



Tablets

Information for the supply of

EROPID

50 mg film-coated tablets

Sildenafil

Contents Page

Introduction	03
Understanding Erectile Dysfunction	04
About Eropid	06
Patient Eligibility of Eropid	08
The Pharmacy Checklist	10
Advice for Men Who are Suitable for Eropid	12
Advice for Men who are Not Suitable for Eropid	13
Advice for All Men	14
Resources for Further Information	15
Essential Information	16
References	20

Introduction

This booklet is part of the information and training material to support pharmacists in providing Eropid as an over the counter treatment for Erectile Dysfunction (ED), also known as impotence.

This document contains essential information you will need to know and consider when assessing patients as suitable candidates for the use of Eropid.

One 'Pharmacy Checklist' is enclosed in the middle of this booklet, additional 'Pharmacy Checklists' can be found on our website that may be used electronically or to be printed out at www.somexpharma.com.

Whilst this document provides the comprehensive information required, pharmacists are still required to use their professional judgement

Understanding Erectile Dysfunction

What Erectile Dysfunction is

Erectile dysfunction (ED) or impotence is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. ^[1]

It can occur at any age but becomes more common with increasing age. It's an issue that affects nearly half of men over the age of 40 years ^[2], and it significantly negatively impacts the quality of life and life satisfaction of the affected individual as well as their partner. ^[3]

Causes of Erectile Dysfunction

It is of importance to identify the cause of erectile dysfunction, as it is a symptom and not a disease. It can be indicative of many conditions including, but not limited to: diabetes mellitus, hypogonadism, vascular disease, depression and renal failure. Identification allows patients to be managed more appropriately for their conditions. ^[4]

Broadly, the causes of erectile dysfunction fall into three categories: ^[5]

- **Organic causes** ^[6]
 - The most common cause is of vasculogenic nature, that is due to disease such as cardiovascular disease (CVD), hypertension, hyperlipidaemia, diabetes mellitus, smoking, major pelvic surgery (radical prostatectomy) or radiotherapy of the pelvis. ^[7]
 - Other organic causes include central neurogenic disease (multiple sclerosis, Parkinson's disease), stroke, spinal cord trauma or disease, central nervous system tumour.
 - Peripheral neurogenic diseases that may cause erectile dysfunction are diabetes mellitus, renal failure, polyneuropathy or urethral surgery.
 - Anatomical or structural causes of erectile dysfunction include Peyronie's disease, penile cancer, congenital curvature of the penis, micropenis and other disease that cause a deformity of the penis
 - Hormonal causes include hypogonadism, hyperprolactinaemia, hyper/hypothyroidism, Cushing's disease and multiple endocrine disorders including hypopituitarism
- **Psychogenic causes**
 - This may be generalised, such as due to a lack of arousal and disorders of sexual intimacy
 - Or situational, for example due to performance or partner related issues (low self-esteem or indifference), stress (e.g. money worries and bereavement) and psychiatric illnesses (e.g. depression, anxiety and schizophrenia)
- **Causes associated with specific drugs include** ^[8-12]
 - **Antihypertensives**
 - Beta blockers – impairs vasodilation of the corpora cavernosa
 - ACEIs and ARBs – Interfere with smooth muscle relaxation
 - **Diuretics**
 - Spironolactone and thiazides – Believed to interfere with smooth muscle relaxation
 - **Antidepressants**
 - SSRIs, TCAs and MAOIs – Decrease arousal and desire
 - **Antiarrhythmic drugs**

- **Antiepileptics**
 - Carbamazepine, phenytoin, barbiturates – Affect sex hormone levels
- **Methyldopa**
- **Antipsychotics**
 - Chlorpromazine and haloperidol – increase prolactin levels
- **Hormones or hormone-modifying drugs**
 - Antiandrogens, LHRH agonists (goserelin, leuprorelin), corticosteroids, 5-alpha reductase inhibitors – Decrease sex hormone levels and androgen receptors, reducing sexual desire
- **Histamine (H₂) antagonists**
 - Cimetidine and ranitidine – increase prolactin levels, reducing sexual desire
- **Recreational drugs**
 - Alcohol, heroin, cocaine, marijuana, methadone and synthetic drugs – cause vasoconstriction and/or impacts on neurotransmitters in the erectile pathway

About Eropid

Eropid contains 50mg of sildenafil as a pharmacy only medicine (P medicine) that treats erectile dysfunction (ED) in men aged 18 year and over.

It is a well-established drug that is tolerated well and provides patients with direct legal access via a registered pharmacy under the supervision of a registered pharmacist, no longer requiring a valid prescription from a doctor.

The drug improves erectile function to alleviate erectile dysfunction in affected patients ^[13]. This provides patients to fully engage in sexual intercourse, whilst also providing emotional benefits. Including helping patients to regain their self-esteem, self-confidence and relationship satisfaction ^[14]. It was also shown to improve depressive symptoms in patients with erectile dysfunction. ^[15]

Mechanism of Action

Sildenafil, the active ingredient is a phosphodiesterase type-5 (PDE5) inhibitor.

Penile erection is achieved when sexual stimulation causes a release of nitric oxide (NO) from the cavernous nerved at the nerve endings in the penis. The nitric oxide diffuses across the endothelial cells into smooth muscle to stimulate the enzyme guanylate cyclase, to convert guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP). This initiates a series of cascades causing blood vessels in the penis to expand, increasing blood flow, resulting in an erection.

