ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sildenafil ratiopharm 25 mg film-coated tablets
Sildenafil ratiopharm 50 mg film-coated tablets
Sildenafil ratiopharm 100 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sildenafil ratiopharm 25 mg film-coated tablets
Each film-coated tablet contains sildenafil citrate equivalent to 25 mg of sildenafil.

Sildenafil ratiopharm 50 mg film-coated tablets
Each film-coated tablet contains sildenafil citrate equivalent to 50 mg of sildenafil.

Sildenafil ratiopharm 100 mg film-coated tablets
Each film-coated tablet contains sildenafil citrate equivalent to 100 mg of sildenafil.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

Sildenafil ratiopharm 25 mg film-coated tablets
White to off-white, oblong film-coated tablet with edge.

Sildenafil ratiopharm 50 mg film-coated tablets
White to off-white, oblong film-coated tablet with edge and score line on one side. The tablet can be divided into equal doses.

Sildenafil ratiopharm 100 mg film-coated tablets
White to off-white, oblong film-coated tablet with edge and score line on one side. The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Sildenafil ratiopharm is indicated in adult men with erectile dysfunction, which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance.

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

4.2 Posology and method of administration

Posology

Use in adults
The recommended dose is 50 mg taken as needed approximately one hour before sexual activity. Based on efficacy and tolerability, the dose may be increased to 100 mg or decreased to 25 mg. The maximum recommended dose is 100 mg. The maximum recommended dosing frequency is once per day. If sildenafil is taken with food, the onset of activity may be delayed compared to the fasted state (see section 5.2).

Special populations

Elderly
Dosage adjustments are not required in elderly patients (≥ 65 years old).

Renal impairment
The dosing recommendations described in 'Use in adults' apply to patients with mild to moderate renal impairment (creatinine clearance = 30-80 mL/min).

Since sildenafil clearance is reduced in patients with severe renal impairment (creatinine clearance < 30 mL/min), a 25 mg dose should be considered. Based on efficacy and tolerability, the dose may be increased step-wise to 50 mg up to 100 mg as necessary.

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, the dose may be increased step-wise to 50 mg up to 100 mg as necessary.

Paediatric population
Sildenafil ratiopharm is not indicated for individuals below 18 years of age.

Use in patients taking other medicinal products
With the exception of ritonavir for which co-administration with sildenafil is not advised (see section 4.4), a starting dose of 25 mg should be considered in patients receiving concomitant treatment with CYP3A4 inhibitors (see section 4.5).

In order to minimise the potential of developing postural hypotension in patients receiving alpha-blocker treatment, patients should be stabilised on alpha-blocker therapy prior to initiating sildenafil treatment. In addition, initiation of sildenafil at a dose of 25 mg should be considered (see sections 4.4 and 4.5).

Method of administration

For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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

The co-administration of PDE5 inhibitors, including sildenafil, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension (see section 4.5).

Agents for the treatment of erectile dysfunction, including sildenafil, should not be used in men for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders such as unstable angina or severe cardiac failure).

Sildenafil is contraindicated in patients who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure (see section 4.4).

The safety of sildenafil has not been studied in the following sub-groups of patients and its use is therefore contraindicated: severe hepatic impairment, hypotension (blood pressure < 90/50 mmHg), recent history of stroke or myocardial infarction and known hereditary degenerative retinal disorders such as *retinitis pigmentosa* (a minority of these patients have genetic disorders of retinal phosphodiesterases).

4.4 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 5.1). 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 the hypotensive effect of nitrates (see section 4.3).

Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular arrhythmia, cerebrovascular haemorrhage, transient ischaemic attack, hypertension and hypotension have been reported post-marketing in temporal association with the use of sildenafil. Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many events were reported to occur during or shortly after sexual intercourse and a few were reported to occur shortly after the use of sildenafil without sexual activity. It is not possible to determine whether these events are 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).

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

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

Effects on vision
Cases of visual defects have been reported spontaneously in connection with the intake of sildenafil and other PDE5 inhibitors (see section 4.8). Cases of non-arteritic anterior ischaemic optic neuropathy, a rare condition, have been reported spontaneously and in an observational study in connection with the intake of sildenafil and other PDE5 inhibitors (see section 4.8). Patients should be advised that in the event of any sudden visual defect, they should stop taking sildenafil and consult a physician immediately (see section 4.3).

Concomitant use with ritonavir
Co-administration of sildenafil with ritonavir is not advised (see section 4.5).

Concomitant use with alpha-blockers
Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the co-administration may lead to symptomatic hypotension in a few susceptible individuals (see section 4.5). This is most likely to occur within 4 hours post sildenafil dosing. In order to minimise the potential for developing postural hypotension, patients should be haemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Initiation of sildenafil at a dose of 25 mg should be considered (see section 4.2). In addition, physicians should advise patients what to do in the event of postural hypotensive symptoms.

Effect on bleeding
Studies with human platelets indicate that sildenafil potentiates the 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.

Women
Sildenafil ratiopharm is not indicated for use by women.

Excipient

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other medicinal products on sildenafil

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

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

Co-administration of the HIV protease inhibitor ritonavir, which is a highly potent P450 inhibitor, at steady state (500 mg twice daily) with sildenafil (100 mg single dose) resulted in a 300% (4-fold) increase in sildenafil C_{max} and a 1,000% (11-fold) increase in sildenafil plasma AUC. At 24 hours, the plasma levels of sildenafil were still approximately 200 ng/mL, compared to approximately 5 ng/mL when sildenafil was administered alone. This is consistent with ritonavir's marked effects on a broad range of P450 substrates. Sildenafil had no effect on ritonavir pharmacokinetics. Based on these pharmacokinetic results co-administration of sildenafil with ritonavir is not advised (see section 4.4) and in any event the maximum dose of sildenafil should under no circumstances exceed 25 mg within 48 hours.

Co-administration of the HIV protease inhibitor saquinavir, a CYP3A4 inhibitor, at steady state (1200 mg three times a day) with sildenafil (100 mg single dose) resulted in a 140% increase in sildenafil C_{max} and a 210% increase in sildenafil AUC. Sildenafil had no effect on saquinavir pharmacokinetics (see section 4.2). Stronger CYP3A4 inhibitors such as ketoconazole and itraconazole would be expected to have greater effects.

When a single 100 mg dose of sildenafil was administered with erythromycin, a moderate CYP3A4 inhibitor, at steady state (500 mg twice daily for 5 days), there was a 182% increase in sildenafil systemic exposure (AUC). In normal healthy male volunteers, there was no evidence of an effect of azithromycin (500 mg daily for 3 days) on the AUC, C_{max}, t_{max}, elimination rate constant, or subsequent half-life of sildenafil or its principal circulating metabolite. Cimetidine (800 mg), a cytochrome P450 inhibitor and non-specific CYP3A4 inhibitor, caused a 56% increase in plasma sildenafil concentrations when co-administered with sildenafil (50 mg) to healthy volunteers.

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

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

Although specific interaction studies were not conducted for all medicinal products, population pharmacokinetic analysis showed no effect of concomitant treatment on sildenafil pharmacokinetics when grouped as CYP2C9 inhibitors (such as tolbutamide, warfarin, phenytoin), CYP2D6 inhibitors (such as selective serotonin reuptake inhibitors, tricyclic antidepressants), thiazide and related diuretics, loop and potassium sparing diuretics, angiotensin converting enzyme inhibitors, calcium channel blockers, beta-adrenoreceptor antagonists or inducers of CYP450 metabolism (such as rifampicin, barbiturates). In a study of healthy male volunteers, co-administration of the endothelin antagonist, bosentan, (an inducer of CYP3A4 [moderate], CYP2C9 and possibly of CYP2C19) at steady state (125 mg twice a day) with sildenafil at steady state (80 mg three times a day) resulted in 62.6% and 55.4% decrease in sildenafil AUC and C_{max}, respectively. Therefore, concomitant administration of strong CYP3A4 inducers, such as rifampin, is expected to cause greater decreases in plasma concentrations of sildenafil.

