

Essential information  
for the supply of

Simarax  
50 mg Film Coated Tablets  
(sildenafil)

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# INTRODUCTION

# INTRODUCTION

This booklet is part of a package of information and training materials that Macleods Pharma UK Limited have put in place to support the launch of Simarax as an OTC treatment for Erectile Dysfunction. This document contains essential information you will need to know and consider when assessing men as suitable candidates for use of Simarax.

**This training can form part of your CPD training and once completed can be recorded at [www.uptodate.org](http://www.uptodate.org).**

The sections in this booklet contain the following information:

## **SECTION 1** **Understanding erectile dysfunction and Simarax.**

Provides an understanding of Simarax and how it works.

## **SECTION 2** **Who can use Simarax?**

Details the types of men who can safely use Simarax taking into account comorbidities and concomitant drug use.

## **SECTION 3** **What is the Simarax checklist?**

The Simarax Checklist is provided as an optional tool to help accurately assess patients and to validate their suitability for treatment.

## **SECTION 4** **Providing advice about Simarax**

Information on the advice you can offer patients who are suitable for Simarax and follow-up advice for those who are found to be not suitable.

## **SECTION 5** **Patient supply scenarios**

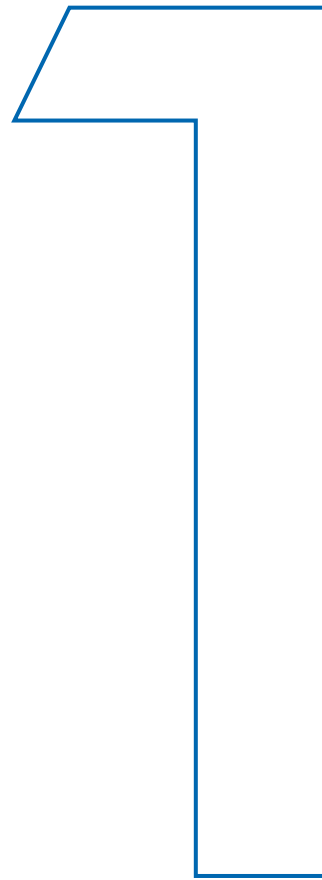
Test your knowledge with a number of patient supply scenarios to which you can apply your professional judgement and check against the suggested supply outcomes.

## **SECTION 6** **Case study responses**

## **SECTION 7** **Essential information**

The essential information from the Summary of Product Characteristics.

**Section**



# UNDERSTANDING ERECTILE DYSFUNCTION AND SIMARAX

## What is Erectile Dysfunction?

Erectile Dysfunction (ED) has been defined as the inability to attain and/or maintain an erection hard enough for satisfactory sexual intercourse<sup>1</sup>. It can occur occasionally or frequently and men are able to self-recognize the condition, which can vary in severity from mild (a soft erection) to severe (no erection at all).

## Causes of ED?

Understanding the causes and conditions associated with ED can help you manage the sufferer appropriately. In general, ED is due to 3 main causes:<sup>2</sup>

- Physical causes
- Psychological causes
- Some types of medication

### 1. Physical causes:

ED usually has an underlying physical cause, and it is useful to bear this in mind when managing patients who have co-morbidities that may predispose them to ED. These include hypertension, diabetes, hypercholesterolaemia or cardiovascular disease (CVD) and lower urinary tract symptoms (LUTS).<sup>3,4</sup>

CVD and most physical causes of ED are linked to vascular endothelial dysfunction, and many men with ED also have CV risk factors.<sup>5</sup>

### 2. Psychological causes:

Psychological causes inhibit normal stimuli to and from the brain and can interfere with the ability to achieve a normal erection. Although there can be a perception that ED is a psychological issue, the reality is, purely psychological causes account for only 1 in 10 cases.<sup>6</sup>

Psychological causes can include:<sup>7</sup>

- Performance anxiety in relation to ED and the fear that it will keep occurring
- Depression - the link with ED appears to be bidirectional. In depressed men, ED may be a symptom of depression and in men with ED, the emotional stress commonly associated with loss of sexual function may lead to depression
- Lack of arousal and/or inhibition between partners
- Other sexual dysfunction (e.g. premature ejaculation)
- Major life stress such as; money worries, bereavement, work-related stress, etc
- Low self-esteem - this can be due to prior episodes of ED (thus a feeling of inadequacy) or can be the result of other issues unrelated to sexual performance
- Indifference - this may come about as a result of age and a subsequent loss of interest in sex, or stem from problems in a couple's relationship

### 3. Medication-induced

Although some drugs can directly cause erection problems (iatrogenic cause), many of the drugs shown in Table 1 are used to treat diseases that are themselves associated with ED.

Recreational drugs, including alcohol, can also cause erection problems

Table 1: Medications that can cause ED <sup>8-14</sup>

Therapy area	Drug class or drug	Impact on ED
<b>Cardiovascular</b>	Diuretics	Not determined, but believed to interfere with smooth muscle relaxation
	ACE inhibitors and ARBs	Interferes with smooth muscle relaxation
	Aldosterone antagonists	An anti-adrenergic action
	Beta-blockers	Affects sex hormones, impairs vasodilation of the corpora cavernosa
	Clonidine	Depresses adrenergic output
<b>Psychotropic</b>	Anti-depressants: selective serotonin reuptake inhibitors, tricyclics, monoamine oxidase inhibitors, lithium	Decreases arousal and desire
	Anti-psychotics: phenothiazines, butyrophenones	Increases prolactin levels
<b>Anti-epileptics</b>	Carbamazepine, Phenytoin, Barbiturates	Affects sex hormone levels
<b>Endocrine drugs</b>	Testosterone antagonists/ oestrogen agonists Anabolic steroids Luteinising hormone-releasing hormone analogues	Affects androgen receptors, reducing sexual desire



**Table 1 continued**

<b>Therapy area</b>	<b>Drug class or drug</b>	<b>Impact on ED</b>
<b>Recreational drugs</b>	Alcohol, heroin, cocaine, marijuana, methadone	Causes vasoconstriction and/or impacts on neurotransmitters in the erectile pathway
<b>Other</b>	H2 antagonists, ranitidine and cimetidine	Increases prolactin levels, reducing sexual desire
	Cytotoxics, e.g. cyclophosphamide, methotrexate	The effect of nausea and general malaise associated with such drugs often diminish libido

## **What is Simarax and what is it used for?**

Simarax contains sildenafil 50 mg and is a pharmacy-only (P) medicine to treat erectile dysfunction (ED) in men aged 18 years and over. It is a well-established and well-tolerated treatment and provides men with access without prescription to an approved and regulated ED medication and professional health advice from the pharmacy.