Phosphodiesterase type-5 (PDE5) inhibitors, prevent the inactivation and recycling of cGMP, resulting in elevated levels of cGMP.

PDE5 is found in particularly high concentrations in the corpus cavernosum, erectile tissue of the penis.

Increased cGMP results in vasodilation which facilitates the generation and maintenance of an erection.

Efficacy of Eropid (Sildenafil 50mg)

Sildenafil is recommended as first-line treatment in erectile dysfunction by:

- National Institute for Health and Care Excellence (NICE) Clinical Knowledge Summaries Erectile dysfunction (December 2017) ^[16]
- British Society for Sexual Medicine (BSSM) Guidelines on the management of erectile dysfunction ^[17]
- European Association of Urology (EAU) Guidelines on male sexual dysfunction ^[18]

In some patients 50mg may not be adequate and require a referral to the GP for an increased strength prescription.

Other patients who have renal or hepatic impairment, interacting medications or those who have tolerability issues should be referred to their doctor.

Sexual intercourse was successful in 69% of all attempts for the men receiving sildenafil, versus 22% for a placebo. The mean numbers of successful attempts per month were 5.9 for men receiving sildenafil versus 1.5 for those receiving a placebo. ^[19]

Long-term effectiveness of sildenafil was assessed after 12 months and at 3 years, with satisfaction and improvement in ability to engage in sexual activity reported in 96% and 99% of patients respectively. ^[20]

The efficacy of sildenafil in almost every subgroup of patients with ED is more than established: [21]

Response rates in elderly men (≥ 65 years) are comparable with the general population regardless of age. [22]

No differences in response rates were demonstrated in ethnic groups [23].

In type 1 diabetic patients, 66.6% reported improved erections and 63% reported successful intercourse attempts compared with 28.6% and 33% by those taking a placebo, respectively. [24]

In patients after bilateral nerve-sparing radical prostatectomy, 76% responded to treatment with sildenafil. [25]

A favourable response was observed to sildenafil in patients with ischemic heart disease who were receiving beta blockers and/or angiotensin-converting enzyme inhibitors and/or calcium channel blockers. [26]

Similar results presented in patients with hypertension (taking different or multiple antihypertensive drugs). High efficacy rates presented in patients on chronic dialysis for renal failure (lower doses and longer intervals between treatments are usually required) [27] [28], after renal transplantation [29] [30], in spinal cord injuries [31] [32] and patients with depression (treated with selective serotonin reuptake inhibitors or not) [33] [34] or patients treated with antipsychotic agents [35].

Patient Eligibility of Eropid

The provided 'Pharmacy Checklist' within this booklet or available on our website (www.somexpharma.com) contains a checklist to aid pharmacists in determining patient suitability for this product.

Exclusion criteria:

- **Under 18s**, as this medicine is not indicated for this patient group and those with issues relating to erectile dysfunction should be directed to their GP
- **Women**, this medicine is only indicated for men aged 18 years of over. If a female is interested in the product for their male partner, it's important to encourage their partner to visit the pharmacy (or doctor) for advice
- **Those who do not have ED, this medicine will not enhance men's erections, sexual performance** or help with problems such as premature ejaculation – such patients with the latter should be advised to speak with their GP for advice
- **Those who are allergic to sildenafil** or any other ingredient in the medicine

Patients with the following health problems must not use Eropid:

- **Hypotension (<90/50 mmHg)**
- Previously diagnosed mild, moderate or severe **hepatic impairment**
- Previously diagnosed severe **renal impairment**
- **Anatomical deformities of the penis**, such as angulation, cavernosal fibrosis or Peyronie's disease
- With **sickle cell anaemia, multiple myeloma** or **leukaemia**
- Loss of vision in one eye because of **non-arteric anterior optic neuropathy (NAION)**, regardless of any connection with PDE5i exposure
- Inherited eye disease such as **retinitis pigmentosa**
- **Bleeding issues (e.g. haemophilia)** or suffer from **stomach ulcers**
- Rare hereditary issues of **galactose intolerance**, Lapp lactase deficiency or glucose-galactose malabsorption) – Due to lactose within the product
- **With the following cardiovascular issues:**
 - **Breathlessness or chest pains** during light or moderate physical activity e.g. Walking briskly for 20 minutes or climbing two flights of stairs
 - Patients who have been advised against sexual activity because of a **cardiovascular problem**
 - Patients who have had a **stroke** or a **myocardial infarction** within the last six months
 - Patients with increased susceptibility to vasodilators including those with **left ventricular outflow obstruction (e.g. aortic stenosis)**, or those with a rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure
 - **Patients previously diagnosed with the following:**
 - **Uncontrolled hypertension**
 - **Hypotension**
 - **Unstable angina**
 - **Moderate to severe valvular disease**
 - **Left ventricular dysfunction**
 - **Hypertrophic obstructive and other cardiomyopathies**
 - **Significant arrhythmias**
 - **Severe cardiac failure**

Such patients with the aforementioned health problems should be advised to consult with their GP before requesting the use of this product.

Note: Eropid may be suitable for some low risk cardiovascular patients who have been advised by their doctor that they can resume sexual activity; those with asymptomatic controlled hypertension, mild valvular disease or who had had successful coronary artery bypass grafting, stenting or angioplasty.

