



SPECIAL REPORT



ED TREATMENT IN THE PHARMACY

Viagra Connect[®], a branded sildenafil 50mg, was made available as a pharmacy medicine in the UK in 2018. Since then, two studies have been published that look into supply through pharmacy and how it has affected men's health. Pharmacists can use the findings to consider how they can improve the services they offer to men in their pharmacy and have a greater impact on men's health in their area.

Viagra Connect[®] is licensed for men over 18 years of age affected by erectile dysfunction (ED). ED may also be called erection problems (EPs) or impotence. Both the terms EP and ED are used in this report.

This report gives a summary of a PASS results assessment report and a paper that was published in the *International Journal of Clinical Practice*, and then considers what it could mean in practice.

1. *J Lem, J Collins. Survey of Pharmacists to Evaluate the Effectiveness of the Viagra Connect[®] National Additional Risk Minimisation Measures (aRMMs) in the United Kingdom (UK). July 2019.*

2. *Lee L, Maguire T, Maculaitis M, Emir B, Li V, Jeffress M, Li J, Zou K, Donde S, Taylor D. Increasing access to erectile dysfunction treatment via pharmacies to improve healthcare provider visits and quality of life: Results from a prospective real-world observational study in the United Kingdom; 2020/12/01; 75 DO 10.1111/ijcp.13849; International Journal of Clinical Practice.*

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1. RISK MINIMISATION REPORT

Summary

A web-based study of UK pharmacists to assess the effectiveness of Viagra Connect[®] additional risk minimisation measures programme

Additional risk minimisation measures (aRMMs) were implemented to support the reclassification of sildenafil citrate 50mg from a prescription only medicine (POM) to a pharmacy medicine (P) in the UK. These aRMMs were training materials and an optional checklist for pharmacists to assist them in making supply decisions. The aim of this study was to evaluate the effectiveness of these aRMMs by assessing participation in training, knowledge of the key risk messages (KRM) and whether the checklist was used. This was a web-based survey of a random sample of community pharmacists. The survey was completed by 345 pharmacists (40.3% of whom were male, aged 41-60 years) between 28th January and 31st March 2019.

A high knowledge of the KRM was displayed, and nearly all reported use of the checklist at supply and said that the training materials were useful or very useful. The study concluded that the aRMMs were effective for education and subsequent consultations, ensuring supply decisions for Viagra Connect[®] were appropriate.



Key findings and discussion

Pharmacists widely used the training materials and found the checklist helpful for consultations, and would take a risk-averse approach if in doubt of making supply and refer the patient to their GP.

Most pharmacists correctly responded to questions about concomitant diseases which may be contributing to ED.

The lowest correct response rate had 41.4%, to the following question:

Men who had a heart attack or stroke more than six months ago should NOT be supplied Viagra Connect®, but should be referred to their GP.

The correct answer, FALSE, was only given by 41.4% of respondents. Viagra Connect® can be supplied to those who were affected more than six months ago, assuming that their cardiovascular health is stable.

This response could be related to being risk averse and wanting to refer potential cardiac issues to a GP, or a misunderstanding of the supporting training materials.

Areas that did not meet the target of 80% correct in relation to the use of Viagra Connect® with other medicines were that the following patients are not suitable for supply:

- Riociguat users (riociguat is predicted to increase the risk of hypotension if used with sildenafil)
- Patients using other strength sildenafil or other ED treatments on prescription.

Other areas that did not meet the 80% target and may be useful revision points for pharmacists and pharmacy team members were:

- Headache and nausea are common side-effects of sildenafil and do not need medical referral
- Hypertension and hypercholesterolaemia are possible causes of ED
- Use of beta-blockers is not a contraindication (those on alpha-blockers should be referred to their GP for a lower dose)

The findings may have implications for future product launches; the study found that pharmacists said that printed

materials in the mail was the most popular format, followed by online training. Of those who did not complete the training, most said that they were not aware of the training available (some were already trained due to offering a related PGD), so ensuring wide reach and awareness of training materials is key to a successful POM to P reclassification.