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

Effects of sildenafil on other medicinal products

In vitro studies
Sildenafil is a weak inhibitor of the cytochrome P450 isoforms 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 (IC_{50} > 150 µM). Given sildenafil peak plasma concentrations of approximately 1 µM after recommended doses, it is unlikely that sildenafil will alter the clearance of substrates of these isoenzymes.

There are no data on the interaction of sildenafil and non-specific phosphodiesterase inhibitors such as theophylline or dipyridamole.

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

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

Concomitant administration of sildenafil to patients taking alpha-blocker therapy may lead to symptomatic hypotension in a few susceptible individuals. This is most likely to occur within 4 hours post sildenafil dosing (see sections 4.2 and 4.4). In three specific drug-drug interaction studies, the alpha-blocker doxazosin (4 mg and 8 mg) and sildenafil (25 mg, 50 mg, or 100 mg) were administered

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

No significant interactions were shown when sildenafil (50 mg) was co-administered with tolbutamide (250 mg) or warfarin (40 mg), both of which are metabolised by CYP2C9.

Sildenafil (50 mg) did not potentiate the increase in bleeding time caused by acetyl salicylic acid (150 mg).

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

Pooling of the following classes of antihypertensive medication, diuretics, beta-blockers, ACE inhibitors, angiotensin II antagonists, antihypertensive medicinal products (vasodilator and centrally-acting), adrenergic neurone blockers, calcium channel blockers and alpha-adrenoceptor blockers, showed no difference in the side effect profile in patients taking sildenafil compared to placebo treatment. In a specific interaction study, where sildenafil (100 mg) was co-administered with amlodipine in hypertensive patients, there was an additional reduction on supine systolic blood pressure of 8 mmHg. The corresponding additional reduction in supine diastolic blood pressure was 7 mmHg. These additional blood pressure reductions were of a similar magnitude to those seen when sildenafil was administered alone to healthy volunteers (see section 5.1).

Addition of a single dose of sildenafil to sacubitril/valsartan at steady state in patients with hypertension was associated with a significantly greater blood pressure reduction compared to administration of sacubitril/valsartan alone. Therefore, caution should be exercised when sildenafil is initiated in patients treated with sacubitril/valsartan.

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

In healthy male volunteers, sildenafil at steady state (80 mg t.i.d.) resulted in a 49.8% increase in bosentan AUC and a 42% increase in bosentan C_{max} (125 mg b.i.d.).

4.6 Fertility, pregnancy and lactation

Sildenafil ratiopharm is not indicated for use by women.

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

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

There was no effect on sperm motility or morphology after single 100 mg oral doses of sildenafil in healthy volunteers (see section 5.1).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

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.

4.8 Undesirable effects

Summary of the safety profile
The safety profile of sildenafil is based on 9,570 patients in 74 double-blind placebo-controlled clinical studies. The most commonly reported adverse reactions in clinical studies among sildenafil treated patients were headache, flushing, dyspepsia nasal congestion, dizziness, nausea, hot flush, visual disturbance, cyanopsia and vision blurred.

Adverse reactions from post-marketing surveillance has been gathered covering an estimated period > 10 years. Because not all adverse reactions are reported to the Marketing Authorisation Holder and included in the safety database, the frequencies of these reactions cannot be reliably determined.

Tabulated list of adverse reactions
In the table below all medically important adverse reactions, which occurred in clinical trials at an incidence greater than placebo are listed by system organ class and frequency [very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000)]. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

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

System Organ Class	**Very common** ***(≥ 1/10)***	**Common** ***(≥ 1/100 and < 1/10)***	**Uncommon** ***(≥ 1/1,000 and < 1/100)***	**Rare** ***(≥ 1/10,000 and < 1/1,000)***
Infections and infestations			Rhinitis	
Immune system disorders			Hypersensitivity	
Nervous system disorders	Headache	Dizziness	Somnolence, Hypoaesthesia	Cerebrovascular accident, Transient ischaemic attack, Seizure*, Seizure recurrence*, Syncope
Eye disorders		Visual colour distortions**, Visual disturbance, Vision blurred	Lacrimation disorders***, Eye pain, Photophobia, Photopsia, Ocular hyperaemia, Visual brightness, Conjunctivitis	Non-arteritic anterior ischaemic optic neuropathy (NAION)*, Retinal vascular occlusion*, Retinal haemorrhage, Arteriosclerotic retinopathy, Retinal disorder, Glaucoma, Visual field defect, Diplopia, Visual acuity reduced, Myopia, Asthenopia, Vitreous floaters, Iris disorder, Mydriasis,

System Organ Class	**Very common** ***(≥ 1/10)***	**Common** ***(≥ 1/100 and < 1/10)***	**Uncommon** ***(≥ 1/1,000 and < 1/100)***	**Rare** ***(≥ 1/10,000 and < 1/1,000)***
				Halo vision, Eye oedema, Eye swelling, Eye disorder, Conjunctival hyperaemia, Eye irritation, Abnormal sensation in eye, Eyelid oedema, Scleral discoloration
Ear and labyrinth disorders			Vertigo, Tinnitus	Deafness
Cardiac disorders			Tachycardia, Palpitations	Sudden cardiac death*, Myocardial infarction, Ventricular arrhythmia*, Atrial fibrillation, Unstable angina
Vascular disorders		Flushing, Hot flush	Hypertension, Hypotension	
Respiratory, thoracic and mediastinal disorders		Nasal congestion	Epistaxis, Sinus congestion	Throat tightness, Nasal oedema, Nasal dryness
Gastrointestinal disorders		Nausea, Dyspepsia	Gastro oesophagael reflux disease, Vomiting, Abdominal pain upper, Dry mouth	Hypoaesthesia oral
Skin and subcutaneous tissue disorders			Rash	Stevens-Johnson Syndrome (SJS)*, Toxic Epidermal Necrolysis (TEN)*
Musculoskeletal and connective tissue disorders			Myalgia, Pain in extremity	
Renal and urinary disorders			Haematuria	
Reproductive system and breast disorders				Penile haemorrhage, Priapism*,

System Organ Class	Very common *(≥ 1/100 and < 1/10)*	Common *(≥ 1/100 and < 1/10)*	Uncommon *(≥ 1/1,000 and < 1/100)*	Rare *(≥ 1/10,000 and < 1/1,000)*
				Haematospermia, Erection increased
General disorders and administration site conditions			Chest pain, Fatigue, Feeling hot	Irritability
Investigations			Heart rate increased	

*****Reported during post-marketing surveillance only
**Visual colour distortions: Chloropsia, Chromatopsia, Cyanopsia, Erythropsia and Xanthopsia
***Lacrimation disorders: Dry eye, Lacrimal disorder and Lacrimation increased

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In single dose volunteer studies of doses up to 800 mg, adverse reactions were similar to those seen at lower doses, but the incidence rates and severities were increased. Doses of 200 mg did not result in increased efficacy but the incidence of adverse reactions (headache, flushing, dizziness, dyspepsia, nasal congestion, altered vision) was increased.