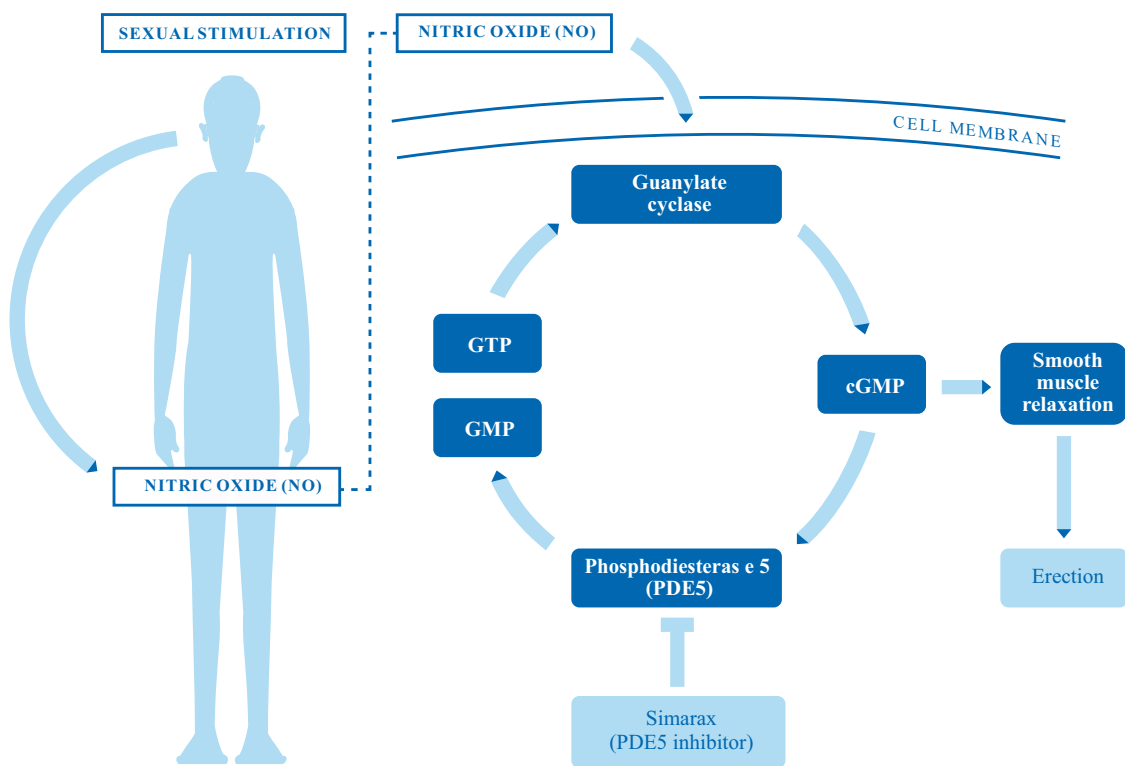
As well as improving their erectile function, allowing men to fully engage in intercourse and/or masturbation, successful treatment with sildenafil can also have emotional benefits for many men with ED, helping them to regain their self-esteem, self-confidence and relationship satisfaction. It can improve their overall quality of life and thus positively impact the wider social implications of erection problems, such as depression.<sup>15</sup>

## How does Simarax work?

When a man is sexually stimulated, impulses from the brain reach the cavernous nerve which releases nitric oxide (NO) at nerve endings in the penis. The NO diffuses across the endothelial cells into smooth muscle and stimulates the enzyme, guanylate cyclase, to convert GTP into cyclic GMP (cGMP). Cyclic GMP starts a further cascade of biochemical reactions which results in smooth muscle relaxation and the cavernous bodies fill with blood and become rigid. Cyclic GMP is normally broken down by the enzyme PDE5 to GMP, which terminates the pathway and produces detumescence. Simarax inhibits the action of this enzyme thus increasing cGMP levels and maintaining these levels for longer. Hence Simarax helps a man attain and maintain an erection in response to sexual stimulation.<sup>16</sup>

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

**Figure 1: Simarax mode of action**



- PDE5 inhibitor augments the normal physiological response to sexual stimulation
- There is no effect in the absence of sexual stimulation

## Simarax Efficacy

Simarax is an efficacious treatment for ED at the recommended 50 mg OTC dose. The efficacy of sildenafil has been demonstrated extensively in numerous clinical trials involving more than 23,000 men.

In some patients, 50 mg may not be efficacious and a referral to the GP is required as the dose may need to be increased to 100 mg. Patients who have renal or hepatic impairment, concomitant medication such as CYP3A4 inhibitors or alpha blockers or who have issues with tolerability should also be referred to their doctor as a 25 mg dose may be appropriate. The 25 mg and 100 mg doses are only available on prescription.

In fixed dose studies, the proportions of patients reporting that treatment improved their erections were 74% (50 mg)<sup>17</sup>. These data show Simarax is effective in men with ED and with a wide range of concomitant diseases.

**Section**

**2**

## WHO CAN USE SIMARAX?

Only adult men aged 18 years or older who have erectile dysfunction (ED) can use the product.

The active ingredient in Simarax, sildenafil, is a part of the class of medicines known as Phosphodiesterase 5 Inhibitors (PDE5i) that are recommended as a first line treatment for ED by:

1. NICE's Clinical Knowledge Summaries<sup>2</sup>
2. The British Association for Urological Surgeons<sup>6</sup>
3. The British Society for Sexual Medicine<sup>18</sup>

Simarax is licensed for packs of 2, 4 and 8 tablets (not all sizes may be marketed).

There are a number of contraindications or special warnings which mean that in certain circumstances the product cannot be used by men with ED, see below.

### Who must not use Simarax?

- **Men aged under 18 years**, as it not indicated for this age group. These men should be directed to their GP for follow up if they believe they have an issue relating to erectile function.
- **Women**, as it is only indicated for men aged 18 years and over. For a woman interested in the product for their male partner, it is important to ask them to encourage their partner to visit the pharmacy or their doctor for additional advice
- **Men who do not have ED. It is important that you establish that the man has a problem getting or keeping an erection which is satisfactory for sexual performance.** Simarax will not enhance men's erections or sexual performance and it will not help problems such as premature ejaculation. Men in the latter group should be directed to their GP for further advice
- **Men allergic to sildenafil** or any other ingredient in the medicine.
- **Men using a different dose** of sildenafil or another ED treatment

### Men with the following health problems must not use Simarax:

- **Men with hypotension (<90/50 mmHg) must not use Simarax.** This is because the safety of sildenafil has not been studied in these sub-groups of patients, and its use is, therefore, contraindicated
- **Men with previously diagnosed mild, moderate or severe hepatic impairment** (e.g. liver cirrhosis), should be advised to talk with their GP about a suitable starting dose or alternative options for the treatment of ED. Men should be asked the questions included in the Checklist (see Section 3) relating to those diagnosed with liver disease or liver problems. If they are under the care of a doctor for liver problems, they will be aware of this and answer 'yes'. As such, this means that you must not supply the product and refer them to their GP
- **Men with previously diagnosed severe renal impairment.** In most cases, patients with severe renal impairment will have some signs or symptoms of the underlying issues and will be under the care of a GP or renal specialist. A question is included in the Checklist which asks the man whether he is suffering from severe kidney problems. If the answer to this is 'yes', then they should be advised to talk with their doctor about alternative options for the

- **Simarax must not be used in patients with anatomical deformation of the penis** (such as angulation, cavernosal fibrosis or Peyronie's disease) **or in patients with sickle cell anaemia, multiple myeloma or leukaemia**. There is an increased risk of priapism with these patients and they should be directed to their GP for further advice
- **Sildenafil is contraindicated in patients who have loss of vision in 1 eye because of non arteritic anterior ischaemic optic neuropathy (NAION)**, regardless of whether this episode was in connection with previous PDE5i exposure or not
- **Men who have an inherited eye disease 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
- **Men who have any bleeding issues** (e.g. haemophilia) **or suffer from stomach ulcers** must not use Simarax and should be directed to see their GP
- **Rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption** must not take Simarax because of the lactose contained within the tablet.
- **Men who have cardiovascular issues**, see section below.

