

Zamantos 50mg film-coated tablets



ESSENTIAL INFORMATION
FOR THE SUPPLY OF
Zamantos 50mg film-coated tablets
(sildenafil)

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Introduction

This booklet is part of a package of information and training materials that Crescent Pharma have put in place to support the launch of Zamantos 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 Zamantos.

While this booklet provides information on the key information to facilitate the assessment as to whether to supply Zamantos, an accompanying, comprehensive booklet, “Essential information for the supply of Zamantos”, provides information on erectile dysfunction, its causes, risk factors, co-morbid links, management, treatment options, Zamantos product information and pharmacist role in supporting the man.

SECTION 1 - Understanding erectile dysfunction and Zamtos

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.¹ It can occur occasionally or frequently and men are able to self-recognise 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:²

- Physical causes
- Psychological causes
- Some types of medication

An overview of the causes is detailed below.

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 could include hypertension, diabetes mellitus, hypercholesterolaemia or CV disease³.

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.⁴

Psychological causes can include:⁵

- 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;
- Antidepressant drugs, such as the tricyclics and selective serotonin reuptake inhibitors, can also cause ED⁶

- Lack of arousal and/or inhibition between partners
- Other sexual dysfunction (*e.g.* premature ejaculation)
- Major life stress such as; money worries, bereavement, 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^{6–12}

| Therapy area | Drug class or drug | Impact on ED |
|------------------------|---|---|
| Cardiovascular | Diuretics | Not determined, but believed to interfere with smooth muscle relaxation |
| | ACE and ARB inhibitors | 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 |
| Psychotropic | Anti-depressants, <i>e.g.</i> selective serotonin reuptake inhibitors tricyclics, monoamine oxidase inhibitors, lithium | Decreases arousal and desire |
| | Anti-psychotics, <i>e.g.</i> phenothiazines, butyrophenones | Increases prolactin levels |
| Anti-epileptics | Carbamazepine Phenytoin Barbiturates | Affects sex hormone levels |
| Endocrine drugs | Testosterone antagonists/ oestrogen agonists Anabolic steroids Luteinising hormone-releasing hormone analogues | Affects androgen receptors, reducing sexual desire |

Table 1: Medications that can cause ED⁶⁻¹² - continued

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

What is Zamantos and what is it used for?

Zamantos 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 a legal ED medication and professional health advice from the pharmacy.

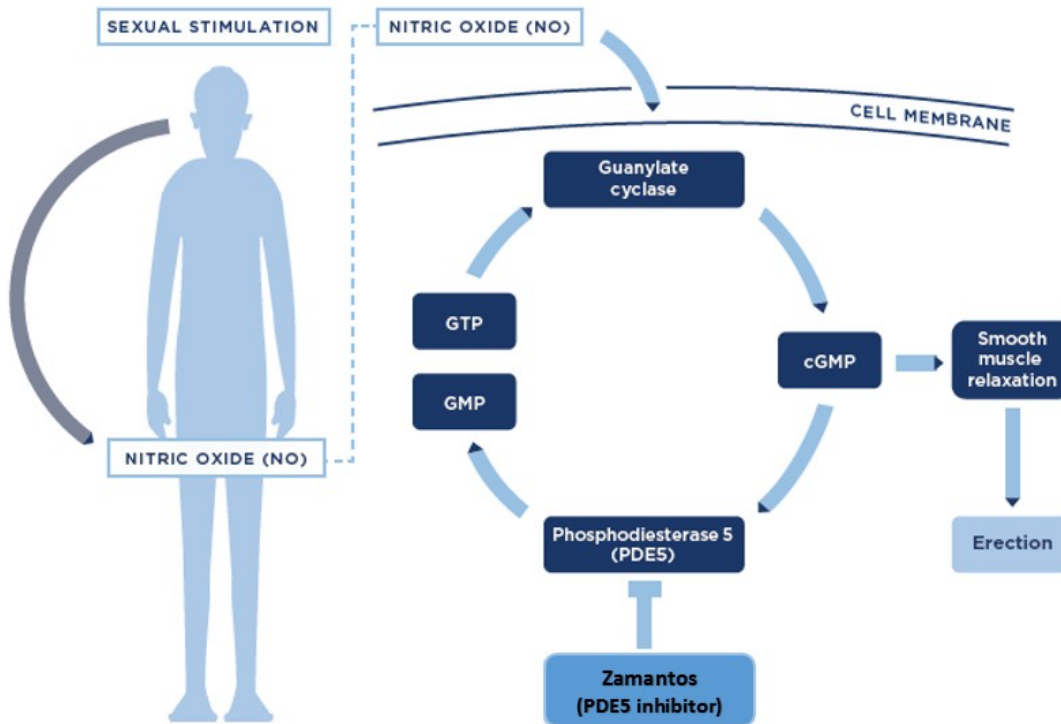
As well as improving their erectile function, allowing men to fully engage in intercourse and/or masturbation, successful treatment with sildenafil can also have emotional benefits for many men with ED, helping them to regain their self-esteem, self-confidence and relationship satisfaction. It can improve their overall quality of life and thus positively impact the wider social implications of erection problems, such as depression.¹³

How does Zamantos 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. Zamantos inhibits the action of this enzyme thus increasing cGMP levels and maintaining these levels for longer. Hence Zamantos helps a man attain and maintain an erection in response to sexual stimulation.¹⁴

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

Figure 1- *Zamantos* mode of action



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

Zamantos Efficacy

Zamantos 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).¹⁵ These data show Zamantos is effective in men with ED and with a wide range of concomitant diseases.