In cases of overdose, standard supportive measures should be adopted as required. Renal dialysis is not expected to accelerate clearance as sildenafil is highly bound to plasma proteins and not eliminated in the urine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals; Drugs used in erectile dysfunction, ATC code: G04BE03

Mechanism of action
Sildenafil is an oral therapy for erectile dysfunction. In the natural setting, i.e. with sexual stimulation, it restores impaired erectile function by increasing blood flow to the penis.

The physiological mechanism responsible for erection of the penis involves the release of nitric oxide (NO) in the corpus cavernosum during sexual stimulation. Nitric oxide 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 is a potent and selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) in the corpus cavernosum, where PDE5 is responsible for degradation of cGMP. Sildenafil has a peripheral site of action on erections. Sildenafil has no direct relaxant effect on isolated human corpus cavernosum but potently enhances the relaxant effect of NO on this tissue. When the NO/cGMP pathway is activated, as occurs with sexual stimulation, inhibition of PDE5 by sildenafil results in

increased corpus cavernosum levels of cGMP. Therefore sexual stimulation is required in order for sildenafil to produce its intended beneficial pharmacological effects.

Pharmacodynamic effects
Studies *in vitro* have shown that sildenafil is selective for PDE5, which is involved in the erection process. Its effect is more potent on PDE5 than on other known phosphodiesterases. There is a 10-fold selectivity over PDE6 which is involved in the phototransduction pathway in the retina. At maximum recommended doses, there is an 80-fold selectivity over PDE1, and over 700-fold over PDE2, 3, 4, 7, 8, 9, 10 and 11. In particular, sildenafil has greater than 4,000-fold selectivity for PDE5 over PDE3, the cAMP-specific phosphodiesterase isoform involved in the control of cardiac contractility.

Clinical efficacy and safety
Two clinical studies were specifically designed to assess the time window after dosing during which sildenafil could produce an erection in response to sexual stimulation. In a penile plethysmography (RigiScan) study of fasted patients, the median time to onset for those who obtained erections of 60% rigidity (sufficient for sexual intercourse) was 25 minutes (range 12-37 minutes) on sildenafil. In a separate RigiScan study, sildenafil was still able to produce an erection in response to sexual stimulation 4-5 hours post-dose.

Sildenafil causes mild and transient decreases in blood pressure which, in the majority of cases, do not translate into clinical effects. The mean maximum decreases in supine systolic blood pressure following 100 mg oral dosing of sildenafil was 8.4 mmHg. The corresponding change in supine diastolic blood pressure was 5.5 mmHg. These decreases in blood pressure are consistent with the vasodilatory effects of sildenafil, probably due to increased cGMP levels in vascular smooth muscle. Single oral doses of sildenafil up to 100 mg in healthy volunteers produced no clinically relevant effects on ECG.

In a study of the haemodynamic effects of a single oral 100 mg dose of sildenafil in 14 patients with severe coronary artery disease (CAD) (> 70% stenosis of at least one coronary artery), the mean resting systolic and diastolic blood pressures decreased by 7% and 6% respectively compared to baseline. Mean pulmonary systolic blood pressure decreased by 9%. Sildenafil showed no effect on cardiac output, and did not impair blood flow through the stenosed coronary arteries.

A double-blind, placebo-controlled exercise stress trial evaluated 144 patients with erectile dysfunction and chronic stable angina who regularly received anti-anginal medicinal products (except nitrates). The results demonstrated no clinically relevant differences between sildenafil and placebo in time to limiting angina.

Mild and transient differences in colour discrimination (blue/green) were detected in some subjects using the Farnsworth-Munsell 100 hue test at 1 hour following a 100 mg dose, with no effects evident after 2 hours post-dose. The postulated mechanism for this change in colour discrimination is related to inhibition of PDE6, which is involved in the phototransduction cascade of the retina. Sildenafil has no effect on visual acuity or contrast sensitivity. In a small size placebo-controlled study of patients with documented early age-related macular degeneration (n = 9), sildenafil (single dose, 100 mg) demonstrated no significant changes in the visual tests conducted (visual acuity, Amsler grid, colour discrimination simulated traffic light, Humphrey perimeter and photostress).

There was no effect on sperm motility or morphology after single 100 mg oral doses of sildenafil in healthy volunteers (see section 4.6).

Further information on clinical trials
In clinical trials sildenafil was administered to more than 8,000 patients aged 19-87. The following patient groups were represented: elderly (19.9%), patients with hypertension (30.9%), diabetes mellitus (20.3%), ischaemic heart disease (5.8%), hyperlipidaemia (19.8%), spinal cord injury (0.6%), depression (5.2%), transurethral resection of the prostate (3.7%), radical prostatectomy (3.3%). The following groups were not well represented or excluded from clinical trials: patients with pelvic

surgery, patients post-radiotherapy, patients with severe renal or hepatic impairment and patients with certain cardiovascular conditions (see section 4.3).

In fixed dose studies, the proportions of patients reporting that treatment improved their erections were 62% (25 mg), 74% (50 mg) and 82% (100 mg) compared to 25% on placebo. In controlled clinical trials, the discontinuation rate due to sildenafil was low and similar to placebo. Across all trials, the proportion of patients reporting improvement on sildenafil were as follows: psychogenic erectile dysfunction (84%), mixed erectile dysfunction (77%), organic erectile dysfunction (68%), elderly (67%), diabetes mellitus (59%), ischaemic heart disease (69%), hypertension (68%), TURP (61%), radical prostatectomy (43%), spinal cord injury (83%), depression (75%). The safety and efficacy of sildenafil was maintained in long-term studies.

Paediatric population
The European Medicines Agency has waived the obligation to submit the results of studies with the reference medicinal product containing sildenafil in all subsets of the paediatric population for the treatment of erectile dysfunction (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption
Sildenafil is rapidly absorbed. Maximum observed plasma concentrations are reached within 30 to 120 minutes (median 60 minutes) of oral dosing in the fasted state. The mean absolute oral bioavailability is 41% (range 25-63%). After oral dosing of sildenafil AUC and C_{max} increase in proportion with dose over the recommended dose range (25-100 mg).

When sildenafil is taken with food, the rate of absorption is reduced with a mean delay in t_{max} of 60 minutes and a mean reduction in C_{max} of 29%.

Distribution
The mean steady state volume of distribution (V_d) for sildenafil is 105 l, indicating distribution into the tissues. After a single oral dose of 100 mg, the mean maximum total plasma concentration of sildenafil is approximately 440 ng/mL (CV 40%). Since sildenafil (and its major circulating *N*-desmethyl metabolite) is 96% bound to plasma proteins, this results in the mean maximum free plasma concentration for sildenafil of 18 ng/mL (38 nM). Protein binding is independent of total drug concentrations.

In healthy volunteers receiving sildenafil (100 mg single dose), less than 0.0002% (average 188 ng) of the administered dose was present in ejaculate 90 minutes after dosing.

Biotransformation
Sildenafil is cleared predominantly by the CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes. The major circulating metabolite results from *N*-demethylation of sildenafil. This metabolite has a phosphodiesterase selectivity profile similar to sildenafil and an *in vitro* potency for PDE5 approximately 50% that of the parent drug. Plasma concentrations of this metabolite are approximately 40% of those seen for sildenafil. The *N*-desmethyl metabolite is further metabolised, with a terminal half-life of approximately 4 h.