### **Men with the following cardiovascular (CV) issues must not use Simarax:**

- **Men who get very breathless or experience chest pains with light or moderate physical activity**, such as walking briskly for 20 minutes or climbing 2 flights of stairs should be referred to their GP.<sup>19</sup>
- **Men who have been advised against sexual activity because of a CV problem**. This group of men are potentially at higher risk due to the burden of over activity on their heart and as such should be referred back to their GP
- **Men with recent history (in the last 6 months) of stroke or myocardial infarction** are also contraindicated from using Simarax and will need to follow up with their GP
- **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
- **Patients previously diagnosed with the following must be advised to consult with their GP before resuming sexual activity:**
  - uncontrolled hypertension
  - hypotension
  - unstable angina
  - moderate to severe valvular disease
  - left ventricular dysfunction
  - hypertrophic obstructive and other cardiomyopathies
  - significant arrhythmias
  - severe cardiac failure

Note: Some low risk cardiovascular patients may be suitable for Simarax, as long as their doctor has advised they can resume sexual activity: those with **asymptomatic controlled hypertension, mild valvular disease or who have had successful coronary artery bypass grafting, stenting or angioplasty.**

## Men taking certain other medicines must not use Simarax

- **Men taking nitrates (e.g. isosorbide mononitrate/dinitrate and glyceryl trinitrate), nitric oxide donors (e.g. nicorandil) or 'poppers' (e.g. amyl nitrate).** Consistent with its known effects on the NO cGMP pathway, sildenafil has been shown to potentiate the hypotensive effects of nitrates, and it is contraindicated for use with nitric oxide donors, nitrates, amyl nitrite (known as the recreational drug 'poppers'), sodium nitroprusside and nicorandil. These men should be directed to their GP for further advice
- **The co-administration of sildenafil with guanylate cyclase stimulators, such as riociguat, is contraindicated** as it may potentially lead to symptomatic hypotension. Again, these men will need to talk with a doctor for further advice
- **Men taking ritonavir**, a potent CYP3A4 inhibitor used in the treatment of HIV, are contraindicated due to the potential for increased blood levels of sildenafil in these patients. They should consult with their doctor for further guidance
- **Men already being treated with another PDE5i** or a higher or lower dose of sildenafil should not use Simarax. Men taking 50 mg of sildenafil can use the product providing they meet the criteria for pharmacy supply and do not exceed 50 mg as a daily dose
- **Men taking CYP3A4 inhibitors or alpha-blockers** (see Table 2 for examples). These patients should be advised to speak with their GP about a lower suitable starting dose which is available on prescription.
- **Men taking sacubitril/valsartan**, if patients are taking sacubitril/valsartan for heart failure they should talk to their doctor, pharmacist before taking sildenafil

**Table 2: Examples of CYP3A4 inhibitors and alpha-blockers**

Antibiotics	Erythromycin, clarithromycin
Antifungals	Itraconazole, ketoconazole
Calcium channel blockers	Diltiazem, verapamil
H2-antagonists	Cimetidine
HIV-protease inhibitors	Amprenavir, fosamprenavir, atazanavir, darunavir, indinavir, lopinavir, ritonavir, saquinavir, tipranavir
Alpha blockers	Phenoxybenzamine, phentolamine, tolazoline, trazodone, alfuzosin, doxazosin, tamsulosin, prazosin, terazosin

# CASE STUDIES

## Case study 1:

### How would you respond to the following patient request?

Mr. P is a man in his mid-50s who is new to your pharmacy. He has walked briskly to the pharmacy as it is raining and asks to see you. The first thing he states is: "I get out of breath so quickly these days; I could do with a sit down." He then goes on to tell you he would like to purchase Simarax.

### How would you handle this conversation? Would you sell Simarax in this situation?

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See page 35 for case study responses



## Case study 2:

### How would you respond to the following patient request?

Mr. G is a 72-year-old man who has asked to talk with you about the 'Simarax'. After questioning, you discover he is a smoker with a history of cardiovascular issues including angina, despite undergoing bypass surgery 3 years ago. He is on a range of cardiac medications including glyceryl trinitrate spray for his chest pains. He also has a number of other issues including type 2 diabetes and benign prostatic hypertrophy treated with tamsulosin. His wife has seen a newspaper advert for the product and reckons it is just what he needs.

**How would you handle this conversation? Would you make a sale of Simarax in this situation?**

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See page 35 for case study responses

**Section**

3

## WHAT IS THE SIMARAX CHECKLIST?

The Simarax Checklist, on pages 20-21 of this document, has been provided as an optional tool to help you when assessing men to accurately validate their suitability for treatment. It also provides information which will enable you to offer valuable health advice for men regardless of whether or not they are suitable for the product.

There is no mandatory requirement to use the Checklist; it is your professional judgement to decide when and how to use as an aid in deciding whether to supply Simarax to the man. The recommendation, however, is to use the supplied questions as a framework to assess suitability. You may also wish to check the patient's Summary Care Record or Patient Medication Record to check their concomitant conditions, such as hepatic disease or renal impairment, and medication intake, such as nitrate use.

The Simarax Checklist includes an assessment of the man's overall fitness for sex, by determining if he gets out of breath or experiences chest pain when he undertakes physical activity. It is also important to understand if the man has any other medical issues that could mean the product is not suitable for him. These may include cardiovascular problems, such as a recent heart attack or stroke which would be revealed through questioning, so the following should be considered:

- There is a degree of cardiac risk associated with sexual activity, although the risk is small in those with stable CVD
- Checking the man's fitness for sex will help identify his CV risk; those with a low risk can be initiated on Simarax and reminded to follow-up with their GP within 6 months
- It also helps identify men at higher risk of CV problems who would benefit from further investigation by their doctor, ideally as soon as possible

Those patients who do not receive the product should be provided with the reason for non-supply and advised to go to the doctor. A tear off piece is included at the bottom of the Checklist for this purpose and contains a section to provide a written explanation of the reason for non-supply. The patient can then take the slip with them to the doctor to help start the conversation

The following has been created as a useful aide-memoire to help determine whether your patient is suitable for Simarax 50 mg film-coated tablets, or whether he should be seen by a doctor for further advice. Use of the checklist is optional, and you should use your professional judgement to decide when and how to use it. You may also wish to review the patient's Summary Care Record or Patient Medication Record to check concomitant conditions or medication use. The Essential Information for the Supply of Simarax provides additional background information in relation to the supply of this product.

