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SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

DYNAFIL 50 mg tablets

DYNAFIL 100 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DYNAFIL 50 mg: Each tablet contains sildenafil citrate equivalent to 50 mg sildenafil.

DYNAFIL 100 mg: Each tablet contains sildenafil citrate equivalent to 100 mg sildenafil.

DYNAFIL contains sugar (lactose monohydrate) in the following quantities:

DYNAFIL 50 mg (124,76 mg), DYNAFIL 100 mg (249,52 mg).

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film coated tablet.

DYNAFIL 50 mg: Blue, elliptical, biconvex, 13,0 x 6,5 mm film coated tablets, with SL50 engraved on one side.

DYNAFIL 100 mg: Blue, elliptical, biconvex, 17,0 x 8,5 mm film coated tablets, with SL100

engraved on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DYNAFIL is indicated only for the treatment of erectile dysfunction.

DYNAFIL IS NOT AN APHRODISIAC.

4.2 Posology and method of administration

Posology

Adults

The recommended oral dose is 50 mg, taken if needed once a day approximately one hour before sexual intercourse.

The dose may be increased depending on the efficacy and toleration to 100 mg, or decreased to 25 mg using another formulation. Neither DYNAFIL 50 mg nor DYNAFIL 100 mg have score lines to permit halving, a 25 mg dose cannot be achieved by splitting these tablets. Another formulation should be used to achieve the 25 mg dose. The maximum recommended dosing frequency is once per day.

Several factors can lead to increased plasma levels of DYNAFIL

Age over 65: This can result in a 40% increase in the area under the curve (AUC).

Liver impairment: Conditions such as cirrhosis can cause an 80% increase.

Severe kidney impairment: Specifically, a creatinine clearance of 30 mL/min or less can lead to a 100% increase.

Concurrent use of strong cytochrome P450 3A4 inhibitors: Examples include erythromycin (182% increase), saquinavir (210% increase), ketoconazole and itraconazole (200% increase), and ritonavir (1000% increase).

Special populations

Elderly and patients with impaired renal or hepatic function

In patients with reduced clearance, increased DYNAFIL plasma levels and an increase in the incidence of adverse events may occur. A starting dose of 25 mg of another formulation should be considered in the following patient groups since neither DYNAFIL 50 mg nor DYNAFIL 100 mg have score lines to permit halving:

- Age > 65 (40 % increase in AUC)
- Hepatic impairment (e.g. cirrhosis, 80 %)
- Severe renal impairment (creatinine clearance < 30 mL/min, 100 %).

Another formulation should be used for patients requiring a dose of 25 mg.

Patients using potent CYP 3A4 inhibitors

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

Patients receiving alpha-blocker treatment

Patients should be haemodynamically stable on alpha-blocker therapy prior to initiating DYNAFIL treatment in order to minimise the potential of developing postural hypotension (see section 4.4). A starting dose of 25 mg of another formulation should be considered, since neither DYNAFIL 50 mg nor DYNAFIL 100 mg have score lines to permit halving.

DYNAFIL administration is contraindicated in patients who use nitric oxide donors or nitrates in any form as it was shown to potentiate the hypotensive effects of nitrates (see section 4.3).

Paediatric population

DYNAFIL is not indicated for use in children below 18 years of age.

Method of administration

For oral use.

4.3 Contraindications

Dynafil is contraindicated in:

- Hypersensitivity to sildenafil or to any of the ingredients of DYNAFIL (see section 6.1)

Consistent with its known effects on the nitric oxide / cGMP pathway (see section 5.1), DYNAFIL 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. Doctors should discuss the contraindication of

DYNAFIL with concurrent organic nitrates with their patients.

Although plasma levels of sildenafil at 24 hours post dose are much lower than at peak concentration, it is unknown whether nitrates can be safely co-administered at this time point.

- Patients with severe hepatic impairment (e.g. cirrhosis), severe impairment of renal function (creatine clearance < 30 mL/min) not on haemodialysis or continuous ambulatory peritoneal dialysis.
- **Concomitant use of DYNAFIL with potent cytochrome P450 3A4 inhibitors (e.g. erythromycin, ritonavir, saquinavir, ketoconazole and itraconazole) (see section 4.5).**
- The co-administration of PDE5 inhibitors, including DYNAFIL, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension (see section 4.5).
- Patients with non-arteritic anterior ischaemic optic neuropathy with loss of vision, regardless of whether this episode was in connection with previous PDE5 inhibitor exposure or not (see section 4.4).