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

Pharmacokinetics in special patient groups

Elderly

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 = 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 up to 126% and up to 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
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 have not been studied.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Hypromellose
Croscarmellose sodium
Magnesium stearate
Calcium hydrogen phosphate
Talc
Macrogol 6000
Titanium dioxide
Iron oxide red

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVdC/PVC/Aluminium blisters.

Sildenafil ratiopharm 25 mg film-coated tablets
Pack sizes of 1, 2, 4, 8, or 12 film-coated tablets.

Sildenafil ratiopharm 50 mg film-coated tablets
Pack sizes of 1, 2, 4, 8, 12 or 24 film-coated tablets.

Sildenafil ratiopharm 100 mg film-coated tablets
Pack sizes of 1, 2, 4, 8, 12, 24 or 48 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

ratiopharm GmbH
Graf-Arco-Straße 3
89079 Ulm
Germany

8. MARKETING AUTHORISATION NUMBER(S)

Sildenafil ratiopharm 25 mg film-coated tablets
EU/1/09/603/001
EU/1/09/603/002
EU/1/09/603/003
EU/1/09/603/004
EU/1/09/603/013

Sildenafil ratiopharm 50 mg film-coated tablets
EU/1/09/603/005
EU/1/09/603/006
EU/1/09/603/007
EU/1/09/603/008
EU/1/09/603/014
EU/1/09/603/017

Sildenafil ratiopharm 100 mg film-coated tablets
EU/1/09/603/009
EU/1/09/603/010
EU/1/09/603/011
EU/1/09/603/012
EU/1/09/603/015
EU/1/09/603/016
EU/1/09/603/018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 December 2009.

Date of latest renewal: 9 September 2014.

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Merckle GmbH
Ludwig-Merckle-Strasse 3
89143 Blaubeuren
Germany

Teva Operations Poland Sp. z o.o.
ul. Mogilska 80
31-546 Kraków
Poland

HBM Pharma s.r.o.
Sklabinská 30
036 80 Martin
Slovak Republic

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Sildenafil ratiopharm 25 mg film-coated tablets
sildenafil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains sildenafil citrate equivalent to 25 mg of sildenafil.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

1 film-coated tablet
2 film-coated tablets
4 film-coated tablets
8 film-coated tablets
12 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ratiopharm GmbH
Graf-Arco-Straße 3
89079 Ulm
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/603/001 1 film-coated tablet
EU/1/09/603/002 4 film-coated tablets
EU/1/09/603/003 8 film-coated tablets
EU/1/09/603/004 12 film-coated tablets
EU/1/09/603/013 2 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sildenafil ratiopharm 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Sildenafil ratiopharm 25 mg film-coated tablets
sildenafil

2. NAME OF THE MARKETING AUTHORISATION HOLDER

ratiopharm

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Sildenafil ratiopharm 50 mg film-coated tablets
sildenafil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains sildenafil citrate equivalent to 50 mg of sildenafil.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

1 film-coated tablet
2 film-coated tablets
4 film-coated tablets
8 film-coated tablets
12 film-coated tablets
24 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ratiopharm GmbH
Graf-Arco-Straße 3
89079 Ulm
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/603/005 1 film-coated tablet
EU/1/09/603/006 4 film-coated tablets
EU/1/09/603/007 8 film-coated tablets
EU/1/09/603/008 12 film-coated tablets
EU/1/09/603/014 2 film-coated tablets
EU/1/09/603/017 24 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sildenafil ratiopharm 50 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Sildenafil ratiopharm 50 mg film-coated tablets
sildenafil

2. NAME OF THE MARKETING AUTHORISATION HOLDER

ratiopharm

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Sildenafil ratiopharm 100 mg film-coated tablets
sildenafil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains sildenafil citrate equivalent to 100 mg of sildenafil.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

1 film-coated tablet
2 film-coated tablets
4 film-coated tablets
8 film-coated tablets
12 film-coated tablets
24 film-coated tablets
48 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ratiopharm GmbH
Graf-Arco-Straße 3
89079 Ulm
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/603/009 1 film-coated tablet
EU/1/09/603/010 4 film-coated tablets
EU/1/09/603/011 8 film-coated tablets
EU/1/09/603/012 12 film-coated tablets
EU/1/09/603/015 2 film-coated tablets
EU/1/09/603/016 24 film-coated tablets
EU/1/09/603/018 48 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Sildenafil ratiopharm 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Sildenafil ratiopharm 100 mg film-coated tablets
sildenafil

2. NAME OF THE MARKETING AUTHORISATION HOLDER

ratiopharm

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Sildenafil ratiopharm 25 mg film-coated tablets

sildenafil

Read all of this leaflet carefully before you start taking 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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Sildenafil ratiopharm is and what it is used for
2. What you need to know before you take Sildenafil ratiopharm
3. How to take Sildenafil ratiopharm
4. Possible side effects
5. How to store Sildenafil ratiopharm
6. Contents of the pack and other information

1. What Sildenafil ratiopharm is and what it is used for

What Sildenafil ratiopharm is
Sildenafil ratiopharm contains the active substance sildenafil which belongs to a group of medicines called phosphodiesterase type 5 (PDE5) inhibitors. This medicine allows an erection to last long enough for you to satisfactorily complete sexual activity. It reduces the action of the natural chemical in your body, which makes erections go away. Sildenafil ratiopharm will only work when you are sexually stimulated.

What Sildenafil ratiopharm is used for
Sildenafil ratiopharm is a treatment for adult men with erectile dysfunction, sometimes known as impotence. This is when a man cannot get or keep a hard, erect penis suitable for sexual activity.

2. What you need to know before you take Sildenafil ratiopharm

Do NOT take Sildenafil ratiopharm
- if you are allergic to sildenafil or any of the other ingredients of this medicine (listed in section 6).
- if you are taking medicines that contain nitrates (e.g. glycerol trinitrate) or nitric oxide donors (e.g. amyl nitrite, also called “poppers”). These medicines are often used to relieve the symptoms of chest pain (angina pectoris). Taking these medicines with Sildenafil ratiopharm could seriously affect your blood pressure. Tell your doctor if you are taking any of these medicines. If you are not certain, ask your doctor or pharmacist.
- if you are taking riociguat. This medicine is used to treat pulmonary arterial hypertension (i.e. high blood pressure in the lungs) and chronic thromboembolic pulmonary hypertension (i.e. high blood pressure in the lungs secondary to blood clots). PDE5 inhibitors, such as sildenafil, have been shown to increase the hypotensive effects of this medicine. If you are taking riociguat or are unsure tell your doctor.
- if you have a severe heart problem.
- if you have recently had a stroke or a heart attack.
- if you have low blood pressure.

- if you have a severe liver problem.
- if you have certain rare inherited eye diseases (such as retinitis pigmentosa).
- if you have ever suffered from loss of vision due to an eye condition known as “stroke of the eye” (non-arteritic anterior ischaemic optic neuropathy, NAION).

Warnings and precautions
Talk to your doctor or pharmacist before taking Sildenafil ratiopharm
- if you have problems with your heart. Your doctor should in that case carefully check whether your heart can take the additional strain of having sex.

- if you suffer from any of the following disorders or symptoms, as you may experience more side effects:
  - an abnormality of the red blood cells (sickle cell anaemia);
  - cancer of the blood (leukaemia);
  - a cancer of the bone marrow (multiple myeloma);
  - any disease or deformity of the penis.

- if you suffer from any of the following disorders, please tell your doctor who will check carefully whether this medicine is suitable for you:
  - if you currently have a stomach ulcer;
  - if you have a blood-clotting disorder (e.g. haemophilia).

