**APPROVED**
**The Order of Ministry of Health of Ukraine**
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# INSTRUCTION
## for medical use

## MOGININ®

***Composition:***
*active substance:* sildenafil;
1 tablet contains sildenafil citrate equivalent to sildenafil 50 mg or 100 mg;
*excipients:* microcrystalline cellulose, dibasic calcium phosphate anhydrous, croscarmellose sodium, hypromellose, magnesium stearate, Opadry 03K80814 blue: hypromellose, titanium dioxide (E 171), triacetin, indigo carmine (E 132).

**Pharmaceutical form.** Film coated tablets.
*Main physicochemical properties:* blue film coated round biconvex tablets smooth on both sides.

**Pharmacotherapeutic group.**
Drugs used in erectile dysfunction. Sildenafil. ATC code G04B E03.

***Pharmacological properties.***
*Pharmacodynamics.*
Mechanism of action. Sildenafil is an oral drug used to treat erectile dysfunction. In combination with sexual stimulation the drug restores the decreased erectile function by increasing blood flow to the penis.
The physiological mechanism that causes erection includes the release of nitric oxide (NO) in the cavernous bodies during sexual stimulation. The released nitric oxide activates the enzyme guanylate cyclase, which stimulates increase in the levels of cyclic guanosine monophosphate (cGMP) which, in turn, causes relaxation of smooth muscles of the cavernous bodies, promoting blood flow.
Sildenafil is a potent and selective inhibitor of type 5 cGMP specific phosphodiesterase (PDE5) in cavernous bodies, where PDE5 is responsible for the decay of cGMP. Effects of sildenafil on erections are peripheral in nature. Sildenafil does not cause immediate relaxation effect on isolated human cavernous bodies, but strongly enhances the relaxation effect of NO on this tissue. Upon activation of metabolic pathways of NO/cGMP that happens during sexual stimulation, inhibition of PDE5 by sildenafil leads to increased level of cGMP in the cavernous bodies. Thus, sexual arousal is required to obtain the necessary pharmacological effect of sildenafil.
Effect on pharmacodynamics. Sildenafil is known to have selective effect on PDE5, which takes active part in the erection process. The effect of sildenafil on PDE5 is more potent than on other known phosphodiesterases. This effect is 10 times more potent than the effect on PDE6 which is involved in the process of photoconversion in the retina. When using the maximum recommended doses, selectivity of sildenafil to PDE5 is 80 times higher than the selectivity to PDE1, 700 times higher than to PDE2, PDE3, PDE 4, PDE7, PDE8, PDE9 and PDE11. In particular, the selectivity of sildenafil to PDE5 in 4000 times higher than its selectivity to PDE3, cGMP-specific phosphodiesterase isoform, involved in the regulation of cardiac contractility.
*Pharmacokinetics.*
Absorption. Sildenafil is rapidly absorbed. Maximum plasma concentrations ($C_{max}$) are reached within 30–120 minutes (medial of 60 minutes) after its oral use under fasting conditions. Mean absolute bioavailability after oral use is 41% (with the range of values from 25 to 63%). In the recommended