4.4 Special warnings and precautions for use

Serious cardiovascular events, including myocardial infarction, sudden cardiac death, ventricular dysrhythmia, cerebrovascular haemorrhage and transient ischaemic attack have been reported post-

marketing in temporal association with the use of sildenafil, as found in DYNAFIL, for erectile dysfunction. Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many of these events were reported to occur during or shortly after sexual activity, and a few were reported to occur shortly after the use of sildenafil, as found in DYNAFIL, without sexual activity. Others were reported to have occurred hours to days after the use of sildenafil, as found in DYNAFIL, and sexual activity. It is not possible to determine whether these events are related directly to sildenafil, as found in DYNAFIL, to sexual activity, to the patient's underlying cardiovascular disease, to a combination of these factors, or to other factors. **The cardiovascular status of patients should be assessed prior to initiating treatment for erectile dysfunction.** DYNAFIL should not be used in men for whom sexual activity is inadvisable.

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

Cardiovascular risk factors:

DYNAFIL has systemic vasodilatory properties that resulted in transient decreases in supine blood pressure in healthy volunteers. Medical practitioners should carefully consider whether their patients with underlying cardiovascular disease could be affected adversely by such vasodilatory effects, especially in combination with sexual activity. Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction (e.g. aortic

stenosis, hypertrophic obstructive cardiomyopathy), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure.

DYNAFIL potentiates the hypotensive effect of nitrates (see section 4.3).

Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular dysrhythmia, cerebrovascular haemorrhage, transient ischaemic attack, hypertension and hypotension have been reported post-marketing in temporal association with the use of DYNAFIL. Some 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 DYNAFIL without sexual activity.

Priapism:

Prolonged erections and priapism have been reported with DYNAFIL in post-marketing experience. Patients should seek immediate medical assistance in the event of an erection that persists longer than 4 hours. Priapism (painful erections longer than 6 hours) should be treated immediately, as penile tissue damage and permanent loss of potency could result.

DYNAFIL 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).

Concomitant use with alpha-blockers:

Caution is advised when DYNAFIL is co-administered to patients taking an alpha-blocker; administration may lead to symptomatic hypotension (see section 4.5). This is most likely to occur within 4 hours post DYNAFIL dosing (see section 4.5).

In order to minimise the potential for developing postural hypotension, patients should be haemodynamically stable on alpha-blocker therapy prior to initiating DYNAFIL treatment. Initiation of DYNAFIL at a dose of 25 mg should be considered (see section 4.2). In addition, doctors should advise patients what to do in the event of postural hypotensive symptoms.

Sensorineural deafness:

A sudden unilateral or bilateral decrease or loss of hearing (sensorineural deafness) with or without associated vestibular symptoms has been reported with the use of PDE5 inhibitors, including DYNAFIL.

There is insufficient information regarding the reversibility of the hearing loss and the role of underlying risk factors for hearing loss in individual subjects (see section 4.8).

In case of sudden decrease or loss of hearing, patients should be advised to stop taking DYNAFIL and consult a medical practitioner promptly.

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

Combinations of DYNAFIL with other treatments for erectile dysfunction is not recommended as the safety and efficacy of such combinations have not been studied.

Effects on vision:

Non-arteritic anterior ischaemic optic neuropathy (NAION) with some loss of vision or irreversible blindness has been reported with the use of selective phosphodiesterase type-5

inhibitors including sildenafil (contained in DYNAFIL). NAION appears to be a class effect of these medicines. Most of these patients had risk factors such as low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidaemia and smoking. Patients should be advised that in the event of any sudden visual defect they should stop taking DYNAFIL and consult their doctor immediately.

Individuals who have already experienced NAION are at increased risk of NAION recurrence. Therefore, medical practitioners should discuss this risk with these patients and whether they could be adversely

affected by use of PDE5 inhibitors. PDE5 inhibitors, including DYNAFIL, should be used with caution in these patients and the patient's NAION risk factors should be evaluated when considering prescribing DYNAFIL.

NAION appears to be a class effect of these medicines.

A minority of patients with the inherited condition retinitis pigmentosa have genetic disorders of retinal phosphodiesterases. There is no safety information on the administration of DYNAFIL to patients with

retinitis pigmentosa, therefore, DYNAFIL should be administered with caution to these patients.

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

- Patients who have suffered a myocardial infarction, stroke, or life-threatening dysrhythmia within the last 6 months.
- Patients with resting hypotension (BP < 90/50 mmHg) or hypertension (BP > 170/110

mmHg).

- Patients with cardiac failure or coronary artery disease causing unstable angina.