Interacting Medications

Patients taking the following medications must not use Eropid:

- **Nitrates; isosorbide mononitrate/dinitrate and glyceryl trinitrate, Nitric oxide donors; nicorandil and 'Poppers'; amyl nitrate** – Affects the NO cGMP pathway which sildenafil potentiates the hypotensive effects of
- **Guanylate cyclase stimulators e.g. Riociguat** – may lead to symptomatic hypotension
- **Ritonavir** – A potent CYP3A4 inhibitor that increase sildenafil plasma concentrations
- **Already taking another PDE5i**
- **Alpha blockers;** Phenoxybenzamine, phentolamine, tolazoline, trazodone, alfuzosin, doxazosin, tamsulosin, prazosin, terazosin
- **CYP3A4 inhibitors**
 - Antibiotics; erythromycin, clarithromycin, rifampicin
 - Antifungals; itraconazole, ketoconazole
 - Calcium channel blockers; diltiazem, verapamil
 - H2 antagonists; cimetidine
 - HIV-protease inhibitors; amprenavir, fosamprenavir, atazanavir, darunavir, indinavir, lopinavir, ritonavir, saquinavir, tipranavir

The Pharmacy Checklist

This information pack has been created to help you determine if your patient is suitable for Eropid (Sildenafil). Within this pack is an optional checklist below and overleaf, that you may use to help assess the suitability of your patient. **In ALL cases your professional judgement should be used to decide when and how to use it.** Further information and copies of this checklist can be found at www.somexpharma.com

Who Eropid is for:

Eropid is solely intended for men 18 years and older who are experiencing erectile dysfunction (ED), also known as impotence; this is the inability to attain and/or maintain penile erection sufficient for satisfactory sexual performance. It's important to confirm if the patient's already receiving treatment for the condition, those who are currently prescribed 50 mg of sildenafil can be supplied this product if the patient meets the criteria for pharmacy supply, given that they do not take more than 50 mg daily. Remind the patient to follow up with his doctor within the first 6 months of use. Should the patient be using a different dose of sildenafil or another ED treatment, they should be referred to their doctor.

Causes of erectile dysfunction:

Erectile dysfunction has multiple causes which should be considered and support should be offered to patients, regardless of suitability for this product. This may include undiagnosed depression, anxiety, stress or worry. Other causes include side effects of medications such as: diuretics, anti-hypertensives, corticosteroids, anticonvulsants and recreational drugs. Patients should be made aware of other risk factors that include excessive drinking, smoking, obesity and a lack of exercise.

Suitability checklist:

These are questions to ask your patients, in order to determine their suitability.

If the patient answers yes to any of the following, do NOT supply the product and refer the patient to their doctor.

Please put Yes / No into the respective check boxes

Y N 1. Check the patient's CARDIOVASCULAR (CV) HEALTH by asking the following:

- Have you been advised by your doctor that you are not fit enough for any physical or sexual activity?
- Do you feel very breathless or experience chest pain with light/moderate physical activity e.g. walking briskly for twenty minutes or climbing two flights of stairs
- Have you had a heart attack or stroke within the last six months?
- Do you have any other heart problems or are under a doctor's care for any of the following?
 - Low blood pressure or uncontrolled high blood pressure
 - Unstable angina (chest pain), irregular heartbeat or palpitations (arrhythmia)
 - A problem with one of the valves in your heart (valvular heart disease)
 - A problem where your heart muscle becomes inflamed and doesn't work as well as it should (cardiomyopathy)
 - Heart problems causing blood flow issues (e.g. left ventricular outflow obstruction, aortic narrowing) or severe cardiac failure

Y N 2. Check the patient's CURRENT MEDICATIONS for interactions by asking the following:

- Are you taking any nitrates for chest pain? (nicorandil or other nitric oxide donors e.g. glyceryl trinitrate, isosorbide mononitrate or isosorbide dinitrate)
- Are you using drugs called 'poppers' (amyl nitrite) for recreational purposes?
- Are you taking riociguat or other guanylate cyclase stimulators for lung problems?
- Are you taking ritonavir (for HIV infection)?
- Are you taking any CYP3A4 inhibitors e.g. saquinavir (to treat HIV infection), cimetidine (for heartburn), itraconazole or ketoconazole (to treat fungal infections), erythromycin or rifampicin (antibiotics) or diltiazem (for high blood pressure)?
- Are you taking any alpha-blockers, such as alfuzosin, doxazosin or tamsulosin, which are medicines used to treat urinary problems due to an enlarged prostate (benign prostatic hyperplasia) or occasionally to treat high blood pressure?

Y N 3. Check for OTHER CONTRAINDICATIONS:

- Do you have Peyronie's disease or any other disease, injury or deformation of the penis?
- Have you ever had loss of vision because of damage to the optic nerve (e.g. non-arteric anterior ischaemic optic neuropathy [NAION]) or have an inherited eye disease (e.g. retinitis pigmentosa)?
- Do you have intolerance to galactose, Lapp lactase deficiency or glucose-galactose malabsorption?
- Do you have previously diagnosed hepatic (liver) disease (including liver cirrhosis), or severe renal (kidney) impairment?
- Do you have any of the following: sickle cell anaemia, multiple myeloma or leukaemia?
- Do you have any bleeding issues (e.g. haemophilia) or any active stomach ulcers?