dosage range AUS and $C_{max}$ values of sildenafil after its oral use increase proportionally to the dose.
When using sildenafil with meal, the degree of absorption is reduced with mean increase in $T_{max}$ to 60 minutes and mean decrease in $C_{max}$ by 29%.
Distribution. Mean steady-state volume of distribution ($V_d$) is 105 litres, showing the distribution of the drug in the body tissues. After single oral administration of sildenafil 100 mg, mean maximum total plasma concentration of sildenafil is approximately 440 ng/ml (variability index is 40%). Since binding of sildenafil and its main N-desmethyl metabolite with plasma proteins is 96%, mean maximum plasma concentration of free sildenafil is 18 ng/ml (38 nmol). The degree of protein binding is independent of total concentration of sildenafil.
In healthy volunteers receiving 100 mg single dose of sildenafil, less than 0.0002% (average 188 ng) of the administered dose was present in ejaculate 90 minutes after dosing.
Biotransformation. Metabolism of sildenafil is mainly mediated by liver microsomal isoenzymes CYP3A4 (major pathway) and CYP2C9 (minor pathway). The major circulating metabolite is formed by N-demethylation of sildenafil. The selectivity of the metabolite for PDE5 is comparable to the selectivity of sildenafil, and the activity of the metabolite for PDE5 is approximately 50% of the activity of the starting material. Plasma concentrations of this metabolite are approximately 40% of sildenafil plasma concentrations. The N-demethylated metabolite undergoes further metabolism, and its half-life is approximately 4 hours.
Elimination. Total clearance of sildenafil is 41 L/hour, causing its half-life period duration of 3–5 hours. Both after oral and intravenous administration, sildenafil in the form of metabolites is excreted mainly in the feces (approximately 80% of the administered oral dose) and to a lesser extent in the urine (approximately 13% of the administered oral dose).
*Pharmacokinetics in special groups of patients.*
Elderly patients. Healthy elderly volunteers (65 years or over) had a reduced clearance of sildenafil, 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 was approximately 40%.
Renal insufficiency. In volunteers with mild to moderate renal impairment (creatinine clearance is 30–80 mL/min), the pharmacokinetics of sildenafil were not altered after receiving a 50 mg single oral dose. The mean AUC and $C_{max}$ of the N-desmethyl metabolite increased 126% and 73% respectively, compared to age-matched volunteers with no renal impairment. However, due to high inter-subject variability, these differences were not statistically significant. In volunteers with severe renal impairment (creatinine clearance < 30 mL/min), sildenafil clearance was reduced, resulting in mean increases in AUC and $C_{max}$ of 100% and 88% respectively compared to age-matched volunteers with no renal impairment. In addition, N-desmethyl metabolite AUC and $C_{max}$ values were significantly increased by 200% and 79% respectively.
Hepatic insufficiency. Hepatic insufficiency. In volunteers with mild to moderate hepatic cirrhosis (Child-Pugh A and B) sildenafil clearance was reduced, resulting in increases in AUC (84%) and $C_{max}$ (47%) compared to age-matched volunteers with no hepatic impairment. The pharmacokinetics of sildenafil in patients with severely impaired hepatic function has not been studied.

**Clinical characteristics.**
***Indications.***
Moginin® is recommended for men with erectile dysfunction, defined as the inability to achieve or maintain an erection of the penis necessary for successful sexual intercourse.
Sexual arousal is necessary for the effective action of Moginin®.

***Contraindications.***
- Hypersensitivity to the active substance or any of the excipients of the drug.
- Concomitant use with nitric oxide donors (such as amyl nitrite) or nitrates in any form is contraindicated since sildenafil is known to affect the ways of metabolism of nitric acid/cyclic guanosine monophosphate (cGMP) and potentiate the hypotensive effect of nitrates.
- Concomitant use of PDE5 inhibitors (including sildenafil) with guanylate cyclase stimulants such as

riociguate is contraindicated as it may lead to symptomatic hypotension (see section "Interaction with other medicinal products and other forms of interaction").
- Conditions when sexual activity is inadvisable (e.g. severe cardiovascular disorders such as unstable angina or severe heart failure).
- Loss of vision in one eye due to non-arteritic anterior ischaemic optic neuropathy, regardless whether this condition is associated with prior use of PDE5 inhibitors.
- Such diseases as severe live dysfunction, arterial hypotension (blood pressure below 90/50 mm Hg), recent stroke or myocardial infarction and known inherited retinal degenerative diseases, such as retinitis pigmentosa, (some patients may have genetic disorders of retinal phosphodiesterases) because safety of sildenafil has not been investigated in these subgroups of patients.

***Interaction with other medicinal products and other forms of interaction.***

*Effect of other medicinal products on sildenafil.*

*In vitro* studies.