Concomitant use with ritonavir:

Co-administration of DYNAFIL with ritonavir is not advised (see section 4.3 and 4.5).

Effect on bleeding:

There are no controlled clinical data on the safety or efficacy of DYNAFIL in patients with bleeding disorders or active peptic ulceration, therefore, DYNAFIL should be administered with caution. DYNAFIL has no effect on bleeding time, including during co-administration with aspirin. Therefore, DYNAFIL should be administered with caution in these patients.

Doctors should counsel patients on the following:

DYNAFIL offers no protection against sexually transmitted diseases. Counselling of patients about the protective measures necessary to guard against sexually transmitted diseases, including the Human Immunodeficiency Virus (HIV), may be considered.

The use of DYNAFIL could increase the risk for unwanted pregnancy and suitable contraceptive measures should be taken.

There is potential of prolonged erections greater

than 4 hours and priapism in patients taking Dynafil and organic nitrates. The co-administration of Dynafil with regular and/or intermittent use of organic nitrates is contraindicated.

Lactose:

DYNAFIL contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take DYNAFIL.

Women:

DYNAFIL is not indicated for use by women.

4.5 Interaction with other medicines and other forms of interaction

Sildenafil may potentiate the hypotensive effect of acute and chronic nitrates. Therefore, the concomitant use of DYNAFIL and nitrates or nitric oxide donors is contraindicated (see section 4.3).

Ritonavir increases the plasma concentration of sildenafil significantly and such combinations should not be given (see section 4.4).

Preclinical studies showed additive systemic blood pressure lowering effect when PDE5 inhibitors were combined with riociguat. Concomitant use of riociguat with PDE5 inhibitors, including sildenafil, is contraindicated (see section 4.3).

Effects of other medicines on DYNAFIL

Inhibitors of cytochrome P450 (CYP) isoforms 3A4 (major route of sildenafil) and 2C9 (minor route of sildenafil) which may reduce sildenafil clearance, include the following: cimetidine, erythromycin, itraconazole, ketoconazole, mibefradil, HIV-protease inhibitors such as saquinavir.

Inducers of cytochrome P450 (CYP) isoform 3A4 may increase the metabolism and clearance of sildenafil such as rifampicin

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 as in DYNAFIL.

No effect of concomitant medication on sildenafil pharmacokinetics acting as CYP2C9 inhibitors

(such as tolbutamide, warfarin), CYP2D6 inhibitors (such as selective serotonin reuptake inhibitors, tricyclic antidepressants), thiazide and related diuretics, loop and potassium sparing diuretics, ACE inhibitors, calcium channel blockers, beta-adrenoreceptor antagonists.
Single doses of antacid (magnesium hydroxide/aluminium hydroxide) did not affect the bioavailability of DYNAFIL.

Effects of DYNAFIL on other medicines

Concomitant use of DYNAFIL and other antihypertensive medicines may potentiate the antihypertensive effect of these medicines. A mean additional reduction in supine blood pressure (systolic, 8 mmHg; diastolic, 7 mmHg) was observed in concomitant use of sildenafil and amlodipine (see sections 4.2 and 4.4).
Concomitant administration of DYNAFIL 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). 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.
Grapefruit juice is a weak inhibitor of CYP3A4 gut wall metabolism and may give rise to modest increases in plasma levels of sildenafil.
DYNAFIL did not potentiate the increase in bleeding time caused by aspirin.
No significant interactions were shown between DYNAFIL and tolbutamide (250 mg) or warfarin (40 mg), both being metabolised by CYP2C9 isoenzyme.

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

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.).

Addition of a single dose of DYNAFIL 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 DYNAFIL is initiated in patients treated with sacubitril/valsartan.

4.6 Fertility, pregnancy and lactation

DYNAFIL is not indicated for use in women. DYNAFIL was not found to be carcinogenic, teratogenic, embryotoxic or fetotoxic in animal studies. Single 100 mg oral doses of sildenafil did not impair sperm motility or morphology.

4.7 Effects on ability to drive and use machines

DYNAFIL may have a minor influence on the ability to drive and use machines.
DYNAFIL can lead to dizziness and altered vision.
Patients should be advised not to drive or operate hazardous machinery or perform hazardous tasks, until they know how DYNAFIL affects them.