**If the patient has previously been supplied with Simarax, he should be asked if anything has changed with respect to his health status or medicines usage. There is no need to repeat the questions below prior to resupply in that case. Remind him to follow up with his doctor within the first 6 months of use. If any factors have changed, Sections 2-4 should be reviewed again. The repeat supply tear-off slip (below) can also be given to the man.**

### Additional advice

You should consider possible causes of erectile dysfunction, such as undiagnosed depression, anxiety, excessive alcohol use and taking certain medicines. Examples of classes of medicines that cause ED include diuretics, anti-hypertensives, corticosteroids, anticonvulsants and recreational drugs. Whilst it may be appropriate to supply the product, you should provide lifestyle advice and recommend a follow-up with a doctor.

### 1. Why Simarax 50 mg film-coated tablets for?

**Simarax is only intended for men 18 years and older who are experiencing erectile dysfunction (ED) (i.e. difficulty in getting and/or maintaining an erection satisfactory for sexual performance). This product must not be supplied to men who do not have ED.**

It is important to confirm if the man is already receiving treatment for the condition. Men currently prescribed 50 mg of sildenafil can be supplied this product if they meet the criteria for pharmacy supply, provided they do not take more than 50 mg daily. If the man is using a different dose of sildenafil or another ED treatment, he should be referred to his doctor.

### 2. Check patient's cardiovascular (CV) health

If the patient answers **YES** to any of the following: **do not supply the product** and refer to the doctor. If you have any reason to consider, based on physical status, the patient should not be using this product, refer to the doctor.

- Has your doctor advised that you are not fit enough for any physical and/or sexual activity?
- Do you feel very breathless or experience chest pain with light or moderate physical activity, such as walking briskly for 20 minutes or climbing two flights of stairs?
- Have you had a heart attack or stroke within the last 6 months?
- Do you have any other heart problems or are you under a doctor's care for any of the following:
- Low blood pressure or uncontrolled high blood pressure
  - Unstable angina (chest pain), irregular heart beat or palpitations (arrhythmia)
  - A problem with one of the valves in your heart (valvular heart disease)
  - A problem where the heart muscle becomes inflamed and does not 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

### 3. Check concomitant medication use

**Please check what other medicines the patient is taking.**

If the patient answers **YES** to any of the following: **do not supply the product** and refer to the doctor.

- Are you taking nitrates (nicorandil or other nitric oxide donors e.g. glyceryl trinitrate, isosorbide mononitrate or isosorbide dinitrate) for chest pain?
- Are you using drugs called 'poppers' for recreational purposes (e.g. amyl nitrite)?
- 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 (a heartburn treatment), 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 to treat urinary problems due to enlarged prostate (benign prostatic hyperplasia) or occasionally to treat high blood pressure?
- Are you taking sacubitril/valsartan to treat heart failure?

### 4. Check concomitant conditions

If the patient answers **YES** to any of the following: **do not supply product** and refer to the doctor.

- Do you have Peyronie's disease or any other deformation of the penis?  
Have ever had loss of vision because of damage to the optic nerve (such as non-arteritic anterior ischaemic optic neuropathy [NAION]) or have an inherited eye disease (such as retinitis pigmentosa)?
- Do you have galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption?
- Do you have previously diagnosed hepatic (liver) disease (including cirrhosis of the liver) 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 have active stomach ulcers?



Dear Doctor,

Please can you review this patient in relation to erectile dysfunction. We had a discussion in my pharmacy, but he was not suitable for supply of Simarax due to his [delete as appropriate] 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 Simarax.

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 time you received the product.

Pharmacist signature:..... Date:.....

PHARMACY  
STAMP

# Points for counselling and other information

Please follow these points to ensure that your patient is counseled appropriately whether they are supplied the product or not.

## Advice for men who have not been supplied Simarax

Men who have not been supplied Simarax because of their cardiovascular health, interacting medicines or another concern must be told to see their GP as soon as they can within 6 months. The tear-off slip (below) can be filled in and given to the man to facilitate his discussion with the doctor.

## Advice for men who have been supplied Simarax

Men should be advised:

- Simarax is only intended for men 18 years and older who have erectile dysfunction (ED). Men who do not have ED will not benefit from using this product.
- Take one tablet approximately 1 hour before planning to have sexual intercourse. Simarax can start to work within 30 minutes.
- Take with or without food, but Simarax may take longer to work after a high-fat meal.
- Do not take with grapefruit or grapefruit juice, as it may affect the way the medicine works.
- The maximum recommended dosing frequency is one 50 mg tablet per day.
- They may need to take Simarax 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.
- Medicines containing any nitrates (e.g. glyceryl trinitrate, isosorbide mononitrate, isosorbide dinitrate, amyl nitrite also known as 'poppers'), or nitric oxide donors (e.g. sodium nitroprusside or nicorandil), must NOT be used at the same time as Simarax as this combination may lead to a dangerous fall in blood pressure.
- Men should tell their doctor that they have started taking Simarax, especially if they are started on any new medicines.
- Remind patients about common side effects. These include: headache, flushing, dyspepsia, nasal congestion, dizziness, nausea, visual disturbance, cyanopsia (blue-tinted vision) and blurred vision.

**Note: If any of these become a concern, advise the patient to talk with a pharmacist or doctor.**

**Men should be advised to STOP TAKING Simarax and seek medical attention IMMEDIATELY if they experience any of the following SERIOUS side effects. Side effects can be reported by patients or pharmacists via the Yellow Card Scheme at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).**

- Chest pains: If this occurs before, during or after intercourse, they should get into a semi-sitting position and try to relax. Nitrates must NOT be used to treat chest pains.
- A persistent and sometimes painful erection lasting longer than 4 hours.
- A sudden decrease or loss of vision.
- An allergic reaction. Symptoms include sudden wheeziness, difficulty breathing or dizziness, swelling of the eyelids, face, lips or throat.
- Serious skin reactions such as Stevens - Johnson syndrome (SJS) and Toxic Epidermal Syndrome (TEN). Symptoms may include severe peeling and swelling of the skin, blistering of the mouth, genitals and around the eyes, fever.
- Seizures or fits.

## Follow up advice for all men

- ED can be associated with a number of contributing conditions, e.g. hypertension, diabetes mellitus, hypercholesterolaemia or cardiovascular disease. As a result, all men with ED should be advised to consult their doctor within 6 months for a clinical review of potential underlying conditions and risk factors associated with ED.
- Provide appropriate advice on lifestyle factors and general healthy living, including:
  - Losing weight
  - Giving up smoking
  - Cutting back on alcohol/recreational drugs
  - Exercising regularly
  - Reducing stress
- You may also want to check if the man is buying products from unregulated sources. It is important to explain these products are not tested for their safety or effectiveness, may not contain the ingredients listed within them and are therefore potentially dangerous, unlike product sourced from a pharmacy and medicines obtained via prescription from the doctor.