Sildenafil is metabolized primarily by isoform 3A4 (main pathway) and isoform 2C9 (secondary pathway) of the cytochrome P450 (CYP). Therefore the inhibitors of these isoenzymes can reduce sildenafil clearance, whereas inducers of these isoenzymes may increase sildenafil clearance.

*In vivo* studies.

Reduction in sildenafil clearance has been shown in its simultaneous use with CYP3A4 inhibitors (such as ketoconazole, erythromycin, cimetidine). Although in concomitant use of sildenafil and CYP3A4 inhibitors no increase in the frequency of adverse effects has been seen, the recommended initial dose of sildenafil is 25 mg.

Concomitant use of HIV protease inhibitor ritonavir, a very potent P450 inhibitor, in steady state concentration (500 mg 1 time per day) and sildenafil (a single dose of 100 mg) led to an increase in sildenafil $C_{max}$ by 300% (4-fold) and AUC by 1000% (11-fold). After 24 hours, plasma levels of sildenafil were still approximately 200 ng/ml, compared to about 5 ng/ml characteristic of the use of sildenafil alone, which corresponds to a significant effect of ritonavir on a wide spectrum of P450 substrates. Sildenafil has no effect on the pharmacokinetics of ritonavir. Given these pharmacokinetic data concomitant use of sildenafil and ritonavir is not recommended; in any case, the maximum dose of sildenafil in no circumstances should exceed 25 mg within 48 hours.

Concomitant use of HIV-protease inhibitor saquinavir, CYP3A4 inhibitor, at a dose that provides the steady-state concentration (1200 mg three times per day) and sildenafil (a single dose of 100 mg) led to an increase in sildenafil $C_{max}$ by 140% and an increase in systemic exposure (AUC) of sildenafil by 210%. No effect of sildenafil on pharmacokinetics of saquinavir has been found (see section "Administration and dosage"). It is assumed that more potent inhibitors of CYP3A4, such as ketoconazole and itraconazole, will have a more pronounced effect.

When using sildenafil (a single dose of 100 mg) and erythromycin, a specific CYP3A4 inhibitor, in the steady state (500 mg two times per day during 5 days) an increase in systemic exposure (AUC) of sildenafil by 182% has been seen. In healthy male volunteers, no effect of azithromycin (500 mg per day during 3 days) on AUC, $C_{max}$, $T_{max}$, elimination rate constant and further half-life of sildenafil or its main circulating metabolite has been observed. Cimetidine (cytochrome P450 inhibitor and nonspecific CYP3A4 inhibitor) at a dose of 800 mg concomitantly used with sildenafil at a dose of 50 mg in healthy volunteers increased plasma concentrations of sildenafil by 56%.

Grapefruit juice is a weak inhibitor of CYP3A4 in the intestinal wall and it may cause moderate increase in plasma levels of sildenafil.

Single use of antacids (magnesium hydroxide/aluminum hydroxide) does not affect the bioavailability of sildenafil.

Though there have been no studies of specific interaction with all medicinal products, according to the data of population pharmacokinetic analysis, pharmacokinetics of sildenafil remained unchanged in case if its concomitant use with medicinal products belonging to the group of CYP2C9 inhibitors (tolbutamide, warfarin, phenytoin), the group of CYP2D6 inhibitors (such as selective serotonin reuptake inhibitors, tricyclic antidepressants), the group of thiazide and thiazide-like diuretics, loop and potassium-sparing diuretics, angiotensin-converting enzyme inhibitors, calcium antagonists, beta-adrenergic receptors antagonists or inducers of CYP450 metabolism (such as rifampicin, barbiturates).