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4.8 Undesirable effects

a.) Summary of the safety profile

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 blurred vision.

b.) Tabulated summary of adverse effects

System Organ Class	Frequency	Side effects
Infections and infestations	Frequent Less frequent	Flu syndrome Respiratory tract infection, herpes simplex, pharyngitis, bronchitis, sinusitis, urinary tract infection, laryngitis
Blood and lymphatic system disorders	Less frequent	Anaemia, leukopenia
Immune system disorders	Less frequent Frequency unknown	Allergic reaction Hypersensitivity (including skin reactions)*
Metabolism and nutrition disorders	Less frequent	Thirst, oedema, gout, unstable diabetes, hyperglycaemia, hyperuricaemia, hypoglycaemic reaction, hypernatraemia

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Psychiatric disorders	Less frequent	Depression, abnormal dreams
Nervous system disorders	Frequent	Insomnia, headache, dizziness, pyrexia
	Less frequent	Ataxia, hypertonia, neuralgia, neuropathy, paraesthesia, tremor, vertigo, somnolence, migraine, decreased reflexes, hypoaesthesia
	Frequency unknown	Seizure*, seizure recurrence*
Eye disorders	Frequent	Abnormal vision (increased perception of light, blurred vision), chromatopsia (mild and transient, predominantly colour tinge to vision)
	Less frequent	Conjunctivitis, photophobia, dry eyes, eye haemorrhage, eye pain, cataract
	Frequency unknown	Ocular redness*, mydriasis*, diplopia*, temporary vision loss/decreased vision*, lacrimation disorders*, photopsia*, ocular hyperaemia*, non-arteritic anterior ischaemic optic neuropathy (NAION)*, retinal vascular occlusion*, retinal haemorrhage*,

		arteriosclerotic retinopathy*, retinal disorder*, glaucoma*, visual field defect*, visual acuity reduced*, myopia*, asthenopia*, vitreous floaters*, iris disorder*, halo vision*, eye oedema*, eye swelling*, eye disorder*, conjunctival hyperaemia*, eye irritation*, abnormal sensation in eye*, eyelid oedema*, scleral discolouration*
Ear and labyrinth disorders	Less frequent	Tinnitus, deafness, ear pain
Cardiac disorders	Frequent Less frequent Frequency unknown	Palpitations Cerebrovascular haemorrhage, transient ischaemic attack, tachycardia, angina pectoris, unstable angina, AV block, cardiac arrest, heart failure, abnormal electrocardiogram, cardiomyopathy, atrial fibrillation Myocardial infarction*, sudden cardiac death*, ventricular dysrhythmia*

Vascular disorders	Frequent Less frequent	Vasodilation, flushing, hot flushes Hypotension, hypertension, syncope, postural hypotension, epistaxis, shock
Respiratory, thoracic and mediastinal disorders	Frequent Less frequent	Nasal congestion, rhinitis Respiratory disorders, dyspnoea, asthma, cough increased, sputum increased, throat tightness, nasal oedema, nasal dryness
Gastrointestinal disorders	Frequent Less frequent	Dyspepsia Vomiting, glossitis, colitis, dysphagia, gastritis, gastroenteritis, oesophagitis, stomatitis, dry mouth, diarrhoea, nausea, abdominal pain, gingivitis, rectal haemorrhage, gastro-oesophagael reflux disease (GORD)
Hepatobiliary disorders	Frequent	Liver function tests abnormal

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Skin and subcutaneous tissue disorders	Frequent Less frequent Frequency unknown	Flushing, erythema Urticaria, pruritus, sweating, skin ulcer, contact dermatitis, exfoliative dermatitis, photosensitivity reaction, face oedema, erythema Stevens Johnson Syndrome*, Toxic Epidermal Necrolysis (TEN)*
Musculoskeletal, connective tissue and bone disorders	Less frequent	Arthralgia, myalgia, back pain, tenosynovitis, synovitis, arthritis, tendon rupture, arthrosis, bone pain, myasthenia
Renal and urinary disorders	Less frequent	Cystitis, nocturia, urinary frequency/incontinence, haematuria
Reproductive system and breast disorders	Less frequent Frequency unknown	Gynaecomastia, abnormal ejaculation, prostatic disorder, genital oedema, penile haemorrhage, haematospermia, anorgasmia Priapism*
General disorders and administrative site conditions	Less frequent	Asthenia, pain, chest pain, chills, peripheral oedema, feeling hot, thirst, irritability
Injury and poisoning	Less frequent	Accidental injury/fall

***Reported during post-marketing surveillance only

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website. An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

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

Side effects may be exacerbated or exaggerated (see section 4.8).

Management of overdose:

Supportive measures should be adopted as required, in the event of an overdose.

Renal dialysis is not expected to accelerate clearance as sildenafil is highly bound to plasma proteins and not eliminated in the urine.