53% of pharmacists reported that discussing Viagra Connect® in the pharmacy made some patients uncomfortable and less willing to disclose information, but only 5.2% of pharmacists felt uncomfortable counselling on the product, so putting patients at ease seems to be an ongoing area for development.

IN PRACTICE



Consider the areas below to help identify actions for you or the team.

Training:

- Can all new pharmacists/returning workers/locums access the training and checklist?
- Is there a need to revise some of the areas that were not identified correctly in the study, or pass on to others involved in consultations?

Current consultation process:

- Do customers prefer to use the consultation room?
- How welcoming is the pharmacy?
- Is there room for improvement in relation to consultation skills?

Pharmacists widely used the training materials and found the checklist helpful



2. LONGITUDINAL STUDY

Summary

Increasing access to erectile dysfunction treatment via pharmacies to improve healthcare provider visits and quality of life: Results from a prospective real-world observational study in the United Kingdom

A one-year prospective real-world study (March 2018 to April 2019) was conducted to track men's health behaviour; particularly how they used healthcare, as well as quality of life both before and after the availability of sildenafil as a pharmacy medicine (sildenafil-P) in the UK.

The quality of life (QoL) outcomes were measured using the following tools:

- Self-Esteem and Relationship questionnaire (SEAR) is a validated, 14-item measure focusing on the impact of ED on psychosocial functioning and wellbeing
- 2-item Patient Health Questionnaire (PHQ-2) is a screening tool for major depressive disorder
- Ratings of sexual satisfaction (1-5 responses to a single question)

Linear models were used to assess the association of sildenafil-P use with total physician/nurse practitioner and pharmacist visits. The survey was completed by 1,162 men at all the follow-up time points, with around 55% reporting moderate or severe ED. Of these, 234 reported using sildenafil-P at some point, while 928 were never users of sildenafil-P.

ED is often a result of underlying conditions (such as hypertension and hypercholesterolaemia) and it has an impact on a man's quality of life. Despite this, men often delay seeking treatment as they do not want to discuss ED with their GP. The reclassification was expected to increase access to healthcare visits for men.

The study did find that the reclassification of sildenafil 50mg was associated with a higher number of visits to physicians/nurse practitioners or pharmacists for any reason and better ED-specific quality of life in the 12 months following the switch.

The reclassification was associated with a **higher number of visits to physicians, nurse practitioners or pharmacists**



Key findings and discussion

ED adversely affects a patient's QoL and is associated with physical and psychological conditions, including performance anxiety and depressive symptoms. ED is both underdiagnosed and undertreated, and an increased uptake of treatment could improve wellbeing. Conversations about ED can also lead to early diagnosis and subsequent management of co-morbidities.

Increased public awareness of the availability of phosphodiesterase-5 inhibitors has been shown to shorten the time between someone having symptoms and accessing treatment. Pharmacy availability will facilitate broader access to treatment and more opportunities for health conversations by pharmacists.

Sildenafil-P users tended to be younger than non-users (54.87 ±13.21 years vs 60.06 ±11.53 years).

The most reported risk factors for ED were being overweight, hypertension and hypercholesterolaemia. Lifestyle factors to consider were smoking and alcohol use. Around 1 in 5 of those surveyed reported using a prescription medicine for ED. Overall, just under 63% had never tried anything.

Approximately 17% of men screened positive for depression on the PHQ-2 at baseline and 12-month follow-up.

Sildenafil-P users reported significantly more visits to physicians/nurse practitioners and to pharmacists for any reason, and sildenafil-P users reported marginally more pharmacist visits for sexual functioning discussion than never-users.

The results suggest that men are following the recommendation of pharmacists to see their GP within 6 months of first supply of sildenafil-P, which is important for the secondary prevention of cardiovascular disease, diabetes and depression.

The results suggest that the reclassification has resulted in men seeking further advice on other health issues from pharmacists.