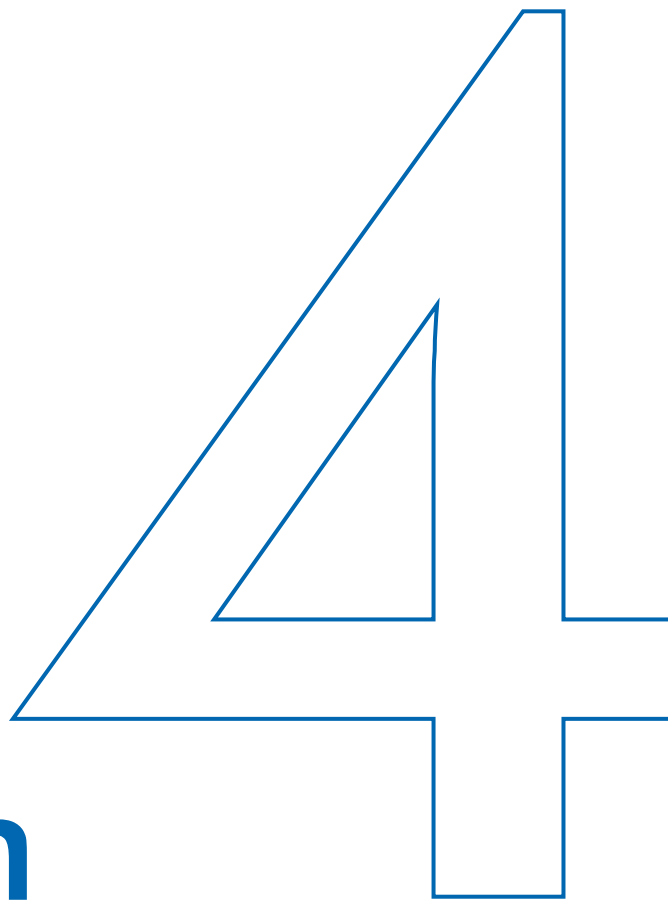
CHECKLIST/SILD/V01/JULY/2023



Your Pharmacist has supplied you with Simarax today for your personal use.  
Please ensure that you make an appointment to see your GP within 6 months of the date of first receiving Simarax (see date on reverse).

You have not been provided with Simarax for ED today as it may not be suitable for you to take without consulting your doctor. You should go to see your doctor to discuss other suitable options.  
Please make an appointment to see your GP as soon as you can within the next 6 months and present this slip.

# Section



## ADVICE FOR MEN WHO ARE SUITABLE FOR SIMARAX

### Advise patients:

- The product is only for men aged 18 years and over who have ED. Men who do not have ED will not benefit from this product
- To avoid taking nitrates (e.g. glyceryl trinitrate, isosorbide mononitrate, isosorbide dinitrate), nitric oxide donors (e.g. sodium nitroprusside or nicorandil) or amyl nitrite (“poppers”) as these can cause a dangerous drop in blood pressure when used in combination with Simarax.
- During any interaction with their doctor men should tell their doctor that they have started taking Simarax, especially if they are started on any new medicines
- Men should not take after excessive drinking as Simarax may be less effective. Excessive alcohol consumption can impact sexual function, as it acts as a central nervous system depressant and can impair motor and cognitive function
- How to take Simarax
  - Take 1 tablet approximately 1 hour before planning to have sexual intercourse or to masturbate
  - Swallow the tablet whole, with water
  - Do not take more than 1 tablet per day
  - Simarax can start to work within 30 minutes, but men are still able to obtain an erection in response to sexual stimulation for up to 4 hours post-dose
  - Simarax can be taken with or without food but may take longer to work after a high-fat meal
  - Avoid grapefruit juice as this may increase sildenafil levels in the blood
- For most men, Simarax will work the first or second time they try it. For men who have not been able to have sexual intercourse for some time, it can take additional attempts to obtain maximum benefit. 74% of men will respond to Simarax (sildenafil 50 mg).<sup>17</sup>

If after several attempts (up to 8 separate dosing occasions) 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 their doctor.
- One Simarax tablet can be taken daily, men should be advised to visit their doctor within 6 months of starting the product for a general health check-up. Once reviewed by their doctor, they can continue using the product, providing there is no change in their circumstances (health or medication).
- If they experience any of the serious side effects detailed in the Side Effect section below, they should stop taking Simarax and seek IMMEDIATE medical advice.

### What if a patient takes more than the recommended dose of Simarax?

Data show that at doses 16 times the Simarax dosage, adverse reactions were similar to those seen at lower doses, but the incidence rates and severities were increased. If you are concerned a patient has taken an overdose, refer them immediately to the nearest Accident and Emergency facility or their on-call GP

### Are there any side effects associated with Simarax?

Sildenafil is generally well tolerated and side effects reported in association with its use are usually transient and mild-to-moderate in intensity.

## **Patients who experience any of the following after taking Simarax should be advised to STOP TAKING Simarax and seek IMMEDIATE medical advice:**

- **If chest pain occurs before, during or after sex, patients should be advised to get in a semi-sitting position and try to relax. Do NOT use nitrates to treat your chest pain**
- **A persistent and sometimes painful erection that lasts more than 4 hours**
- **A sudden decrease in vision or hearing**
- **Allergic reaction including sudden wheeziness, difficulty breathing, dizziness or swelling of eyelids, face, lips and throat**
- **Serious skin reactions which include severe peeling and swelling of the skin, blistering of mouth, genitals and around the eyes, and fever**
- **Seizure or fits**

A full list of side effects experienced with Simarax can be found in the SmPC<sup>17</sup>

The most commonly reported side effects in the use of Simarax are:

- Headache
- Facial flushing, hot flush
- Dyspepsia
- Nausea
- Nasal congestion
- Dizziness
- Visual disturbance, blurred vision and blue-tinted vision (cyanopsia)
- Temporary change in colour vision

## **Advice for men who are not suitable for Simarax**

Please see Section 2 for men who must not take Simarax

If unsuitable for Simarax, it is important to advise the man of the reason they are not suitable (e.g. it may be a contraindication or that he doesn't have ED). All men with ED should be referred to their GP to explore other suitable options and advised that they should do this within the next 6 months. Men should be encouraged to seek advice from their doctor for two reasons- because ED may be a symptom of other conditions that need medical attention and because, although Simarax is not suitable for them, the doctor may be able to prescribe medicines which are suitable.

## **Advice for all men**

ED can be associated with a number of underlying conditions, e.g. hypertension, diabetes mellitus, hypercholesterolaemia or cardiovascular disease. As a result, all men with ED should be advised to consult their doctor within 6 months for a clinical review of potential underlying conditions and risk factors associated with ED.

Lifestyle advice and guidance should be provided to all men, as it can help to reduce the risk factors for ED:

- Weight management
- Healthy eating
- Regular exercise
- Reducing stress
- Quitting smoking
- Moderating alcohol consumption
- Avoiding recreational drugs

As well as helping to improve ED, these changes can also improve general health and may help to reduce the risk of CVD.



### Case study 3:

#### How would you respond to the following patient request?

Mr. W is back at your pharmacy having purchased Simarax for the first time a few days ago. He tells you he's taken a tablet, but it didn't work and he doesn't know why.

