking KAMAGRA and contact a doctor right away.

The most common side effects of KAMAGRA are:
- headache
- flushing
- upset stomach
- abnormal vision, such as changes in color vision (such as having a blue color tinge) and blurred vision
- stuffy or runny nose
- back pain
- muscle pain
- nausea
- dizziness
- rash

In addition, heart attack, stroke, irregular heartbeats and death have happened rarely in men taking KAMAGRA. Most, but not all, of these men had heart problems before taking KAMAGRA. It is not known if KAMAGRA caused these problems.

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all the possible side effects of KAMAGRA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects.

5. How to store KAMAGRA

Keep this medicine out of the sight and reach of children.

Store at a temperature below 30°C. Protect from light.

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

6. Contents of the pack and other information
What KAMAGRA contains:

Kamagra 50 (Sildenafil Citrate Tablets 50 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil 50 mg

Kamagra 100 (Sildenafil Citrate Tablets 100 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil 100 mg

List of Excipients:
Sodium Starch Glycolate (Type A), Povidone, Isopropyl Alcohol, Microcrystalline Cellulose, Purified Talc, Magnesium Stearate, Insta Moistshield Aqua II A22D20470 Green and Purified Water.

What KAMAGRA looks like and contents of the pack
4 Tablets in a Blister Pack in a Printed Carton along with Package Insert.

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : 022-6913 2111/2112 Fax : 022-6913 2070 Email : info@ajantapharma.com	Ajanta Pharma Limited Z/103/A, Dahej SEZ II, Bharuch-392 130, Dist. Bharuch, Gujarat State. Tel : 91-0361-7188500/ +91-0361-7188511

For any information about this medicinal product, please contact Manufacturing Authorization Holder.

DATE OF PUBLICATION OR REVISION
Aug 18, 2023

KAMAGRA
(Sildenafil Citrate Tablets)

Patient Information Leaflet

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

1. What KAMAGRA is and what it is used for

KAMAGRA is a prescription medicine used to treat erectile dysfunction (ED). You will not get an erection just by taking this medicine. KAMAGRA helps a man with erectile dysfunction get and keep an erection only when he is sexually excited (stimulated).

KAMAGRA is not for use in women or children.

It is not known if KAMAGRA is safe and effective in women or children under 18 years of age.

2. What you need to know before you use Kamagra

KAMAGRA can cause your blood pressure to drop suddenly to an unsafe level if it is taken with certain other medicines. Do not take KAMAGRA if you take any other medicines called “nitrates.” Nitrates are used to treat chest pain (angina). A sudden drop in blood pressure can cause you to feel dizzy, faint, or have a heart attack or stroke.

Do not take KAMAGRA if you take medicines called guanylate cyclase stimulators which include:

Riociguat a medicine that treats pulmonary arterial hypertension and chronic-thromboembolic pulmonary hypertension.

Tell all your healthcare providers that you take KAMAGRA.

If you need emergency medical care for a heart problem, it will be important for your healthcare provider to know when you last took KAMAGRA.

Stop sexual activity and get medical help right away if you get symptoms such as chest pain, dizziness, or nausea during sex.

Sexual activity can put an extra strain on your heart, especially if your heart is already weak from a heart attack or heart disease. Ask your doctor if your heart is healthy enough to handle the extra strain of having sex.

KAMAGRA does not protect you or your partner from getting sexually transmitted diseases, including HIV—the virus that causes AIDS.

Do not take KAMAGRA if you:

• take medicines called nitrates (such as nitroglycerin)

• use street drugs called "poppers" such as amyl nitrate or amyl nitrite, and butyl nitrate

• take any medicines called guanylate cyclase stimulators such as riociguat.

• are allergic to sildenafil, as contained in KAMAGRA and REVATIO, or any of the ingredients in KAMAGRA. See the end of this leaflet for a complete list of ingredients in KAMAGRA.

Before you take KAMAGRA, tell your healthcare provider if you:

• have or have had heart problems such as a heart attack, irregular heartbeat, angina, chest pain, narrowing of the aortic valve or heart failure

• have had heart surgery within the last 6 months

• have pulmonary hypertension

• have had a stroke

• have low blood pressure, or high blood pressure that is not controlled

• have a deformed penis shape

• have had an erection that lasted for more than 4 hours

• have problems with your blood cells such as sickle cell anemia, multiple myeloma, or leukemia

• have retinitis pigmentosa, a rare genetic (runs in families) eye disease

• have ever had severe vision loss, including an eye problem called non-arteritic anterior ischemic optic neuropathy (NAION)

• have bleeding problems

• have or have had stomach ulcers

• have liver problems

• have kidney problems or are having kidney dialysis

• have any other medical conditions

Tell your healthcare provider about all the medicines you take*,

Including prescription and over-the-counter medicines, vitamins, and herbal supplements.