Concomitant use of endothelin antagonist, bosentan, (moderate inducer of CYP3A4, CYP2C9, and probably CYP2C19) at a dose that provides steady state concentration (125 mg twice per day) with sildenafil at a dose that provides steady state concentration (80 mg three times per day) resulted in a decrease of AUC and $C_{max}$ values of sildenafil by 62.6% and 55.4%, respectively. Therefore, concomitant administration of strong CYP3A4 inducers, such as rifampin, is expected to cause greater decreases in plasma concentrations of sildenafil.
Nicorandil is a hybrid of calcium channel activator and nitrate. The nitrate component determines the possibility of its serious interaction with sildenafil.
*Effect of sildenafil on other medicinal products.*
*In vitro* studies.
Sildenafil is a weak inhibitor of 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 (IK50> 150 μmol) isoforms of cytochrome P450. Since peak plasma concentrations of sildenafil is equal to about 1 μmol, the effect of sildenafil on clearance of substrates of these isoenzymes is unlikely.
There are no data regarding the interaction between sildenafil and such nonspecific phosphodiesterase inhibitors as theophylline and dipyridamole.
*In vivo* studies.
Since it is known that sildenafil affects the metabolism of nitric oxide/cyclic guanosine monophosphate (cGMP), it has been found that sildenafil potentiates the hypotensive effect of nitrates, therefore, its concomitant use with nitric oxide donors or nitrates in any form is contraindicated (see section "Contraindications").
Riociguate. There are preclinical data on the additive systemic effect of lowering blood pressure with concomitant use of PDE5 inhibitors with reciguate. Clinical trials have shown that riociguate potentiates the hypotensive effect of PDE5 inhibitors. In population studies, there was no evidence of a favorable clinical effect from the combined use of PDE5 inhibitors with riociguate. Concomitant use of riociguat with PDE5 inhibitors (including sildenafil) is contraindicated (see section "Contraindications").
Concomitant use of sildenafil and α-adrenoceptor blockers may lead to the development of symptomatic hypotension in some predisposed patients. This reaction most often occurred within 4 hours after sildenafil administration (see sections "Special warnings and precautions for use" and "Admnistration and dosage"). In 3 drug-specific interaction studies, the α-adrenoceptor blocker doxazosin (4 mg and 8 mg) and sildenafil (25 mg, 50 mg and 100 mg) were co-administered to patients with benign prostatic hyperplasia whose stabilization was achieved with doxazosin. In these populations, there was a mean additional reduction in blood pressure in the supine position at 7/7 mm Hg, 9/5 mm Hg and 8/4 mm Hg and the average decrease in blood pressure in the position of the patient standing at 6/6 mm Hg, 11/4 mm Hg, 4/5 mm Hg respectively. Symptomatic orthostatic hypotension has sometimes been reported with concomitant use of sildenafil and doxazosin in patients whose stabilization was achieved with doxazosin. These reports included cases of dizziness and fainting, but without syncope.
No significant interactions were shown when sildenafil (50 mg) was co-administered with tolbutamide (250 mg) or warfarin (40 mg), which are metabolized by CYP2C9.
Sildenafil (50 mg) did not potentiate the increase in bleeding time caused by acetyl salicylic acid (150 mg).
Sildenafil (50 mg) did not potentiate the hypotensive effects of alcohol in healthy volunteers with mean maximum blood ethanol levels of 80 mg/dl.
No difference in the side effect profile in patients taking sildenafil compared to placebo treatment has been observed in concomitant use of such classes of antihypertensive medication as diuretics, beta-blockers, ACE inhibitors, angiotensin II antagonists, antihypertensive medicinal products (vasodilator and centrally-acting), adrenergic neuron blockers, calcium channel blockers and alpha-adrenoceptor blockers.
In a specific interaction study, where sildenafil (100 mg) was co-administered with amlodipine in hypertensive patients, there was an additional reduction on supine systolic blood pressure of 8 mmHg. The corresponding reduction in supine diastolic blood pressure was 7 mmHg. These additional blood pressure reductions were of a similar magnitude to those seen when sildenafil was administered alone to healthy volunteers.
Sildenafil at a dose of 100 mg had no effect on pharmacokinetic values of HIV-protease inhibitors, saquinavir and ritonavir, both of which are CYP3A4 substrates.