**How would you handle this conversation? What advice would you give?**

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See page 35 for case study responses

## Case study 4:

### How would you respond to the following patient request?

Mr. R is a 58-year-old smoker who, reluctantly, asks if there is anywhere he can speak to you in private. You take him into the consultation area, where you establish he has ED. Mr. R asks to buy 2 packs of Simarax, but does not want to go into any details about his issue. You ask him how long he has had the problem and he explains that he has been drinking more since he lost his mother last year. He tells you his partner asked him to come to the pharmacy amid worries about his sexual and mental health.

### How would you handle this conversation? Would you make a sale of Simarax in this situation? What other advice could you offer?

**Remember:** ED may not be the only concern; Mr. R has some signs that could indicate untreated depression

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See page 35 for case study responses

## **Case study 5:**

### **How would you respond to the following patient request?**

After purchasing Simarax for the first time a month ago, Mr. S returns to ask for a repeat supply but he is also worried that the tablets give him a mild headache and sometimes make him feel a bit sick. He wants to be sure that he can continue taking Simarax.

### **How would you handle this conversation? Would you provide a repeat supply in this situation? What advice would you give?**

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See page 35 for case study responses

## Case study 6:

### How would you respond to the following patient request?

Mr. O visits the pharmacy and asks to speak with you privately. He saw an advertisement for Simarax online and is eager to give it a try as he has had trouble getting and keeping an erection for the last few months. After briefly discussing his medical history, Mr. O tells you that he that he struggles with his weight, and suffers from high blood pressure and high cholesterol. His current medications are candesartan, hydrochlorothiazide and rosuvastatin.

### How would you handle this conversation? What advice would you give?

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See page 35 for case study responses

**Section**

**5**

## PATIENT SUPPLY SCENARIOS

While the decision to supply Simarax or not will be straight forward in the majority of cases, there would be some situations where the decision is less clear cut. In this section, you will find some less frequent, but more thought-provoking supply scenarios to consider.

Which of the following patients do you feel are suitable for Simarax?

(For some suggested actions see page 32.)

- S1:** Mr. S is a 57-year-old man and has been a widower for 3 years. He has started a new relationship and is very anxious that this goes well and reveals that he has been having problems with his erectile function for the last 8 months. At his regular health check-up at his doctor 5 months ago, there was nothing untoward found in his assessment. He is in relatively good health and takes ibuprofen for osteoarthritis; he was a smoker (20-a-day) but gave up about 8 years ago.
- S2:** Mr. T has had difficulty controlling his hypertension over the last 12 months. After many changes (including following lifestyle advice), he has been stabilized for the past 3 months on a thiazide-related diuretic and an angiotensin-II receptor antagonist combination. Although he is happy with his cardiovascular status, he is having problems with his ability to keep an erection and wonders if Simarax would be suitable for him.
- S3:** Mr. B has been discharged into the care of his GP having had a heart attack 9 months ago that resulted in bypass surgery. After an intense period of cardiac rehabilitation, he is no longer experiencing any chest pain or breathlessness. He explains he is interested in using Simarax, as he and his wife have missed the physical side of their relationship and his GP has advised him to talk with you about the OTC options available. He is on a standard regimen of drugs including aspirin, a statin and an ACE inhibitor and he also takes a non-steroidal anti-inflammatory drug for osteoarthritis.
- S4:** Mr. F is a 36-year-old man and wants a quiet word with you. He is in good health and follows a good diet and exercise regime, but tells you his new girlfriend is hard to satisfy. While he has no issues with having sexual intercourse, he is finding it is taking him longer to recover post coitus and as such wants something to 'pep him up'.
- S5:** Mr. M came to see you a few weeks ago for a Medicines Use Review (MUR). During that process, you advised him to talk to his doctor about his prescription for a sublingual glyceryl trinitrate spray. Although he has held a prescription for this drug for a number of years, he has not needed to use this. His MUR shows he is on a standard combination of other drugs to control his symptoms, and as a result of your intervention, his doctor has removed the nitrate from his drug regimen. He is now back and is keen to discuss whether or not Simarax would be suitable for him as he is experiencing erectile dysfunction. You see from his drug records there are no other contraindicated medicines and he is well with no overt cardiovascular related symptoms.

- S6:** Mr. A asks for Simarax as he has recently found it more difficult to perform sexually. On questioning him, you note he is a diabetic and takes a number of tablets for the condition. He also tells you he likes a drink and has been using alcohol more frequently of late. The diabetic nurse has warned him that he may need to start using insulin as his sugar control is very poor.
- S7:** Mr. Y has been coming to your pharmacy on a regular basis and has been purchasing Simarax. In fact, it is 7 months since his first purchase and although you have repeatedly reminded him he needs to follow up with his doctor, he hasn't done so. He has promised he will make an appointment right after he finishes in the pharmacy and tells you it has kept slipping his mind.
- S8:** Mr. K came into your pharmacy last week and after taking him through the Simarax Checklist you supplied an 8-tablet pack of Simarax. He is back this week and has asked for a further supply of 8 tablets.
- S9:** Mr. L is a regular patient who was started on a course of treatment with an SSRI for depression about 6 weeks ago by his GP. Whilst Mr. L is feeling much happier, he has noticed he has had trouble getting and keeping an erection. He is keen to try Simarax.
- S10:** Mr. D is a 70-year-old gentleman who has recently started a new relationship. He tells you he is concerned about the quality of his erection and that he has difficulties maintaining this during sexual intercourse. You ask him about his medication history and he tells you he takes a product for BPH. On further questioning you ascertain the drug is finasteride, which he has been taking for 18 months. He has not had sex since he lost his wife 3 years ago, and he is keen to try Simarax.
- S11:** Mr. J is a 65-year-old man who is interested in purchasing Simarax. You take him through the Checklist and when it comes to questions about his cardiovascular status, all you can ascertain from him is that he has some problems with his heart. As he is a regular customer you check his patient medication record and find he is prescribed the following in the last 12 months: Atenolol 100 mg, Hydrochlorothiazide 25 mg and 2.5 mg amiloride. What advice would you give him?
- S12:** Mr. V visits the pharmacy to enquire about Simarax. He recently filled a prescription for Simarax but feels the treatment hasn't worked and is unsure why. Mr. V asks whether he could take Simarax as well, thinking that the combination would work better.
- S13:** Mr. R, a 58-year-old prior smoker, has approached you in the pharmacy and asks to speak in private. He tells you that he saw an advertisement for Simarax and would be interested in giving it a try. You take Mr. R through the checklist and learn that he has chronic obstructive pulmonary disease (COPD). He was also diagnosed with pulmonary hypertension 6 months ago, which can leave him short of breath and low in energy. He is currently taking riociguat in addition to an inhaler for his COPD.