Your pharmacist has supplied you with Eropid today for your personal use.

Please ensure that you make an appointment to see your GP within 6 months of the date of receiving Eropid (see date on reverse)

You have not been provided with Eropid (sildenafil) for ED today, as it may not be suitable for you to take without consulting a doctor first.

You should go to see your doctor as soon as you can to discuss other suitable options, please present this slip to your GP

Counselling Points for Patients and Other Information

Please follow these points to ensure that your patient is counselled appropriately, regardless of product supply:

Advice for patients who have not been supplied Eropid:

Should a patient not have been supplied Eropid because of their cardiovascular health, interacting medicines or other concerns, they must be told to see their GP as soon as they can within six months.

Advice for patients who have been supplied Eropid:

- Eropid is only intended for men 18 years and older who have erectile dysfunction and others who don't, won't benefit from using this product
- Take one tablet approximately 1 hour before planning to have sexual intercourse, Eropid can start working within 30 minutes. Sexual stimulation (foreplay) and arousal is still required to attain an erection.
- Take Eropid with or without food, but Eropid can take longer to work after a high-fat meal
- Avoid taking with grapefruit or grapefruit juice, as it may affect the way the medicine works
- Large amounts of alcohol should be avoided, as it can increase the risk and incidence of side effects
- The maximum dose frequency is one 50 mg tablet per day
- Eropid may need to be taken a number of times on different occasions, before they can achieve a penile erection sufficient for satisfactory sexual activity. If after several failed attempts in achieving an erection sufficient for satisfactory sexual activity, they should consult a doctor
- Patients should be warned not to take any medicines called nitrates or nitric oxide donors, (such as glyceryl trinitrate, isosorbide mononitrate, isosorbide dinitrate, for the relief of chest pain or heart failure or amyl nitrite also known as "poppers", nicorandil or sodium nitroprusside), as the combination may lead to a dangerous fall in blood pressure;
- Patients should notify their doctor and pharmacists that they have started taking Eropid, especially if they are started on any new medicines
- Patients may experience some normal side effects including, but not limited to: headache, facial flushing, hot flush, dyspepsia, nausea, nasal congestion, dizziness, visual disturbance, cyanopsia (blue-tinted vision) and blurred vision – should any of these become a concern, advise the patient to talk with a pharmacist or doctor
- **Should any of the following serious side effects occur, the patient should stop taking Eropid and seek immediate medical attention:**
 - o Chest pains. If these occur before, during or after intercourse get into a semi-sitting position and try to relax. Nitrates must NOT be used to treat chest pain.
 - o A persistent and sometimes painful erection lasting longer than 4 hours
 - o A sudden decrease or loss of vision
 - o An allergic reaction - symptoms include: sudden wheeziness, difficulty breathing or dizziness, swelling of the face, eyelids, lips or throat, peeling and swelling of the skin, blistering of the mouth, genitals and around the eyes, fever
 - o Seizures or fits
 - o Patient should inform their doctor if they have started taking Eropid.
 - o Eropid contains tartrazine: May cause allergic reactions as it contains Tartrazine (E-102). It can worsen asthma

Side effects can be reported by patients or pharmacists via the Yellow Card scheme at www.mhra.gov.uk/yellowcard/ or search for MHRA Yellow Card in the Google Play or Apple App Store.

The tear off slip should be filled in and provided to the man to facilitate discussion with their doctor.

Follow up advice for all patients:

- Erectile dysfunction can be associated with a number of contributing conditions (e.g. hypertension, hypercholesterolaemia or cardiovascular disease. As a result, ALL patients with erectile dysfunction should be advised to consult their doctor within six months for a clinical review of potential underlying conditions and risk factors associated with erectile dysfunction
- Provide appropriate advice on lifestyle factors and general healthy living, including:
 - o Losing weight, if obese
 - o Giving up smoking, recommend smoking cessation services
 - o Cutting back on alcohol and/or recreational drug use
 - o Exercising regularly
 - o Reducing stress
 - o Eating a healthy diet
- Also check if the patient is buying products from unregulated sources and explain the importance of the products not having been tested for their safety or effectiveness, may not contain the ingredients listed on their labels and therefore are potentially dangerous, unlike products sourced from a pharmacy and obtained via a prescription from the doctor.

If the patient has previously been supplied with Eropid, they should be asked if anything has changed with respect to their health status or medicines usage, there is no need to repeat the checklist again.

Give the patient a reminder to follow up with their doctor within the first 6 months of use.

If any factors have changed, the suitability checklist should be reviewed again.