- if you suffer from kidney or liver problems. Please tell your doctor about this. In this case, he/she may decide to give you a lower dose.

You should NOT take this medicine
- if you are already undergoing other treatments for erectile dysfunction.
- if you are already undergoing treatments for pulmonary arterial hypertension (PAH) containing sildenafil or any other PDE5 inhibitors.
- if you do not have erectile dysfunction.
- if you are a woman.

If you experience sudden decrease or loss of vision, stop taking Sildenafil ratiopharm and contact your doctor IMMEDIATELY.

Children and adolescents
This medicine should NOT be given to children and adolescents under the age of 18.

Other medicines and Sildenafil ratiopharm
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In a medical emergency, you must tell anyone treating you that you have taken Sildenafil ratiopharm.

Do NOT take Sildenafil ratiopharm if you are taking medicines that contain nitrates (e.g. glycerol trinitrate) or nitric oxide donors (e.g. amyl nitrite, also called “poppers”). These medicines are often used to relieve the symptoms of chest pain (angina pectoris). Simultaneous intake of nitrates or nitric oxide donors with Sildenafil ratiopharm can have severe effects on your blood pressure.

Tell your doctor or pharmacist if you are already taking riociguat.

Taking Sildenafil ratiopharm together with some medicines may lead to problems. Therefore, tell your doctor if you are taking any of the following medicines:
- ritonavir or saquinavir (medicines for the treatment of HIV infections);
- ketoconazole or itraconazole (medicines for the treatment of fungal infections);
- erythromycin (an antibiotic);
- cimetidine (medicine for the treatment of heartburn and peptic ulcers);

- alpha blockers (group of medicines for the treatment of high blood pressure or an enlarged prostate [benign prostatic hyperplasia]).
  Some patients taking alpha blockers may experience dizziness or light-headedness when getting up. These are symptoms of a fall in blood pressure upon rising quickly from sitting or lying (postural hypotension). These symptoms usually occur within 4 hours of taking Sildenafil ratiopharm. In order to reduce the probability of these symptoms occurring, you should start taking Sildenafil ratiopharm only when you are already well controlled on a regular daily dose of your alpha blocker.
- medicines containing sacubitril/valsartan, used to treat heart failure.

If you are taking one of these medicines, your doctor may start you on the lowest dose (25 mg) of Sildenafil ratiopharm. If you are taking ritonavir, you may not exceed a maximum dose of 25 mg sildenafil within a period of 48 hours.

Sildenafil ratiopharm with food, drink and alcohol
When this medicine is taken with food, it may take a little longer for Sildenafil ratiopharm to work.

Alcoholic drink can make erection difficulties worse. In order to get the maximum benefit from your medicine, it is recommended that you avoid alcohol before intake of this medicine.

Driving and using machines
This medicine might make some people feel dizzy or affect their vision or hearing. If you feel dizzy, or if your vision or hearing is affected after taking Sildenafil ratiopharm, do not drive or operate any tools or machines.

Sildenafil ratiopharm contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

3. How to take Sildenafil ratiopharm

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is
Take 1 film-coated tablet of Sildenafil ratiopharm about 1 hour before sexual activity. Swallow the film-coated tablet whole with a glass of water.

You should not take more film-coated tablets than your doctor tells you to.

You should not take Sildenafil ratiopharm more than once a day.

This medicine will only help you to get an erection if you are sexually stimulated. The amount of time Sildenafil ratiopharm takes to work varies from person to person, but it normally takes between half an hour and one hour. You may find that this medicine takes longer to work if you take it with a heavy meal.

If this medicine does not help you to get an erection, or if your erection does not last long enough for you to complete sexual intercourse, you should tell your doctor.

If you take more Sildenafil ratiopharm than you should
Men who take too much Sildenafil ratiopharm may experience more side effects or may get severe muscle pain. If you take more Sildenafil ratiopharm than you should, tell your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects reported in association with the use of sildenafil are usually mild to moderate and of a short duration.

If you experience any of the following serious side effects stop taking Sildenafil ratiopharm and seek medical help immediately:

- An allergic reaction - this occurs **uncommonly** (may affect up to 1 in 100 people). Symptoms include sudden wheeziness, difficulty in breathing or dizziness, swelling of the eyelids, face, lips or throat.

- Chest pains - this occurs **uncommonly.**
  If this occurs during or after intercourse:
  - Get in a semi-sitting position and try to relax.
  - **Do not use nitrates** to treat your chest pain.

- Prolonged and sometimes painful erections - this occurs **rarely** (may affect up to 1 in 1,000 people).
  If you have an erection, which lasts for more than 4 hours, you should contact a doctor immediately.

- A sudden decrease or loss of vision - this occurs **rarely.**

- Serious skin reactions - this occurs **rarely.**
  Symptoms may include severe peeling and swelling of the skin, blistering of the mouth, genitals and around the eyes, fever.

- Seizures or fits - this occurs **rarely.**

Other side effects:

Very common (may affect more than 1 in 10 people): headache.

Common (may affect up to 1 in 10 people): nausea, facial flushing, hot flush (symptoms include a sudden feeling of heat in your upper body), indigestion, colour tinge to vision, blurred vision, visual disturbance, stuffy nose and dizziness.

Uncommon (may affect up to 1 in 100 people): vomiting, skin rash eye irritation, bloodshot eyes/red eyes, eye pain, seeing flashes of light, visual brightness, light sensitivity, watery eyes, pounding heartbeat, rapid heartbeat, high blood pressure, low blood pressure, muscle pain, feeling sleepy, reduced sense of touch, vertigo, ringing in the ears, dry mouth, blocked or stuffy sinuses, inflammation of the lining of the nose (symptoms include runny nose, sneezing and stuffy nose), upper abdominal pain, gastro-oesophageal reflux disease (symptoms include heartburn), presence of blood in urine, pain in the arms or legs, nosebleed, feeling hot and feeling tired.

Rare (may affect up to 1 in 1,000 people): fainting, stroke, heart attack, irregular heartbeat, temporary decreased blood flow to parts of the brain, feeling of tightening of the throat, numb mouth, bleeding at the back of the eye, double vision, reduced sharpness of vision, abnormal sensation in the eye, swelling of the eye or eyelid, small particles or spots in your vision, seeing halos around lights, dilation of the pupil of the eye, discolouration of the white of the eye, penile bleeding, presence of blood in semen, dry nose, swelling of the inside of the nose, feeling irritable and sudden decrease or loss of hearing.

From post-marketing experience cases of unstable angina (a heart condition) and sudden death have been reported rarely. Of note, most, but not all, of the men who experienced these side effects had

heart problems before taking this medicine. It is not possible to determine whether these events were directly related to Sildenafil ratiopharm.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Sildenafil ratiopharm

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

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

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Sildenafil ratiopharm contains
- The active substance is sildenafil.
  Each film-coated tablet contains sildenafil citrate equivalent to 25 mg of sildenafil.
- The other ingredients are: microcrystalline cellulose, hypromellose, croscarmellose sodium, magnesium stearate, calcium hydrogen phosphate, talc, macrogol 6000, titanium dioxide, iron oxide red.

What Sildenafil ratiopharm looks like and contents of the pack
Sildenafil ratiopharm are white to off-white, oblong film-coated tablets with edge.

Sildenafil ratiopharm are supplied in packs of 1, 2, 4, 8 or 12 film-coated tablets in blisters. Not all pack sizes may be marketed.