In male volunteers the use of sildenafil at steady state (80 mg three times a day) increased bosentan AUC and $C_{max}$ (125 mg two times a day) by 49.8% and 42%, respectively.

***Special warnings and precautions for use.***
A medical history and physical examination should be undertaken to diagnose erectile dysfunction and determine potential underlying causes, before pharmacological treatment is considered.
*Cardiovascular risk factors.*
Prior to initiating any treatment for erectile dysfunction, physicians should consider the cardiovascular status of their patients, since there is a degree of cardiac risk associated with sexual activity. Sildenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure (see section "Pharmacodynamics"). 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.
Sildenafil potentiates hypotensive effect of nitrates (see section "Contraindications").
Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular arrhythmia, cerebrovascular hemorrhage, transient ischaemic attack, hypertension and hypotension have been reported in temporal association with the use of sildenafil. Most patients along with this had cardiovascular risk factors. Most adverse reactions have been observed during or shortly after sexual intercourse and a few occurred shortly after the use of the drug without sexual activity. Therefore, it is impossible to determine whether the development of such adverse reactions is related directly to these factors or to other factors.
*Priapism.*
Agents for the treatment of erectile dysfunction, including 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 anaemia, multiple myeloma or leukaemia).
There are data about prolonged erection and priapism when taking sildenafil.
If erection persists for more than 4 hours, the patients should seek immediate medical attention. In the absence of immediate treatment, priapism may lead to damage of penile tissue and permanent loss of potency.
*Concomitant use with other PDE5 inhibitors or other drugs for treatment of erectile dysfunction.*
The safety and efficacy of concomitant use of sildenafil with other PDE5 inhibitors or other drugs for treatment of pulmonary artery hypertension that contain sildenafil, or with other drugs for treatment of erectile dysfunction have not been studied. Therefore, the use of such combinations is not recommended.
*Effects on vision.*
Cases of visual defects and non-arteritic anterior ischaemic optic neuropathy when using sildenafil and other PDE5 inhibitors have been reported (see section "Adverse reactions"). Cases of non-arterial anterior ischemic optic neuropathy, a rare condition, have been reported spontaneously and have been reported in a follow-up study as associated with sildenafil and other PDE5 inhibitors (see section "Adverse reactions"). Patients should be advised that in the event of any sudden visual defect, they should stop taking Moginin® and consult a physician immediately (see section "Contraindications").
*Concomitant use with ritonavir.*
Co-administration of sildenafil with ritonavir is not advised (see section "Interaction with other medicinal products and other forms of interaction").
*Concomitant use with α-adrenoceptor blockers.*
Caution is advised when sildenafil is administered to patients taking α-adrenoceptor blockers; as such combination may lead to symptomatic hypotension in a few susceptible individuals. The symptomatic hypotension is most likely to occur within 4 hours post sildenafil dosing. In order to minimize the potential for developing postural hypotension in patients using α-adrenoceptor blockers, their condition should be stabilized on α-adrenoceptor blockers prior to initiating sildenafil treatment. The possibility of