The tear-off slip below can be provided to the patient to present for a repeat supply:

Dear Doctor, Please can you review this patient in relation to erectile dysfunction. We had a discussion in my pharmacy, but they were not suitable for Eropid (sildenafil) due to their cardiovascular health/interacting medicines/ other condition: Pharmacist signature:Date:	PHARMACY STAMP	Please keep this slip and present to the pharmacist when you next wish to purchase Eropid Before resupply, your pharmacist will need to assess you to ensure that there have been no changes in your health or medications since the last supply. Pharmacist signature:Date:	PHARMACY STAMP
--	-------------------	--	-------------------

Advice for Men Who are Suitable for Eropid

- Eropid (sildenafil 50mg) is used for men 18 years and older with Erectile Dysfunction (ED), those who don't have ED won't benefit from this product
- Do not take Eropid if you have taken any medicines called nitrates or nitric oxide donors, (such as glyceryl trinitrate, isosorbide mononitrate, isosorbide dinitrate, for the relief of chest pain or heart failure or amyl nitrite also known as "poppers", nicorandil or sodium nitroprusside), as the combination may lead to a dangerous fall in blood pressure;
- Take one dose (single 50mg tablet) with a full glass of water approximately 1 hour before planning to have sexual intercourse or masturbate, with a maximum of one single dose per 24 hours
- It can be taken with or without food, but best to avoid a high fat meal, as it can cause the medicine to take longer to begin its effect
- Eropid can start working within 30 minutes, but patients are still able to obtain an erection in response to sexual stimulation for up to 4 hours after taking the dose
- Sexual arousal and stimulation (foreplay) is still required to achieve an erection
- Avoid consuming grapefruit or grapefruit juice, as it may increase drug levels in the blood
- Large amounts of alcohol should be avoided, as it can side effects of Eropid and can impact sexual function
- For most patients, sildenafil will work on the first instance. However, for others it can take additional attempts to obtain maximum benefit. If after 8 separate occasions the patient is still suffering from erectile dysfunction, they should be advised to consult their doctor
- Patients should be advised to visit their doctor within 6 months of starting to take Eropid for a general health check-up and may continue using the product after a review, provided there's no change in their health or medication circumstances
- Patients may experience some normal side effects, which include:
 - Headache; advise the patient to drink plenty of water
 - Facial flushing, nausea, indigestion, blocked nose; these should soon pass
 - Feeling dizzy, visual changes such as blurred vision or colour distortion; affected patients should not drive, use tools or operate heavy machinery until reactions/vision returns back to normal
- **Should any of the following side effects occur, patients should be advised to stop taking Eropid and seek immediate medical attention:**
 - Chest pains. If these occur before, during or after intercourse get into a semi-sitting position and try to relax. Nitrates must NOT be used to treat chest pain.
 - A persistent and sometimes painful erection that lasts for more than 4 hours
 - A sudden decrease in hearing or loss of vision
 - An allergic reaction - symptoms include: sudden wheeziness, difficulty breathing or dizziness, swelling of the face, eyelids, lips or throat, peeling and swelling of the skin, blistering of the mouth, genitals and around the eyes, fever
 - Seizure or fits
 - A full list can be found in the Summary of Product Characteristics.
- If a patient takes more than the recommended dose, they should be referred immediately to the nearest Accident and Emergency facility or their on-call GP

Advice for Men who are Not Suitable for Eropid

Should a patient not have been supplied Eropid because of their cardiovascular health, interacting medicines or other concerns, they should be made aware of the reason why and be told to see their GP as soon as possible.

This should be encouraged as erectile dysfunction can be indicative of undiagnosed disease states including diabetes, **hypertension, cardiovascular disease** and **renal failure** etc.

Doctors may also be able to prescribe more suitable medicines or sildenafil at a different dose, to treat the patient's erectile dysfunction.

Advice for All Men

Affected individuals should be advised to consult their doctor within 6 months for a clinical review of potential underlying conditions or causes of their erectile dysfunction.

Lifestyle advice should be passed on to patients, in order to reduce or eliminate modifiable risk factors for erectile dysfunction. Such advice includes, but isn't limited to:

- Losing weight, if the patient is overweight
- Healthy eating with a balanced diet
- Regular exercise – recommended at least 150 minutes of moderate aerobic activity (e.g. cycling or brisk walking) every week
- Reducing stress – can recommend mindfulness therapy or yoga
- Giving up smoking – recommend smoking cessation services
- Reducing alcohol intake to moderate levels – max 14 units per week
- Avoiding recreational drug use

Resources for Further Information

Should you or your patient require further information in erectile dysfunction and/or the use of sildenafil, useful information may be found at the following credible and reliable sources:

- BNF - <https://bnf.nice.org.uk/drug/sildenafil.html>
- NICE CKS - <https://cks.nice.org.uk/erectile-dysfunction>
- NHS website - <https://www.nhs.uk/conditions/erection-problems-erectile-dysfunction/>
- Patient info - <https://patient.info/doctor/Erectile-Dysfunction>
- British Association of Urological Surgeons - https://www.baus.org.uk/patients/conditions/3/erectile_dysfunction_impotence

Essential Information

Name of product: Eropid 50mg Film Coated Tablets

Active ingredient(s): Sildenafil

Product licence number: PL 15764/0130

Name and address of the product licence holder: Somex Pharma, 600 High Road, seven Kings, Ilford, Essex, IG3 8BS, United Kingdom

Supply classification: Pharmacy only (P)

Indications: Treatment of men with erectile dysfunction

Side effects:

Very common (>1/10): headache.

Common ($\geq 1/100$ and $<1/10$): Dizziness, Visual colour distortions, Visual disturbance, Vision blurred, Flushing, hot flush, nasal congestion, nausea, dyspepsia.

Uncommon ($\geq 1/1,000$ and $<1/100$): rhinitis, hypersensitivity, Somnolence, Hypoaesthesia, Lacrimation disorders, Eye pain, Photophobia, Photopsia, Ocular hyperaemia, Visual brightness, Conjunctivitis, Vertigo, Tinnitus, Tachycardia, Palpitations, **Hypertension**, Hypotension, Epistaxis, Sinus Congestion, Gastro oesophageal reflux disease, Vomiting, Abdominal pain upper, Dry mouth, Rash, Myalgia, Pain in extremity, Haematuria, Chest pain, Fatigue, Feeling Hot, Heart rate Increased.