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals; Drugs used in erectile dysfunction.

ATC code: G04B E03

Pharmacological classification: A 7.1.5 Vasodilators – peripheral

Mechanism of action:

Sildenafil is a selective phosphodiesterase type 5 (PDE5) inhibitor, an enzyme responsible for degrading cyclic guanosine monophosphate (cGMP) in the corpus cavernosum.
Sildenafil facilitates the effect of nitric oxide on the corpus cavernosum tissue during sexual stimulation with increased cGMP levels, the smooth muscle is relaxed and blood flows into the corpus cavernosum producing an erection. Without sexual stimulation, sildenafil has no effect on erections. Sildenafil increases blood flow to the penis in response to sexual stimulation, and thereby restores impaired erectile function.

5.2 Pharmacokinetic properties

Absorption:

Sildenafil is rapidly absorbed after an oral dose with a bioavailability of about 40 % (range 25 - 63 %). Peak plasma concentrations are reached within 30 to 120 minutes (median 60 minutes) of oral dosing in the fasted state. The oral pharmacokinetics of sildenafil are proportional over the recommended dose range (25 – 100 mg). A high fat meal reduces absorption of sildenafil as shown by reducing the maximum plasma concentration (C_{max}) by 29 % and delaying time to

peak concentration (T_{max}) by 60 minutes.

Distribution:

The mean steady state volume of distribution (V_{ss}) for sildenafil is 105 litres, indicating distribution into the tissues. Sildenafil and its major circulating N-desmethyl metabolite exhibit very high percentage (96 %) plasma protein binding, independent of total medicine concentrations. Less than 0,002 % (average 188 ng) of sildenafil remained in the semen of healthy volunteers at 90 minutes after dosing.

Biotransformation:

Hepatic metabolism of sildenafil is predominantly by the CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes. Sildenafil is converted by N-demethylation to an active metabolite with a PDE selectivity profile similar to sildenafil and an in vitro potency for PDE5 approximately 50 % that of the parent compound. Plasma concentrations of this metabolite are approximately 40 % of those seen for sildenafil. The N-desmethyl metabolite is further metabolised, with a terminal half-life of approximately 4 hours.

Elimination:

The total body clearance of sildenafil is 41 L/h with a resultant terminal phase half-life of 3 – 5 hours. After either oral or intravenous administration, sildenafil is excreted as metabolites mainly 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 cleared sildenafil less effectively from the plasma than did healthy volunteers 18 to 45 years of age as shown by a 40 % increase of AUC in older adults.

Renal Insufficiency

Sildenafil clearance was reduced in volunteers with severe renal impairment with creatinine clearance values of CLcr ≤ 30 mL/min, resulting in increases in AUC (100 %) and C_{max} (88 %) compared to age-matched volunteers with no renal impairment (see section 4.2). The pharmacokinetics of sildenafil were not altered in persons with mild to moderate renal impairment.

Hepatic insufficiency

Sildenafil clearance was reduced in volunteers with hepatic cirrhosis (Child-Pugh A and B), resulting in increases in AUC by 84 % and C_{max} by 47 % compared to age-matched volunteers with no hepatic impairment (see section 4.2).

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.

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6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cores:

Croscarmellose sodium

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Povidone

Coating - Opadry blue

Hypromellose 6cP

Indigo carmine aluminium lake

Macrogol 6000

Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

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6.4 Special precautions for storage

Store at or below 25 °C. Protect from light and moisture.

Do not remove from outer carton until required for use.

6.5 Nature and contents of container

DYNAFIL 50 mg is packed into hard, silver-coloured aluminium foil / transparent PVC/PVDC film blister strips, containing 2 or 4 tablets each. Each outer carton contains 1 blister strip.

DYNAFIL 100 mg is packed into hard, silver-coloured aluminium foil / transparent PVC/PVDC film blister strips, containing 2 or 4 tablets each. Each outer carton contains 1 blister strip.

6.6 Special precautions for disposal <and other handling>

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER(S)

DYNAFIL 50 mg: A42/7.1.5/1071

DYNAFIL 100 mg: A42/7.1.5/1072

Not all strengths may be marketed.

9. DATE OF FIRST AUTHORISATION

Date of registration: 14 September 2012

10. DATE OF REVISION OF THE TEXT

19 August 2025

DYNAFIL 50 mg: NAM: NS2 13/7.1.5/0086

DYNAFIL 100 mg: NAM: NS2 13/7.1.5/0087

DYNAFIL 50 mg: MOZ 5044

DYNAFIL 100 mg: MOZ 5045