KAMAGRA may affect the way other medicines work, and other medicines may affect the way KAMAGRA works causing side effects. Especially tell your healthcare provider if you take any of the following:

• Medicines called nitrates (see "What is the most important information I should know about KAMAGRA?")

• medicines called guanylate cyclase stimulators, such as riociguat.

• Medicines called alpha blockers such as terazosin, tamsulosin, doxazosin, prazosin, alfuzosin, dutasteride and tamsulosin, or silodosin. Alpha-blockers are sometimes prescribed for prostate problems or high blood pressure. In some patients, the use of KAMAGRA with alpha-blockers can lead to a drop in blood pressure or to fainting.

• medicines called HIV protease inhibitors, such as ritonavir, indinavir sulfate, saquinavir or atazanavir sulfate.

• some types of oral antifungal medicines, such as ketoconazole, and itraconazole.

• some types of antibiotics, such as clarithromycin, telithromycin, or erythromycin

• other medicines that treat high blood pressure

• other medicines or treatments for ED

•KAMAGRA contains sildenafil, KAMAGRA should not be used with other pulmonary arterial hypertension (PAH) treatments containing sildenafil or any other PDE5 inhibitors (such as tadalafil).

Ask your healthcare provider or pharmacist for a list of these medicines, if you are not sure.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

3. How to use KAMAGRA

- Take KAMAGRA exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much KAMAGRA to take and when to take it.
- Your healthcare provider may change your dose if needed.
- Take KAMAGRA about 1 hour before sexual activity. You may take KAMAGRA between 30 minutes to 4 hours before sexual activity if needed.
- KAMAGRA can be taken with or without food. If you take KAMAGRA after a high fat meal (such as a cheeseburger and french fries), KAMAGRA may take a little longer to start working
- **Do not** take KAMAGRA more than 1 time a day.

If you accidentally take too much KAMAGRA, call your doctor or go to the nearest hospital emergency room right away

4. Possible side effects

KAMAGRA can cause serious side effects. Rarely reported side effects include:

- **An erection that will not go away (priapism).** If you have an erection that lastsmore than 4 hours, get medical help right away. If it is not treated right away, priapism can permanently damage your penis.
- **Sudden vision loss in one or both eyes.** Sudden vision loss in one or both eyes can be a sign of a serious eye problem called non-arteritic anterior ischemic optic neuropathy (NAION). It is uncertain whether PDE5 inhibitors directly cause the vision loss. Stop taking KAMAGRA and call your healthcare provider right away if you have sudden vision loss in one or both eyes.
- **Sudden hearing decrease or hearing loss.** Some people may also have ringing in their ears (tinnitus) or dizziness. If you have these symptoms, stop taking KAMAGRA and contacta doctor right away.

The most common side effects of KAMAGRA are:

- headache
- flushing
- upset stomach
- abnormal vision, such as changes in color vision (such as having a blue color tinge) and blurred vision
- stuffy or runny nose
- back pain
- muscle pain
- nausea
- dizziness
- rash

In addition, heart attack, stroke, irregular heartbeats and death have happened rarely in men taking KAMAGRA. Most, but not all, of these men had heart problems before taking KAMAGRA. It is not known if KAMAGRA caused these problems.

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all the possible side effects of KAMAGRA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects.

5. How to store KAMAGRA

Keep this medicine out of the sight and reach of children.

Store at a temperature below 30°C. Protect from light.

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What KAMAGRA contains:

Kamagra 50 (Sildenafil Citrate Tablets 50 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil ..... 50 mg

Kamagra 100 (Sildenafil Citrate Tablets 100 mg)
Each film coated tablet contains:
Sildenafil Citrate
equivalent to Sildenafil ..... 100 mg

List of Excipients:
Sodium Starch Glycolate (Type A), Povidone, Isopropyl Alcohol, Microcrystalline Cellulose, Purified Talc, Magnesium Stearate, Insta Moistshield Aqua II A22D20470 Green and Purified Water.

What KAMAGRA looks like and contents of the pack
4 Tablets in a Blister Pack in a Printed Carton along with Package Insert.

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : 022-6913 2111/2112 Fax : 022-6913 2070 Email : info@ajantapharma.com	Ajanta Pharma Limited Z/103/A, Dahej SEZ II, Bharuch-392 130, Dist. Bharuch, Gujarat State. Tel : 91-0361-7188500/ +91-0361-7188511

For any information about this medicinal product, please contact Manufacturing Authorization Holder.

DATE OF PUBLICATION OR REVISION
Aug 18, 2023

KAMAGRA 100 (Sildenafil Citrate Tablets 100 mg)	
Module 1	Administrative Information and Product Information
Section 1.6	Product Information

1.6.4 Mock -ups & specimens

Please find enclosed herewith the artwork of Carton.