Rare ($\geq 1/10,000$ and $<1/1,000$): Cerebrovascular accident, Transient ischaemic attack, Seizure, Seizure recurrence, Syncope, Non-arteritic anterior ischaemic optic neuropathy (NAION), Retinal vascular occlusion, Retinal haemorrhage, Arteriosclerotic retinopathy, Retinal disorder, Glaucoma, Visual field defect, Diplopia, Visual acuity reduced, Myopia, Asthenopia, Vitreous floaters, Iris disorder, Mydriasis, Halo vision, Eye oedema, Eye swelling, Eye disorder, Conjunctival hyperaemia, Eye irritation, Abnormal sensation in eye, Eyelid oedema, Scleral discoloration, Deafness, Sudden cardiac death, Myocardial infarction, Ventricular arrhythmia, Atrial fibrillation, Unstable angina, Throat tightness, Nasal oedema, Nasal dryness, Hypoaesthesia, oral Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Penile haemorrhage, Priapism, Haemospermia, Erection, increased Irritability.

Precautions: Erectile dysfunction can be associated with a number of contributing conditions, e.g. **hypertension**, *diabetes mellitus*, hypercholesterolaemia or cardiovascular disease. As a result, all men with erectile dysfunction should be advised to consult their doctor within 6 months for a clinical review of potential underlying conditions and risk factors associated with erectile dysfunction (ED). If symptoms of ED have not improved after taking Sildenafil on several consecutive occasions, or if their erectile dysfunction worsens, the patient should be advised to consult their doctor.

Cardiovascular risk factors: Since there is a degree of cardiac risk associated with sexual activity, the cardiovascular status of men should be considered prior to initiation of therapy. Agents for the treatment of erectile dysfunction, including sildenafil, are not recommended to be used by those men who with light or moderate physical activity, such as walking briskly for 20 minutes or climbing 2 flights of stairs, feel very breathless or experience chest pain. The following patients are considered at low cardiovascular risk from sexual activity: patients who have been successfully revascularized (e.g. via coronary artery bypass grafting, stenting, or angioplasty), patients with asymptomatic controlled **hypertension**, and those with mild valvular disease. These patients may be suitable for treatment but should consult a doctor before resuming sexual activity.

Patients previously diagnosed with the following must be advised to consult with their doctor before resuming sexual activity: uncontrolled **hypertension**, moderate to severe valvular disease, left ventricular dysfunction, hypertrophic obstructive and other cardiomyopathies, or significant arrhythmias. Sildenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction (e.g. aortic stenosis), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure. Men with these conditions must not use the product without consulting a doctor. Sildenafil potentiates the hypotensive effect of nitrates. 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: Patients who have conditions which may predispose them to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia), should consult a doctor before using agents for the treatment of erectile dysfunction, including sildenafil. Prolonged erections and priapism have been occasionally 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 treatments for erectile dysfunction: The safety and efficacy of combinations of sildenafil with 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. 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. Patients should be advised that in case of sudden visual defect, they should stop taking sildenafil and consult a physician immediately. Concomitant use with CYP3A4 inhibitors. Pharmacokinetic analysis of clinical trial data indicated a reduction in sildenafil clearance when co-administered with CYP3A4 inhibitors (such as ketoconazole, itraconazole, erythromycin, cimetidine). Although, no increased incidence of adverse events was observed in these patients, they should be advised to consult a doctor before taking Sildenafil as a 25 mg tablet may be more suitable for them.

Concomitant use with alpha-blockers: Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the coadministration may lead to symptomatic hypotension in a few susceptible individuals. 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 hemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Thus, patients taking alpha blockers should be advised to consult their doctor before taking Sildenafil as a 25 mg tablet may be more suitable for them. Treatment should be stopped if symptoms of postural hypotension occur, and patients should seek advice from their doctor on what to do.

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, the use of sildenafil is not recommended in those patients with history of bleeding disorders or active peptic ulceration, and should only be administered after consultation with a doctor.

Hepatic impairment: Patients with **hepatic impairment** must be advised to consult their doctor before taking Sildenafil, since a 25 mg tablet may be more suitable for them.

Renal impairment: Patients with severe **renal impairment** (creatinine clearance <30 mL/min), must be advised to consult their doctor before taking Sildenafil, since a 25 mg tablet may be more suitable for them.

Use with alcohol: Drinking excessive alcohol can temporarily reduce a man's ability to get an erection.

Contra-indications: Hypersensitivity to the active substance or to any of the excipients. The film coating of the Sildenafil tablet contains tartrazine, which may cause allergic reactions. **Tartrazine has been linked with the exacerbation of asthma; however, the clinical evidence is inconclusive.** Consistent with its known effects on the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway, 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. Co-administration of Sildenafil with ritonavir (a highly potent P450 enzyme inhibitor) is contraindicated. The co-administration of phosphodiesterase type 5 (PDE5) inhibitors, including sildenafil, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension. Agents for the treatment of erectile dysfunction, including sildenafil, should not be used by those men for whom sexual activity may be inadvisable, and these patients should be referred to their doctor. This includes patients with severe cardiovascular disorders such as a recent (6 months) acute myocardial infarction (AMI) or stroke, unstable angina or severe cardiac failure. Sildenafil should not be used in patients with severe **hepatic impairment**, hypotension (blood pressure < 90/50 mmHg) and known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterases). This is because the safety of sildenafil has not been studied in these sub-groups of patients, and its use is therefore contraindicated. 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. Sildenafil should not be used in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease). Sildenafil is not indicated for use by women. The product is not intended for men without erectile dysfunction. This product is not intended for men under 18 years of age.