use of a starting dose of 25 mg should be considered (see section "Dosage and administration"). Besides, the patients should be advised what to do in the event of postural hypotensive symptoms.
*Effects on blood clotting.*
Human platelet studies have shown that sildenafil potentiates the antiaggregatory effect of sodium nitroprusside *in vitro*. There is no safety information on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration. Therefore sildenafil should be administered to these patients only after careful benefit-risk assessment.
There was no effect observed on sperm motility or morphology after single 100 mg oral doses of sildenafil in healthy volunteers (see section "Pharmacodynamics").
*Hearing loss.*
Physicians should advice patients to stop using PDE5 inhibitors, including Moginin®, and seek immediate medical attention in case of a sudden decrease or loss of hearing. Such cases, which may also be accompanied by tinnitus and dizziness, have been reported in temporal association with the use of PDE5 inhibitors, including sildenafil. It is not possible to determine whether these events are related directly to the use of PDE5 or to other factors.
*Concomitant use with hypotensive drugs.*
Sildenafil has systemic vasodilator effect and may lead to further decrease of the blood pressure in patients using hypotensive drugs. There are data that in case of concomitant oral administration of amlodipine (5 mg or 10 mg) and sildenafil (100 mg) an average additional decrease of systolic blood pressure by 8 mm Hg and of diastolic by 7 mm Hg was observed.
*Sexually transmitted diseases.*
The use of sildenafil does not protect from sexually transmitted diseases. The possibility to instruct patients about the necessary precautions for protection from sexually transmitted diseases, including human immunodeficiency virus, should be considered.
This drug contains less than 1 mmol (23 mg)/dose of sodium, i.e. virtually free of sodium.

*Use during pregnancy and lactation.*
The drug Moginin® is not indicated for use in women.

*Effects on ability to drive and use machines*.
No studies on the effects on the ability to drive and use other machines have been performed.
Since dizziness and visual disturbances have been reported with sildenafil, patients need to find out their individual response to sildenafil before driving or operating machinery..

***Administration and dosage.***
The drug is used orally.
*Adults.*
The recommended dose of sildenafil is 50 mg and is used approximately one hour before the sexual intercourse.
Based on efficacy and tolerability the dose may be increased to 100 mg or decreased to 25 mg*. The maximum recommended dose is 100 mg.
The recommended frequency of the maximum recommended dose is once per day. If Moginin® is taken with food, the onset of activity may be delayed compared to the fasted state.
*Elderly patients (≥ 65 years old).*
Dosage adjustments are not required in elderly patients.
*Patients with renal impairment.*
The dosing recommendations described in section "Adults" apply to patients with mild to moderate renal impairment (creatinine clearance from 30 to 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. Based on efficacy and tolerability, the dose may be increased step-wise to 50 mg and up to 100 mg.
*Patients with hepatic impairment.*

Since sildenafil clearance is reduced in patients with hepatic impairment (e.g. cirrhosis) a 25 mg* dose should be considered. Based on efficacy and tolerability, if necessary, the dose may be increased step-wise to 50 mg up to 100 mg.
*Patients taking other medicinal products.*
If patients concomitantly use CYP3A4 inhibitors (see section "Interaction with other medicinal products and other forms of interaction"), a starting dose of 25 mg* should be considered (with the exception of ritonavir concomitant use of which with sildenafil is not recommended, see section "Special warnings details").
To minimize the possible development of postural hypotension in patients using α-adrenoceptor blockers, they should be stabilized on α-adrenoceptor blockers prior to initiating sildenafil treatment. Also, a starting dose of 25 mg* should be considered (see section "Interaction with other medicinal products and other forms of interaction" and "Special warnings").
*Use sildenafil in the appropriate dosage.

*Children.*
The drug is not indicated for use in persons below 18 years of age.