Marketing Authorisation Holder
ratiopharm GmbH
Graf-Arco-Straße 3
89079 Ulm
Germany

Manufacturer
Merckle GmbH
Ludwig-Merckle-Straße 3
89143 Blaubeuren
Germany

Teva Operations Poland Sp. z o.o.
ul. Mogilska 80
31-546 Kraków
Poland

HBM Pharma s.r.o.
Sklabinská 30
036 80 Martin
Slovak Republic

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Teva Pharma Belgium N.V./S.A./AG
Tél/Tel: +32 38207373

Lietuva
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България
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Luxembourg/Luxemburg
ratiopharm GmbH
Allemagne/Deutschland
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Tél: +33 155917800

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ratiopharm - Comércio e Industria de Produtos Farmacêuticos, Lda.
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Teva Pharmaceuticals Ireland
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Suomi/Finland
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Sverige
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United Kingdom (Northern Ireland)
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Tel: +44 2075407117

This leaflet was last revised in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the patient

Sildenafil ratiopharm 50 mg film-coated tablets

sildenafil

Read all of this leaflet carefully before you start taking 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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Sildenafil ratiopharm is and what it is used for
2. What you need to know before you take Sildenafil ratiopharm
3. How to take Sildenafil ratiopharm
4. Possible side effects
5. How to store Sildenafil ratiopharm
6. Contents of the pack and other information

1. What Sildenafil ratiopharm is and what it is used for

What Sildenafil ratiopharm is
Sildenafil ratiopharm contains the active substance sildenafil which belongs to a group of medicines called phosphodiesterase type 5 (PDE5) inhibitors. This medicine allows an erection to last long enough for you to satisfactorily complete sexual activity. It reduces the action of the natural chemical in your body, which makes erections go away. Sildenafil ratiopharm will only work when you are sexually stimulated.

What Sildenafil ratiopharm is used for
Sildenafil ratiopharm is a treatment for adult men with erectile dysfunction, sometimes known as impotence. This is when a man cannot get or keep a hard, erect penis suitable for sexual activity.

2. What you need to know before you take Sildenafil ratiopharm

Do NOT take Sildenafil ratiopharm
- if you are allergic to sildenafil or any of the other ingredients of this medicine (listed in section 6).
- if you are taking medicines that contain nitrates (e.g. glycerol trinitrate) or nitric oxide donors (e.g. amyl nitrite, also called “poppers”). These medicines are often used to relieve the symptoms of chest pain (angina pectoris). Taking these medicines with Sildenafil ratiopharm could seriously affect your blood pressure. Tell your doctor if you are taking any of these medicines. If you are not certain, ask your doctor or pharmacist.
- if you are taking riociguat. This medicine is used to treat pulmonary arterial hypertension (i.e. high blood pressure in the lungs) and chronic thromboembolic pulmonary hypertension (i.e. high blood pressure in the lungs secondary to blood clots). PDE5 inhibitors, such as sildenafil, have been shown to increase the hypotensive effects of this medicine. If you are taking riociguat or are unsure tell your doctor.
- if you have a severe heart problem.
- if you have recently had a stroke or a heart attack.
- if you have low blood pressure.

- if you have a severe liver problem.
- if you have certain rare inherited eye diseases (such as retinitis pigmentosa).
- if you have ever suffered from loss of vision due to an eye condition known as “stroke of the eye” (non-arteritic anterior ischaemic optic neuropathy, NAION).

Warnings and precautions
Talk to your doctor or pharmacist before taking Sildenafil ratiopharm
- if you have problems with your heart. Your doctor should in that case carefully check whether your heart can take the additional strain of having sex.

- if you suffer from any of the following disorders or symptoms, as you may experience more side effects:
  - an abnormality of the red blood cells (sickle cell anaemia);
  - cancer of the blood (leukaemia);
  - a cancer of the bone marrow (multiple myeloma);
  - any disease or deformity of the penis.

- if you suffer from any of the following disorders, please tell your doctor who will check carefully whether this medicine is suitable for you:
  - if you currently have a stomach ulcer;
  - if you have a blood-clotting disorder (e.g. haemophilia).

- if you suffer from kidney or liver problems. Please tell your doctor about this. In this case, he/she may decide to give you a lower dose.

You should NOT take this medicine
- if you are already undergoing other treatments for erectile dysfunction.
- if you are already undergoing treatments for pulmonary arterial hypertension (PAH) containing sildenafil or any other PDE5 inhibitors.
- if you do not have erectile dysfunction.
- if you are a woman.

If you experience sudden decrease or loss of vision, stop taking Sildenafil ratiopharm and contact your doctor IMMEDIATELY.

Children and adolescents
This medicine should NOT be given to children and adolescents under the age of 18.

Other medicines and Sildenafil ratiopharm
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In a medical emergency, you must tell anyone treating you that you have taken Sildenafil ratiopharm.

Do NOT take Sildenafil ratiopharm if you are taking medicines that contain nitrates (e.g. glycerol trinitrate) or nitric oxide donors (e.g. amyl nitrite, also called “poppers”). These medicines are often used to relieve the symptoms of chest pain (angina pectoris). Simultaneous intake of nitrates or nitric oxide donors with Sildenafil ratiopharm can have severe effects on your blood pressure.

Tell your doctor or pharmacist if you are already taking riociguat.

Taking Sildenafil ratiopharm together with some medicines may lead to problems. Therefore, tell your doctor if you are taking any of the following medicines:
- ritonavir or saquinavir (medicines for the treatment of HIV infections);
- ketoconazole or itraconazole (medicines for the treatment of fungal infections);
- erythromycin (an antibiotic);
- cimetidine (medicine for the treatment of heartburn and peptic ulcers);

- alpha blockers (group of medicines for the treatment of high blood pressure or an enlarged prostate [benign prostatic hyperplasia]).
  Some patients taking alpha blockers may experience dizziness or light-headedness when getting up. These are symptoms of a fall in blood pressure upon rising quickly from sitting or lying (postural hypotension). These symptoms usually occur within 4 hours of taking Sildenafil ratiopharm. In order to reduce the probability of these symptoms occurring, you should start taking Sildenafil ratiopharm only when you are already well controlled on a regular daily dose of your alpha blocker.
- medicines containing sacubitril/valsartan, used to treat heart failure.

If you are taking one of these medicines, your doctor may start you on the lowest dose (25 mg) of Sildenafil ratiopharm. If you are taking ritonavir, you may not exceed a maximum dose of 25 mg sildenafil within a period of 48 hours.

Sildenafil ratiopharm with food, drink and alcohol
When this medicine is taken with food, it may take a little longer for Sildenafil ratiopharm to work.

Alcoholic drink can make erection difficulties worse. In order to get the maximum benefit from your medicine, it is recommended that you avoid alcohol before intake of this medicine.

Driving and using machines
This medicine might make some people feel dizzy or affect their vision or hearing. If you feel dizzy, or if your vision or hearing is affected after taking Sildenafil ratiopharm, do not drive or operate any tools or machines.

Sildenafil ratiopharm contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

3. How to take Sildenafil ratiopharm

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is
Take ½ or 1 film-coated tablet of Sildenafil ratiopharm as prescribed by your doctor about 1 hour before sexual activity. Swallow the film-coated tablet whole with a glass of water.

You should not take more film-coated tablets than your doctor tells you to.

You should not take Sildenafil ratiopharm more than once a day.

This medicine will only help you to get an erection if you are sexually stimulated. The amount of time Sildenafil ratiopharm takes to work varies from person to person, but it normally takes between half an hour and one hour. You may find that this medicine takes longer to work if you take it with a heavy meal.