Dosage and Method of use: Use in adults: The recommended dose is 50 mg taken with water approximately one hour before sexual activity. 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. Patients should be advised that they may need to take Sildenafil a number of times on different occasions (a maximum of one 50 mg tablet per day), before they can achieve a penile erection satisfactory for sexual activity. If after several attempts on different dosing occasions patients are still not able to achieve a penile erection sufficient for satisfactory sexual activity, they should be advised to consult a doctor.

Special populations:

Use in the elderly: Dosage adjustments are not required in elderly patients (\geq 65 years old).

Use in patients with impaired renal function: No dosage adjustments are required for patients with mild to moderate renal impairment. However, since sildenafil clearance is reduced in individuals with severe renal impairment (creatinine clearance $<30\text{ml/min}$), individuals previously diagnosed with severe renal impairment must be advised to consult their doctor before taking Sildenafil, since a 25 mg tablet may be more suitable for them.

Use in patients with impaired hepatic function: Sildenafil clearance is reduced in individuals with **hepatic impairment** (e.g. cirrhosis). Individuals previously diagnosed with mild to moderate **hepatic impairment** must be advised to consult their doctor before taking Sildenafil, since a 25 mg tablet may be more suitable for them. The safety of sildenafil has not been studied in patients with severe **hepatic impairment**, and its use is therefore contraindicated.

Use in children and adolescents: Sildenafil is not indicated for individuals below 18 years of age.

Use in patients using other medicines: Pharmacokinetic analysis of clinical trial data indicated a reduction in sildenafil clearance when co-administered with CYP3A4 inhibitors (such as ritonavir, ketoconazole, itraconazole, erythromycin, cimetidine). With the exception of ritonavir, for which co-administration with sildenafil is contraindicated in individuals receiving concomitant treatment with CYP3A4 inhibitors must be advised to consult their doctor before taking Sildenafil, since a 25 mg tablet may be more suitable for them (see section 4.4 for further information). In order to minimise the potential of developing postural hypotension in patients receiving alpha blocker treatment (e.g. alfuzosin, doxazosin or tamsulosin), patients should be stabilised on alpha blocker therapy prior to initiating sildenafil treatment. Thus, patients taking alpha blockers must be advised to consult their doctor before taking Sildenafil since a 25 mg tablet may be more suitable for them.

Method of administration: For oral use.

Date: June 2019

References

- [1] British Society for Sexual Medicine (2013)
- [2] Nehra A, Kulaksizoglu H. Global perspectives and controversies in the epidemiology of male erectile dysfunction. *Curr Opin Urol.* 2002;12:493–6.
- [3] Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol.* 1994;151:54–61.
- [4] NIH Consensus Statement Volume 10, Number 4 December 7–9, 1992
- [5] NICE Clinical Knowledge summaries – Erectile Dysfunction. <https://cks.nice.org.uk/erectile-dysfunction> Accessed on June 2019.
- [6] British Society for Sexual Medicine (2013) Guidelines on the management of erectile dysfunction. www.bssm.org.uk
- [7] Randrup, E., Baum, N. and Feibus, A. (2015) Erectile dysfunction and cardiovascular disease. *Postgraduate Medicine* 127(2), 166-172.
- [8] Muneer, A., Kalsi, J., Nazareth, I. et al. (2014) Erectile dysfunction. *British Medical Journal* 348.
- [9] Rajendran, R. and Cummings, M. (2014) Erectile dysfunction: assessment and management in primary care. *Prescriber* 25(12), 25-30.
- [10] Randrup, E., Baum, N. and Feibus, A. (2015) Erectile dysfunction and cardiovascular disease. *Postgraduate Medicine* 127(2), 166-172.
- [11] Muneer, A., Kalsi, J., Nazareth, I. and Arya, M. (2014). Erectile dysfunction. *BMJ*, 348(jan27 7), pp.g129-g129.
- [12] European Association of Urology (2017) Guidelines on male sexual dysfunction. European Association of Urology. www.uroweb.org
- [13] Seidman SN, Roose SP, Menza MA, et al. Treatment of erectile dysfunction in men with depressive symptoms: results of a placebo-controlled trial with sildenafil citrate. *Am J Psychiatry* 2001 Oct;158:1623–30.
- [14] Cappelleri, J., Althof, S., O’Leary, M., Glina, S., King, R., Stecher, V., Carlsson, M. and Siegel, R. (2007). Clinically meaningful improvement on the Self-Esteem And Relationship questionnaire in men with erectile dysfunction. *Quality of Life Research*, 16(7), pp.1203-1210.
- [15] Seidman, S., Roose, S., Menza, M., Shabsigh, R. and Rosen, R. (2001). Treatment of Erectile Dysfunction in Men With Depressive Symptoms: Results of a Placebo-Controlled Trial With Sildenafil Citrate. *American Journal of Psychiatry*, 158(10), pp.1623-1630.
- [16] NICE CKS – Scenario: Management of erectile dysfunction <https://cks.nice.org.uk/erectile-dysfunction#!scenario>
- [17] Hackett, G., Kirby, M., Wylie, K., Heald, A., Ossei-Gerning, N., Edwards, D. and Muneer, A. (2018). British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men—2017. *The Journal of Sexual Medicine*, 15(4), pp.430-457.
- [18] European Association of Urology (2017) Guidelines on male sexual dysfunction. European Association of Urology. <https://uroweb.org/guideline/male-sexual-dysfunction/>
- [19] Goldstein I, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicker PA *N Engl J Med.* 1998 May 14; 338(20):1397-404.
- [20] The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. Carson CC, Burnett AL, Levine LA, Nehra A. *Urology.* 2002 Sep; 60(2 Suppl 2):12-27.
- [21] Hatzimouratidis K. Sildenafil in the treatment of erectile dysfunction: an overview of the clinical evidence. *Clin Interv Aging.* 2006 Dec;1(4):403-14. Epub 2006 Dec. PubMed PMID: 18046917; PubMed Central PMCID: PMC2699643.