SECTION 2 - Who can use Zamantos

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

The active ingredient in Zamantos, 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 Summaries²
2. The British Association for Urological Surgeons⁴
3. The British Society for Sexual Medicine¹⁶

Zamantos is licenced for packs of 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 Zamantos?

- **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.** Zamantos 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 with the following health problems must not use Zamantos:

- **Men with hypotension (<90/50 mmHg) must not use Zamantos.** 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 treatment of ED.
- **Zamantos 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 Zamantos and should be directed to see their GP.
- **Men with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose- galactose malabsorption** must not take Zamantos 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 Zamantos:

- **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.¹⁷
- **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 Zamantos 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 Zamantos, 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 Zamantos

- **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 Zamantos. 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, rifampicin |
| 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 |

SECTION 3 - What is the Zamantos Checklist?

The Zamantos Checklist, on pages 13–16 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 Zamantos 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 Zamantos 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 Zamantos 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.

Pharmacy Checklist

Zamantos 50mg film-coated tablets (sildenafil)

The following has been created as a useful aide-memoire to help determine whether your patient is suitable for Zamantos, 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 Zamantos provides additional background information in relation to the supply of this product.

If the patient has previously been supplied with sildenafil, 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 tear-off slip (included at the bottom) can also be given to the man.

Additional advice

You should consider possible causes of erectile dysfunction (ED), 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. Who is Zamantos for?

Zamantos is only intended for men 18 years and older who are experiencing 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.

- Y N Has your doctor advised that you are not fit enough for any physical and/or sexual activity?
- Y N 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?
- Y N Have you had a heart attack or stroke within the last 6 months?
- Y N 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 heartbeat 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.

- Y N Are you taking nitrates (nicorandil or other nitric oxide donors *e.g.* glyceryl trinitrate, isosorbide mononitrate or isosorbide dinitrate) for chest pain?
- Y N Are you taking sacubitril/valsartan to treat heart failure?
- Y N Are you using drugs called 'poppers' for recreational purposes (*e.g.* amyl nitrite)?
- Y N Are you taking riociguat or other guanylate cyclase stimulators for lung problems?
- Y N Are you taking ritonavir (for HIV infection)?
- Y N 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)?
- Y N 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?

4. Check concomitant conditions

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

- Y N Do you have Peyronie's disease or any other deformation of the penis?
- Y N 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)?
- Y N Do you have galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption?
- Y N Do you have previously diagnosed hepatic (liver) disease (including cirrhosis of the liver) or severe renal (kidney) impairment?
- Y N Do you have any of the following: sickle cell anaemia, multiple myeloma or leukaemia?
- Y N Do you have any bleeding issues (*e.g.* haemophilia) or have active stomach ulcers?

| | | | |
|--|---------------------------|---|---------------------------|
| <p>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 Zamantos due to his [delete as appropriate] cardiovascular health/interacting medicines/other condition: Pharmacist signature:..... Date:</p> | PHARMACY STAMP | <p>Please keep this slip and present to the Pharmacist when you next wish to purchase Zamantos. 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:</p> | PHARMACY STAMP |
|--|---------------------------|---|---------------------------|

Points for counselling and other information

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

Advice for men who have not been supplied Zamantos

Men who have not been supplied Zamantos 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 Zamantos

Men should be advised:

- Zamantos 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. Zamantos can start to work within 30 minutes.
- Take with or without food, but Zamantos 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 Zamantos 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 Zamantos as this combination may lead to a dangerous fall in blood pressure.
- Men should tell their doctor that they have started taking Zamantos, 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 Zamantos 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.

- 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.

- Your Pharmacist has supplied you with Zamantos 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 Zamantos (see date on reverse).

You have not been provided with Zamantos 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 4 - Advice about Zamantos

Advice for men who are suitable for Zamantos

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 Zamantos.
- During any interaction with their doctor men should tell their doctor that they have started taking Zamantos, especially if they are started on any new medicines.
- Men should not take after excessive drinking as Zamantos 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 Zamantos:
 - 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;
 - Zamantos 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;
 - Zamantos 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, Zamantos 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 Zamantos (sildenafil 50 mg).¹⁵ 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 Zamantos 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 Zamantos and seek IMMEDIATE medical advice.

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

Data show that at doses 16 times the Zamantos 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 Zamantos?

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 Zamantos should be advised to STOP TAKING Zamantos and seek IMMEDIATE medical advice:

- Chest pain, dizziness, feeling of faintness or nausea during or after sex. Nitrates must NOT be used to treat chest pains.
- 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 Zamantos can be found in the SmPC.¹⁵

The most commonly reported side effects in the use of Zamantos 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 Zamantos

Please see Section 2 for men who must not take Zamantos.

If unsuitable for Zamantos, 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 Zamantos 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.

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