## Patient scenarios: Suggested actions

- S1:** Simarax can be supplied to Mr. S. From his history, the use of the Checklist which has helped ascertain his low CV risk and fitness for sex as well as your professional judgement, he would appear to be in good health. He has given up smoking and he regularly engages with his doctor. The information he has provided helps with the supply decision. For most men, Simarax will work the first or second time they try it. For men who have not been able to have sexual intercourse for some time, such as Mr. S, it can take additional attempts to obtain maximum benefit (up to 8 separate dosing occasions). If he doesn't respond after 8 doses, he should be advised to consult with his GP. He should also inform his GP he is using the product when he next visits and this consultation should be within 6 months.
- S2:** Simarax can be supplied to Mr. T as his hypertension is now controlled and he is not taking any contraindicated medicines. As an addition to using the Checklist and your professional judgement, it is clear that Mr. T is under the care of a doctor as he has been stabilized with respect to his hypertension. Given what Mr. T has told you it looks like he is fit for sex. Advise Mr. T of the likely side effects of Simarax and get him to mention he is using the product to his doctor and that he should visit the doctor within 6 months. Advise him to come back if he has any problems or if there are any changes to his health or medication.
- S3:** Simarax can be supplied to Mr. B as it has been more than 6 months since his heart attack and he is not taking any contraindicated medications. Provide Mr. B with the usual follow-up advice. The Checklist has meant that the CV health and fitness for sex has been evaluated and in this case the patient has shown very good signs of improvement in relation to his cardiovascular and general health. He has obviously followed his specialist's advice and has done well with his cardiac rehabilitation. It is important for Mr. B to mention he is using the product to his doctor and as usual he should be counselled on using the product correctly and to go back to the doctor within 6 months.
- S4:** Simarax cannot be supplied to Mr. F as it does not help with shortening the refractory period in sexual intercourse. The drug is only indicated for men who have ED and have described their symptoms in line with the definition of the condition. The no supply slip should be completed and he should be advised to visit his doctor for further advice.
- S5:** Simarax can be supplied to Mr. M. Following the questions on the Checklist, it has been ascertained that he is not taking any contraindicated medications and had no other overt CV issues. As the patient's GP is happy to remove his nitrate prescription and he seems in otherwise good health, he looks like a suitable candidate for the product. The Checklist should be used to provide advice to counsel Mr. M in using the product correctly and advise that he return to see his doctor within 6 months.
- S6:** Simarax can be supplied to Mr. A. It is important that he is taken through the checklist especially with a view on fitness for sex. It appears that he can be supplied the product, but in Mr. A's case there are other issues that warrant investigation, e.g. his increased alcohol use could be a symptom of depression, and he should be advised to speak with his GP and/or his diabetic nurse within 6 months.
- S7:** There are no restrictions within the SPC to prevent supply of the product, so the product can be supplied. However, the man should again be reminded that it is very important that he should see his GP and that this may be because there are underlying conditions which may be causing the ED and you may wish to elaborate on these further to help facilitate the man to see his GP. If you get to the point where you feel that the man has not taken your advice, it is longer than 6 months post supply and the man has continued not to see his GP, you are free to use your professional judgement and state you do not wish to supply until you are happy he has been assessed by his GP.



- S8:** Provided there has been no change since Mr. K completed the Simarax Checklist, you can provide a further supply of Simarax. Remind him the maximum dose is 1 tablet per day. It is also important to check that the drug is working for Mr. K and that he is deriving the benefit he needs. The message to see his GP within 6 months should be repeated.
- S9:** Provide Mr. L with positive encouragement that it is good to hear that the antidepressant is working and that he is feeling happier and reiterate that despite this issue he should not stop taking the anti-depressants. State that ED can be a side effect of anti-depressants, but reinforce that Simarax can be supplied. Make sure to advise Mr. L to tell his GP he has started taking Simarax and that he has experienced ED. You should also counsel him on what he should do if Simarax makes no difference and that in this circumstance he should not discontinue his SSRI medication but return to the GP immediately for further advice.
- S10:** Simarax can be supplied to Mr. D as the checklist has meant that you have ascertained he is fit for sex, he has good cardiovascular health and is not taking any contraindicated medicines. Provide advice on using the product, particularly as he has not had sex for 3 years, it may take several attempts before it works. For most men, Simarax will work the first or second time they try it. For men who have not been able to have sexual intercourse for some time, it can take additional attempts to obtain maximum benefit (up to 8 separate dosing occasions). If it doesn't work after 8 different dosing occasions (a maximum of one 50 mg tablet per day) he should see his GP. He should also be advised to see the GP within 6 months of taking Simarax for a health check.
- S11:** Mr J's medications could be causing erectile dysfunction as a side effect, and they are not contraindicated with Simarax. His medications may also give an indication of the conditions he may have. He could be taking atenolol for hypertension, angina or cardiac arrhythmias, and the hydrochlorothiazide/amiloride combination for hypertension or congestive heart failure. Given he has had the same prescriptions for the past 12 months, it is likely that his blood pressure is stable, but you won't be able to know that all other conditions are controlled. It is important to check the patient's CV health status, including fitness for sex, as per the Checklist, as this may not be clear from his medications alone.
- If following further evaluation using the Checklist, you decide that Mr J is suitable for Simarax, it will be important to advise Mr J on how to use the product. If the CV health status and suitability cannot be deduced from your discussions with the man, then it is probably best to refuse supply and refer him to his doctor.
- S12:** Simarax cannot be supplied to Mr. V because he is already being treated with the same medication on prescription. Explain that Simarax cannot be supplied to men who are already taking a treatment for erection problems but reassure him that Simarax treatment may not work immediately for some people. The no supply slip should be completed, and he should be advised to visit his doctor if he does not have a satisfactory response after completing his prescription
- S13:** Simarax cannot be supplied to Mr. R because co-administration with guanylate cyclase stimulators, such as riociguat, is contraindicated. You should explain to Mr. R that treatments like Simarax are known to interact with riociguat, so these treatments cannot be used in combination. The no supply slip should be completed and he should be advised to speak to his doctor for further advice.

**Section**



## CASE STUDY RESPONSES

### CASE STUDY 1

Given that ED can be an early sign of the development of underlying CVD and coupled with the fact Mr. P is getting out of breath quickly, it is important that he is advised to visit his doctor for a check-up. There is an opportunity to discuss Mr. P's lifestyle and provide him with some information around this, but it is important he is not supplied the product and advised to take further advice from his GP. This guide and the Checklist provide more information around these issues.

### CASE STUDY 2

Mr. G falls in the category of patients using nitrates and in this case you must not supply Simarax to him. Taking a nitrate and Simarax together may lead to a significant drop in blood pressure. You should advise Mr. G of this fact and advise him to speak to his GP about this. In addition, it is important to provide counselling around his other medical issues and again ask him to speak to his doctor about his current health status. You can also offer him advice around his lifestyle choices.

### CASE STUDY 3

For some patients Simarax may not work on taking the first few doses. This can be for a variety of reasons; the man may have been out of practice for a while or may need a higher dose or an alternative treatment. With Mr. W, it is important to establish, how he used the product, e.g. did he take it on an empty stomach or after a meal? Did he take it one hour before he planned to have sexual intercourse?

Once correct use is established and advised on, it will be important to understand what his situation is. For example, is this a new relationship or an existing one? Was he nervous because he hadn't had sex for some time? Experts advise men may need to take up to 8 doses of a PDE5i on different occasions before they are considered a non-responder. In this case it may be worth advising Mr. W to try the product on his own to get used to the effects before proceeding to sexual intercourse. If after a few attempts the product is still not providing a satisfactory response, Mr. W should be advised to come back to speak to you or to visit his GP for further advice.