- [22] Sildenafil citrate (VIAGRA) improves erectile function in elderly patients with erectile dysfunction: a subgroup analysis. Wagner G, Montorsi F, Auerbach S, Collins M J *Gerontol A Biol Sci Med Sci*. 2001 Feb; 56(2):M113-9
- [23] Efficacy and safety of sildenafil citrate (Viagra) in black and Hispanic American men. Young JM, Bennett C, Gilhooly P, Wessells H, Ramos DE *Urology*. 2002 Sep; 60(2 Suppl 2):39-48.
- [24] Sildenafil citrate for treatment of erectile dysfunction in men with type 1 diabetes: results of a randomized controlled trial. Stuckey BG, Jadzinsky MN, Murphy LJ, Montorsi F, Kadioglu A, Fraige F, Manzano P, Deerochanawong C. *Diabetes Care*. 2003 Feb; 26(2):279-84.
- [25] Long-term intracavernous therapy responders can potentially switch to sildenafil citrate after radical prostatectomy. Raina R, Lakin MM, Agarwal A, Ausmundson S, Montague DK, Zippe CD. *Urology*. 2004 Mar; 63(3):532-7; discussion 538.
- [26] Efficacy and safety of sildenafil citrate for the treatment of erectile dysfunction in men with cardiovascular disease. Olsson AM, Persson CA, Swedish Sildenafil Investigators Group. *Int J Clin Pract*. 2001 Apr; 55(3):171-6
- [27] Clinical efficacy of sildenafil in patients on chronic dialysis. Chen J, Mabjeesh NJ, Greenstein A, Nadu A, Matzkin H J *J Urol*. 2001 Mar; 165(3):819-2
- [28] The efficacy of sildenafil for the treatment of erectile dysfunction in male peritoneal dialysis patients. Mahon A, Sidhu PS, Muir G, Macdougall IC *Am J Kidney Dis*. 2005 Feb; 45(2):381-7
- [29] Treatment with sildenafil citrate in renal transplant patients with erectile dysfunction. Prieto Castro RM, Anglada Curado FJ, Regueiro López JC, Leva Vallejo ME, Molina Sánchez J, Saceda López JL, Requena Tapia MJ. *BJU Int*. 2001 Aug; 88(3):241-3
- [30] Treatment of erectile dysfunction with sildenafil citrate in renal allograft recipients: a randomized, double-blind, placebo-controlled, crossover trial. Sharma RK, Prasad N, Gupta A, Kapoor R. *Am J Kidney Dis*. 2006 Jul; 48(1):128-33.
- [31] Efficacy and safety of sildenafil citrate (Viagra) in men with erectile dysfunction and spinal cord injury: a review. Derry F, Hultling C, Seftel AD, Sipski ML. *Urology*. 2002 Sep; 60(2 Suppl 2):49-57
- [32] Male erectile dysfunction following spinal cord injury: a systematic review. Deforge D, Blackmer J, Garritty C, Yazdi F, Cronin V, Barrowman N, Fang M, Mamaladze V, Zhang L, Sampson M, Moher D. *Spinal Cord*. 2006 Aug; 44(8):465-73
- [33] Treatment of erectile dysfunction in men with depressive symptoms: results of a placebo-controlled trial with sildenafil citrate. Seidman SN, Roose SP, Menza MA, Shabsigh R, Rosen RC *Am J Psychiatry*. 2001 Oct; 158(10):1623-30.
- [34] Depression, antidepressant therapies, and erectile dysfunction: clinical trials of sildenafil citrate (Viagra) in treated and untreated patients with depression. Nurnberg HG, Seidman SN, Gelenberg AJ, Fava M, Rosen R, Shabsigh R *Urology*. 2002 Sep; 60(2 Suppl 2):58-66
- [35] Sildenafil in the treatment of antipsychotic-induced erectile dysfunction: a randomized, double-blind, placebo-controlled, flexible-dose, two-way crossover trial. Gopalakrishnan R, Jacob KS, Kuruvilla A, Vasantharaj B, John JK. *Am J Psychiatry*. 2006 Mar; 163(3):494-9