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

***Adverse reactions.***
The most commonly reported adverse reactions were headache, flushing, dyspepsia, nasal congestion, back pain, dizziness, nausea, hot flushes, blurred vision, cyanopsia, and blurred vision.
All clinically relevant adverse reactions observed in clinical trials more frequently than with placebo were listed below according to System-Organ Class and frequency: very common (≥1/10), common (≥1/100 – <1/10), uncommon (≥1000 – <1/100) and rare (≥1/10000 – <1/1000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.
Infections and invasions
*Uncommon:* rhinitis.
Immune system disorders
*Uncommon:* hypersensitivity.
Nervous system disorders.
*Very common:* headache.
*Common:* dizziness.
*Uncommon:* drowsiness, hypoesthesia.
*Rare:* stroke, transient ischemic attack, convulsions*, recurrence of seizures*, syncope.
Eye disorders
*Common:* visual colour distortion**, visual disorders, blurred vision.
*Uncommon:* lacrimation disorders***, pain in the eyes, photophobia, photopsia, hyperaemia of the eyes, eye redness, brightness of vision, conjunctivitis.
*Rare:* non-arteritic anterior ischaemic optic neuropathy*, retinal vascular occlusion*, retinal hemorrhage, arteriosclerotic retinopathy, disorders of the retina, glaucoma, ocular hypertension, visual field defects, diplopia, decrement in visual acuity, myopia, asthenopia, vitreous floaters, iris disorders, mydriasis, appearance of glowing circles around the light source (halo) in the field of vision, eye swelling, eye swelling, disorders of the eyes, hyperemia of the conjunctiva, eye irritation, abnormal sensations in the eyes, eyelid edema, discoloration of sclera.
Ear and labyrinth disorders
*Uncommon:* vertigo, tinnitus.

*Rare:* deafness.
Cardiac disorders.
*Uncommon:* tachycardia, increased heart rate.
*Rare:* sudden cardiac death*, myocardial infarction, ventricular arrhythmia*, atrial fibrillation, unstable angina.
Vascular system disorders.
*Common:* flush, hot feeling.
*Uncommon:* hypertension, hypotension.
Respiratory system, chest and mediastinum disorders.
*Common:* nasal blockage.
*Uncommon:* nasal bleeding, paranasal sinus blockage.
*Rare:* squeezing sensation in the throat, edema of the mucous membranes of the nose, dry nose.
Gastrointestinal tract disorders.
*Common:* nausea, dyspepsia.
*Uncommon:* gastroesophageal reflux disease, vomiting, upper abdominal pain, dry mouth.
*Rare:* hypoesthesia of mouth cavity.
Skin and subcutaneous tissue disorders.
*Uncommon:* skin rash.
*Rare:* Stevens-Johnson syndrome*, toxic epidermal necrolysis*.
Musculoskeletal system and connective tissue.
*Uncommon:* myalgia, pain in the extremities.
Urinary system disorders.
*Uncommon:* haematuria.
Reproductive system and breast disorders.
*Rare*: bleeding from the penis, priapism*, hematospermia, prolonged erection.
General disorders and reactions at the site of drug administration.
*Uncommon:* chest pain, increased tiredness, fever sensation.
*Rare:* irritation.
Examination
*Uncommon:* increased heart rate.
*It was reported only during the study after the drug was released on the market.
**Visual color distortion: chloropsia, chromatopsia, cyanopsia, erythropsia, xanthopsia.
***Lacrimation disorders: dry eyes, lacrimation disorders and increased lacrimation.
The following events were observed in <2% of patients in controlled clinical trials; the causal relationship has not been determined. Reports included events that were likely to be associated with the use of the drug. The phenomena that were not mentioned were mild and the messages were too inaccurate to matter.
*General.* Facial edema, photosensitivity reactions, shock, asthenia, pain, sudden fall, abdominal pain, sudden injury.
*Cardio-vascular system:* angina, AV-blockade, migraine, postural hypotension, myocardial ischemia, cerebrovascular thrombosis, sudden cardiac arrest, ECG abnormalities, cardiomyopathy.
*Gastrointestinal tract disorders:* glossitis, colitis, dysphagia, gastritis, gastroenteritis, esophagitis, stomatitis, abnormal results of liver function tests, rectal bleeding, gingivitis.
*Blood and lymphatic system disorders:* anemia, leukopenia.
*Metabolism and nutrition disorders:* thirst, edema, gout, unstable diabetes, hyperglycemia, peripheral edema, hyperuricemia, hypoglycemia, hypernatremia.
*Musculoskeletal system:* arthritis, arthrosis, tendon rupture, tenosynovitis, bone ache, myasthenia, synovitis.
*Nervous system disorders:* ataxia, neuralgia, neuropathy, paresthesia, tremor, vertigo, depression, insomnia, abnormal dreams, reduced reflexes.
*Respiratory system dirorders:* asthma, dyspnea, laryngitis, pharyngitis, sinusitis, bronchitis, increased salivation, increased cough.
*Skin disorders:* urticaria, herpes, itching, sweating, skin ulcers, contact dermatitis, exfoliative dermatitis.
*Specific sensations:* sudden hearing reduction or hearing loss, hemophthalmia, cataract, dry eyes.
*Urogenital system disorders:* cystitis, nocturia, increased frequency of urination, urinary incontinence,