If this medicine does not help you to get an erection, or if your erection does not last long enough for you to complete sexual intercourse, you should tell your doctor.

If you take more Sildenafil ratiopharm than you should
Men who take too much Sildenafil ratiopharm may experience more side effects or may get severe muscle pain. If you take more Sildenafil ratiopharm than you should, tell your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects reported in association with the use of sildenafil are usually mild to moderate and of a short duration.

If you experience any of the following serious side effects stop taking Sildenafil ratiopharm and seek medical help immediately:

- An allergic reaction - this occurs **uncommonly** (may affect up to 1 in 100 people). Symptoms include sudden wheeziness, difficulty in breathing or dizziness, swelling of the eyelids, face, lips or throat.

- Chest pains - this occurs **uncommonly.**
  If this occurs during or after intercourse:
  - Get in a semi-sitting position and try to relax.
  - **Do not use nitrates** to treat your chest pain.

- Prolonged and sometimes painful erections - this occurs **rarely** (may affect up to 1 in 1,000 people).
  If you have an erection, which lasts for more than 4 hours, you should contact a doctor immediately.

- A sudden decrease or loss of vision - this occurs **rarely.**

- Serious skin reactions -this occurs **rarely.**
  Symptoms may include severe peeling and swelling of the skin, blistering of the mouth, genitals and around the eyes, fever.

- Seizures or fits - this occurs **rarely.**

Other side effects:

Very common (may affect more than 1 in 10 people): headache.

Common (may affect up to 1 in 10 people): nausea, facial flushing, hot flush (symptoms include a sudden feeling of heat in your upper body), indigestion, colour tinge to vision, blurred vision, visual disturbance, stuffy nose and dizziness.

Uncommon (may affect up to 1 in 100 people): vomiting, skin rash, eye irritation, bloodshot eyes/red eyes, eye pain, seeing flashes of light, visual brightness, light sensitivity, watery eyes, pounding heartbeat, rapid heartbeat, high blood pressure, low blood pressure, muscle pain, feeling sleepy, reduced sense of touch, vertigo, ringing in the ears, dry mouth, blocked or stuffy sinuses, inflammation of the lining of the nose (symptoms include runny nose, sneezing and stuffy nose), upper abdominal pain, gastro-oesophageal reflux disease (symptoms include heartburn), presence of blood in urine, pain in the arms or legs, nosebleed, feeling hot and feeling tired.

Rare (may affect up to 1 in 1,000 people): fainting, stroke, heart attack, irregular heartbeat, temporary decreased blood flow to parts of the brain, feeling of tightening of the throat, numb mouth, bleeding at the back of the eye, double vision, reduced sharpness of vision, abnormal sensation in the eye, swelling of the eye or eyelid, small particles or spots in your vision, seeing halos around lights, dilation of the pupil of the eye, discolouration of the white of the eye, penile bleeding, presence of blood in semen, dry nose, swelling of the inside of the nose, feeling irritable and sudden decrease or loss of hearing.

From post-marketing experience cases of unstable angina (a heart condition) and sudden death have been reported rarely. Of note, most, but not all, of the men who experienced these side effects had

heart problems before taking this medicine. It is not possible to determine whether these events were directly related to Sildenafil ratiopharm.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Sildenafil ratiopharm

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

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

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Sildenafil ratiopharm contains
- The active substance is sildenafil.
  Each film-coated tablet contains sildenafil citrate equivalent to 50 mg of sildenafil.
- The other ingredients are: microcrystalline cellulose, hypromellose, croscarmellose sodium, magnesium stearate, calcium hydrogen phosphate, talc, macrogol 6000, titanium dioxide, iron oxide red.

What Sildenafil ratiopharm looks like and contents of the pack
Sildenafil ratiopharm are white to off-white, oblong film-coated tablets with edge and score line on one side. The tablet can be divided into equal doses.

Sildenafil ratiopharm are supplied in packs of 1, 2, 4, 8, 12 or 24 film-coated tablets in blisters. Not all pack sizes may be marketed.

Marketing Authorisation Holder
ratiopharm GmbH
Graf-Arco-Straße 3
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Germany

Manufacturer
Merckle GmbH
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HBM Pharma s.r.o.
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This leaflet was last revised in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Package leaflet: Information for the patient

Sildenafil ratiopharm 100 mg film-coated tablets

sildenafil

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
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- 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.
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What is in this leaflet

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2. What you need to know before you take Sildenafil ratiopharm
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6. Contents of the pack and other information

1. What Sildenafil ratiopharm is and what it is used for

What Sildenafil ratiopharm is
Sildenafil ratiopharm contains the active substance sildenafil which belongs to a group of medicines called phosphodiesterase type 5 (PDE5) inhibitors. This medicine allows an erection to last long enough for you to satisfactorily complete sexual activity. It reduces the action of the natural chemical in your body, which makes erections go away. Sildenafil ratiopharm will only work when you are sexually stimulated.

What Sildenafil ratiopharm is used for
Sildenafil ratiopharm is a treatment for adult men with erectile dysfunction, sometimes known as impotence. This is when a man cannot get or keep a hard, erect penis suitable for sexual activity.

2. What you need to know before you take Sildenafil ratiopharm

Do NOT take Sildenafil ratiopharm
- if you are allergic to sildenafil or any of the other ingredients of this medicine (listed in section 6).
- if you are taking medicines that contain nitrates (e.g. glycerol trinitrate) or nitric oxide donors (e.g. amyl nitrite, also called “poppers”). These medicines are often used to relieve the symptoms of chest pain (angina pectoris). Taking these medicines with Sildenafil ratiopharm could seriously affect your blood pressure. Tell your doctor if you are taking any of these medicines. If you are not certain, ask your doctor or pharmacist.
- if you are taking riociguat. This medicine is used to treat pulmonary arterial hypertension (i.e. high blood pressure in the lungs) and chronic thromboembolic pulmonary hypertension (i.e. high blood pressure in the lungs secondary to blood clots). PDE5 inhibitors, such as sildenafil, have been shown to increase the hypotensive effects of this medicine. If you are taking riociguat or are unsure tell your doctor.
- if you have a severe heart problem.
- if you have recently had a stroke or a heart attack.
- if you have low blood pressure.

- if you have a severe liver problem.
- if you have certain rare inherited eye diseases (such as retinitis pigmentosa).
- if you have ever suffered from loss of vision due to an eye condition known as “stroke of the eye” (non-arteritic anterior ischaemic optic neuropathy, NAION).

Warnings and precautions
Talk to your doctor or pharmacist before taking Sildenafil ratiopharm
- if you have problems with your heart. Your doctor should in that case carefully check whether your heart can take the additional strain of having sex.

- if you suffer from any of the following disorders or symptoms, as you may experience more side effects:
  - an abnormality of the red blood cells (sickle cell anaemia);
  - cancer of the blood (leukaemia);
  - a cancer of the bone marrow (multiple myeloma);
  - any disease or deformity of the penis.

- if you suffer from any of the following disorders, please tell your doctor who will check carefully whether this medicine is suitable for you:
  - if you currently have a stomach ulcer;
  - if you have a blood-clotting disorder (e.g. haemophilia).

- if you suffer from kidney or liver problems. Please tell your doctor about this. In this case, he/she may decide to give you a lower dose.