### CASE STUDY 4

Mr. R should be taken through the Checklist to establish his symptoms and to look at the underlying issues. You know he is a smoker and there is a possibility that he is not in the best of health. The Checklist is designed to help you explore these issues and ascertain his suitability for the product. It is important to remember ED may not be the only concern; Mr. R has some signs that could indicate untreated depression. As such Mr. R should be advised to see his doctor to get a thorough assessment of his physical and mental health. The decision to supply the product will depend on the answers he gives you and this guide will help you with determining this for the wide range of men you may need to talk to.

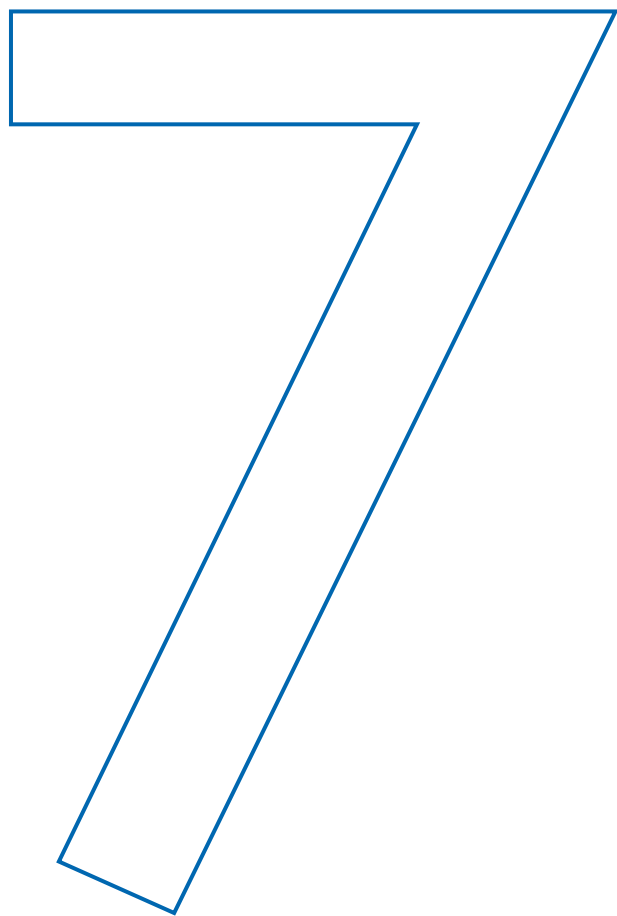
### **CASE STUDY 5**

There is no requirement for Mr. S to stop treatment and seek medical advice due to the headache or nausea he has experienced. You should remind him that headache is a very common side effect of Simarax, and may be experienced by approximately 1 in 10 men. Nausea is also common, but both side effects are generally mild and transient. You can also suggest that if Mr. S gets an occasional headache when taking Simarax, he could take an over-the-counter analgesic such as paracetamol. If he finds his headaches continue or worsen in intensity, Mr. S should be advised to come back to speak to you or visit his GP for further advice.

### **CASE STUDY 6**

Erection problems can be associated with a number of conditions, including hypertension and hypercholesterolaemia. Mr. O's medications could also be contributing to his erectile problems as a side effect, but these are not contraindicated with Simarax. Working through the Checklist will help to determine Mr. O's cardiovascular health status and whether he is suitable for Simarax. You could also offer Mr. O advice and information on lifestyle modifications to reduce the risk factors for erection problems and improve his general health.

**Section**



## ESSENTIAL INFORMATION

**Name of product:** Simarax 50 mg Film Coated Tablets

**Active ingredient(s):** Sildenafil

**Product license number:** PL 34771/0259

**Name and address of the product licence holder:** Macleods Pharma UK Limited, Wynyard Park House, Wynyard Avenue, Wynyard, Billingham, TS22 5TB, United Kingdom

**Supply classification:** P

**Indications:** For Erectile Dysfunction in adult men

**Side Effects:** The safety profile of Simarax is based on > 9,000 patients in > 70 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 Authorization Holder and included in the safety database, the frequencies of these reactions cannot be reliably determined. Very Common ( $\geq 1/10$ ): Headache. Common ( $\geq 1/100$  and  $< 1/10$ ): Dizziness, Visual colour distortions (Chloropsia, Chromatopsia, Cyanopsia, Erythroopsia and Xanthopsia), 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 (Dry eye, Lacrimal disorder and Lacrimation increased) 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 Simarax 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 (see section 5.1). 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 (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: 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 (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 Simarax and consult a physician immediately (see section 4.3). 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 Simarax as a 25 mg tablet may be more suitable for them (see section 4.5 for further information). 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 minimize 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 Simarax 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 anti-aggregatory 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 Simarax, since a 25 mg tablet may

be more suitable for them (see section 4.2 and 5.2 for further information). **Renal impairment:** Patients with severe renal impairment (creatinine clearance <30 mL/min), must be advised to consult their doctor before taking Simarax, since a 25 mg tablet may be more suitable for them (see section 4.2 and 5.2 for further information). **Lactose:** The film coating of the tablet contains lactose. Simarax should not be administered to men with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption. **Use with alcohol:** Drinking excessive alcohol can temporarily reduce a man's ability to get an erection. Men should be advised not to drink large amounts of alcohol before sexual activity.

**Contra-indications:** 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. Co-administration of Simarax with ritonavir (a highly potent P450 enzyme inhibitor) is contraindicated (see section 4.5). 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 (see section 4.5). 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 (see section 4.4). Simarax should not be used in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease). Simarax 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:** For Oral Use: **Adults:** The recommended dose is one 50 mg tablet taken with water approximately one hour before sexual activity. The maximum recommended dosing frequency is once per day. If Simarax is taken with food, the onset of activity may be delayed compared to the fasted state (see section 5.2). Patients should be advised that they may need to take Simarax 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. **Elderly:** Dosage adjustments are not required in elderly patients ( $\geq 65$  years old). **Renal Impairment:** 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 <30ml/min), individuals previously diagnosed with severe renal impairment must be advised to consult their doctor before taking Simarax, since a 25 mg tablet may be more suitable for them (see section 4.4 for further information). **Hepatic Impairment:** 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 Simarax, since a 25 mg tablet may be more suitable for them (see section 4.4 for further information). The safety of sildenafil has not been studied in patients with severe hepatic impairment, and its use is therefore contraindicated (see section 4.3). **Paediatric population:** Simarax is not indicated for individuals below 18 years of age. **Use in patients taking other medicinal products:** 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 coadministration with sildenafil is contraindicated (see section 4.3), individuals receiving concomitant treatment with CYP3A4 inhibitors must be advised to consult their doctor before taking Simarax, since a 25 mg tablet may be more suitable for them (see section 4.4 for further information). In order to minimize the potential of developing postural hypotension in patients receiving alpha blocker treatment (e.g. alfuzosin, doxazosin or tamsulosin), patients should be stabilized on alpha blocker therapy prior to initiating sildenafil treatment. Thus, patients taking alpha blockers must be advised to consult their doctor before taking Simarax since a 25 mg tablet may be more suitable for them (see sections 4.4 and 4.5).

Date: 10/2022

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