breast enlargement, urinary incontinence, ejaculation disorders, genital edema, anorgasmia.
Post-marketing experience. After the drug was launched on the market, the following adverse effects were identified. Since such reactions are reported voluntarily and are reported from an unknown population, it is not always possible to reliably estimate their frequency and establish a causal relationship with drug exposure. These phenomena were noted both because of their severity, frequency of reporting, lack of a clear alternative link, and because of a combination of these factors.
*Cardiovascular and cerebrovascular events.* Serious cardiovascular, cerebrovascular and vascular events, including cerebrovascular haemorrhage, subarachnoid and intracerebral haemorrhage, and pulmonary haemorrhage, have been reported in association with sildenafil. Most patients had cardiovascular risk factors. Most of these events occurred during or immediately after sexual activity and several occurred immediately after sildenafil use without sexual activity. Other events occurred within hours or days of sildenafil use and after sexual activity. It is not possible to determine whether these effects are related to the use of the drug, to sexual activity, to existing risk factors, or to a combination of these factors, or to other factors.
*Blood and lymphatic systems:* vasoocclusive crisis. In a small, prematurely discontinued study of sildenafil in patients with pulmonary arterial hypertension secondary to sickle cell anemia, the development of vasoocclusive crises requiring hospitalization was reported more frequently than with placebo. The clinical significance of this information for patients using sildenafil for the treatment of erectile dysfunction is unknown.
*Nervous system:* anxiety, transient global amnesia.
*Specific sensations.*
*Hearing.* Cases of sudden decrease or loss of hearing associated with sildenafil have been reported since its launch. In some cases, medical conditions and other factors have been reported that may have played a role in the development of hearing impairments. In many cases, information on further medical follow-up is missing. It is not possible to determine whether these events are directly related to sildenafil use, to the available risk factors for hearing loss, to a combination of these factors, or to other factors.
*Vision.* Temporary loss of vision, redness of the eyes, burning in the eyes, increased intraocular pressure, retinal edema, retinal vascular disease or bleeding, vitreous detachment.
Cases of non-arterial anterior ischemic optic neuropathy that cause vision loss, including persistent vision loss, have been reported in post-marketing experience and have been associated with the use of PDE5 inhibitors, including sildenafil. Many patients had anatomical or vascular risk factors for nonarterial anterior ischemic optic neuropathy, including (but not limited to) low ratio of excavation to optic disc diameter (congestive optic disc), age over 50, hypertension, coronary heart disease, hyperlipidemia and smoking. It is not possible to determine whether these events are directly related to the use of PDE5 inhibitors or to existing anatomical or vascular risk factors, or to a combination of all of these factors, or to other factors.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is an important procedure. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to State Enterprise “State Expert Center of the Ministry of Health of Ukraine” and the applicant through the feedback form on the website: https://kusum.ua/pharmacovigilance/ the local reporting system.

***Shelf life.***
2 years.

**Storage conditions.**
Store in the original package at a temperature below 25°C.
Keep out of the reach of children.

**Package.**
1 or 4 tablets in a blister; 1 blister in a carton package.

**Conditions of supply.**

By prescription.

**Manufacturer.**
KUSUM HEALTHCARE PVT LTD.

**Location of manufacturer and its address of its business activity.**
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

**Date of last revision.**