You should NOT take this medicine
- if you are already undergoing other treatments for erectile dysfunction.
- if you are already undergoing treatments for pulmonary arterial hypertension (PAH) containing sildenafil or any other PDE5 inhibitors.
- if you do not have erectile dysfunction.
- if you are a woman.

If you experience sudden decrease or loss of vision, stop taking Sildenafil ratiopharm and contact your doctor IMMEDIATELY.

Children and adolescents
This medicine should NOT be given to children and adolescents under the age of 18.

Other medicines and Sildenafil ratiopharm
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In a medical emergency, you must tell anyone treating you that you have taken Sildenafil ratiopharm.

Do NOT take Sildenafil ratiopharm if you are taking medicines that contain nitrates (e.g. glycerol trinitrate) or nitric oxide donors (e.g. amyl nitrite, also called “poppers”). These medicines are often used to relieve the symptoms of chest pain (angina pectoris). Simultaneous intake of nitrates or nitric oxide donors with Sildenafil ratiopharm can have severe effects on your blood pressure.

Tell your doctor or pharmacist if you are already taking riociguat.

Taking Sildenafil ratiopharm together with some medicines may lead to problems. Therefore, tell your doctor if you are taking any of the following medicines:
- ritonavir or saquinavir (medicines for the treatment of HIV infections);
- ketoconazole or itraconazole (medicines for the treatment of fungal infections);
- erythromycin (an antibiotic);
- cimetidine (medicine for the treatment of heartburn and peptic ulcers);

- alpha blockers (group of medicines for the treatment of high blood pressure or an enlarged prostate [benign prostatic hyperplasia]).
  Some patients taking alpha blockers may experience dizziness or light-headedness when getting up. These are symptoms of a fall in blood pressure upon rising quickly from sitting or lying (postural hypotension). These symptoms usually occur within 4 hours of taking Sildenafil ratiopharm. In order to reduce the probability of these symptoms occurring, you should start taking Sildenafil ratiopharm only when you are already well controlled on a regular daily dose of your alpha blocker.
- medicines containing sacubitril/valsartan, used to treat heart failure.

If you are taking one of these medicines, your doctor may start you on the lowest dose (25 mg) of Sildenafil ratiopharm. If you are taking ritonavir, you may not exceed a maximum dose of 25 mg sildenafil within a period of 48 hours.

Sildenafil ratiopharm with food, drink and alcohol
When this medicine is taken with food, it may take a little longer for Sildenafil ratiopharm to work.

Alcoholic drink can make erection difficulties worse. In order to get the maximum benefit from your medicine, it is recommended that you avoid alcohol before intake of this medicine.

Driving and using machines
This medicine might make some people feel dizzy or affect their vision or hearing. If you feel dizzy, or if your vision or hearing is affected after taking Sildenafil ratiopharm, do not drive or operate any tools or machines.

Sildenafil ratiopharm contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

3. How to take Sildenafil ratiopharm

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is
Take ½ or 1 film-coated tablet of Sildenafil ratiopharm as prescribed by your doctor about 1 hour before sexual activity. Swallow the film-coated tablet whole with a glass of water.

You should not take more film-coated tablets than your doctor tells you to.

You should not take Sildenafil ratiopharm more than once a day.

This medicine will only help you to get an erection if you are sexually stimulated. The amount of time Sildenafil ratiopharm takes to work varies from person to person, but it normally takes between half an hour and one hour. You may find that this medicine takes longer to work if you take it with a heavy meal.

If this medicine does not help you to get an erection, or if your erection does not last long enough for you to complete sexual intercourse, you should tell your doctor.

If you take more Sildenafil ratiopharm than you should
Men who take too much Sildenafil ratiopharm may experience more side effects or may get severe muscle pain. If you take more Sildenafil ratiopharm than you should, tell your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects reported in association with the use of sildenafil are usually mild to moderate and of a short duration.

If you experience any of the following serious side effects stop taking Sildenafil ratiopharm and seek medical help immediately:

- An allergic reaction - this occurs **uncommonly** (may affect up to 1 in 100 people). Symptoms include sudden wheeziness, difficulty in breathing or dizziness, swelling of the eyelids, face, lips or throat.

- Chest pains - this occurs **uncommonly.**
  If this occurs during or after intercourse:
  - Get in a semi-sitting position and try to relax.
  - **Do not use nitrates** to treat your chest pain.

- Prolonged and sometimes painful erections - this occurs **rarely** (may affect up to 1 in 1,000 people).
  If you have an erection, which lasts for more than 4 hours, you should contact a doctor immediately.

- A sudden decrease or loss of vision - this occurs **rarely.**

- Serious skin reactions - this occurs **rarely.**
  Symptoms may include severe peeling and swelling of the skin, blistering of the mouth, genitals and around the eyes, fever.

- Seizures or fits - this occurs **rarely.**

Other side effects:

Very common (may affect more than 1 in 10 people): headache.

Common (may affect up to 1 in 10 people): nausea, facial flushing, hot flush (symptoms include a sudden feeling of heat in your upper body), indigestion, colour tinge to vision, blurred vision, visual disturbance, stuffy nose and dizziness.

Uncommon (may affect up to 1 in 100 people): vomiting, skin rash, eye irritation, bloodshot eyes/red eyes, eye pain, seeing flashes of light, visual brightness, light sensitivity, watery eyes, pounding heartbeat, rapid heartbeat, high blood pressure, low blood pressure, muscle pain, feeling sleepy, reduced sense of touch, vertigo, ringing in the ears, dry mouth, blocked or stuffy sinuses, inflammation of the lining of the nose (symptoms include runny nose, sneezing and stuffy nose), upper abdominal pain, gastro-oesophageal reflux disease (symptoms include heartburn), presence of blood in urine, pain in the arms or legs, nosebleed, feeling hot and feeling tired.

Rare (may affect up to 1 in 1,000 people): fainting, stroke, heart attack, irregular heartbeat, temporary decreased blood flow to parts of the brain, feeling of tightening of the throat, numb mouth, bleeding at the back of the eye, double vision, reduced sharpness of vision, abnormal sensation in the eye, swelling of the eye or eyelid, small particles or spots in your vision, seeing halos around lights, dilation of the pupil of the eye, discolouration of the white of the eye, penile bleeding, presence of blood in semen, dry nose, swelling of the inside of the nose, feeling irritable and sudden decrease or loss of hearing.

From post-marketing experience cases of unstable angina (a heart condition) and sudden death have been reported rarely. Of note, most, but not all, of the men who experienced these side effects had

heart problems before taking this medicine. It is not possible to determine whether these events were directly related to Sildenafil ratiopharm.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Sildenafil ratiopharm

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

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

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Sildenafil ratiopharm contains
- The active substance is sildenafil.
  Each film-coated tablet contains sildenafil citrate equivalent to 100 mg of sildenafil.
- The other ingredients are: microcrystalline cellulose, hypromellose, croscarmellose sodium, magnesium stearate, calcium hydrogen phosphate, talc, macrogol 6000, titanium dioxide, iron oxide red.

What Sildenafil ratiopharm looks like and contents of the pack
Sildenafil ratiopharm are white to off-white, oblong film-coated tablets with edge and score line on one side. The tablet can be divided into equal doses.

Sildenafil ratiopharm are supplied in packs of 1, 2, 4, 8, 12, 24 or 48 film-coated tablets in blisters. Not all pack sizes may be marketed.

Marketing Authorisation Holder
ratiopharm GmbH
Graf-Arco-Straße 3
89079 Ulm
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Manufacturer
Merckle GmbH
Ludwig-Merckle-Straße 3
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Germany

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