Sildenafil-P users had statistically significant higher SEAR total score, sexual relationship score and self-esteem score compared with never-users. However, the SEAR overall relationship score was lower for sildenafil-P users.

IN PRACTICE



Many men may still not be getting treatment for their erection problems (EPs); raising awareness and making pharmacists accessible for consultations may help improve this.

Having conversations with men about EPs may lead the way to having conversations about other associated medical conditions, such as diabetes, hypertension or high cholesterol, and referral to other healthcare professionals (HCPs). It may be worth considering adding services to help screen for these conditions if not already offered.

Mental health check-ups and sharing referral options when offering ED services may give men the opportunity to seek appropriate advice and counselling.

Discussing the smoking status of men during a consultation can be an opportunity to discuss support for stopping, and to give advice about the association between smoking and ED.

- Are you confident to discuss sexual functioning, mental health and other related health issues associated with EPs?
- What are the local signposting options?
- Can you improve how you and the team seek to engage with men in your local area?
- How can you use EP consultations to effectively engage with your customers and raise awareness of other health services and healthy lifestyle advice?

TO FIND OUT MORE ABOUT VIAGRA CONNECT® VISIT:

- pharmacymagazine.co.uk/viagraconnect-learning
- hcp.viagraconnect.co.uk
- pharmacymagazine.co.uk/viagraconnect-mens-health



Name of product: VIAGRA CONNECT® 50 mg Film-coated Tablets Active ingredient: Sildenafil

Product licence number: PL 50622/0063 **Name and address of the product licence holder:** Upjohn UK Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, UK **Supply classification:** P

Indications: For erectile dysfunction in adult men. **Side Effects:** The safety profile of VIAGRA 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 Authorisation 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, Erythrospia 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, Haematospemia, 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 VIAGRA CONNECT 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 revascularised (e.g. via coronary artery bypass grafting, stenting, or angioplasty), patients with asymptomatic controlled hypertension, and those with mild valvular disease. These patients may be suitable for treatment but should consult a doctor before resuming sexual activity. Patients previously diagnosed with the following must be advised to consult with their doctor before resuming sexual activity: uncontrolled hypertension, moderate to severe valvular disease, left ventricular dysfunction, hypertrophic obstructive and other cardiomyopathies, or significant arrhythmias. Sildenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction (e.g., aortic stenosis), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure. Men with these conditions must not use the product without consulting a doctor. Sildenafil potentiates the hypotensive effect of nitrates (see **Contra-indications**). 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 **Side Effects**). 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 **Side Effects**). Patients should be advised that in the event of any sudden visual defect, they should stop taking VIAGRA CONNECT and consult a physician immediately (see **Contra-indications**). 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 VIAGRA CONNECT as a 25 mg tablet may be more suitable for them (see **Precautions**). 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 **Precautions**). This is most likely to occur within 4 hours post sildenafil dosing. In order to minimise the potential for developing postural hypotension, patients should be hemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Thus, patients taking alpha blockers should be advised to consult their doctor before taking VIAGRA CONNECT as a 25 mg tablet may be more suitable for them. Treatment should be stopped if symptoms of postural hypotension occur, and patients should seek advice from their doctor on what to do. Effect on bleeding: Studies with human platelets indicate that sildenafil potentiates the antiaggregatory effect of sodium nitroprusside in vitro. There is no safety information on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration. Therefore the use of sildenafil is not recommended in those patients with history of bleeding disorders or active peptic ulceration, and should only be administered after consultation with a doctor. Hepatic impairment: Patients with hepatic impairment must be advised to consult their doctor before taking VIAGRA CONNECT, since a 25 mg tablet may be more suitable for them (see **Dosage and Method of use**). Renal impairment: Patients with severe renal impairment (creatinine clearance < 30 mL/min), must be advised to consult their doctor before taking VIAGRA CONNECT, since a 25 mg tablet may be more suitable for them (see **Dosage and Method of use**). Lactose: The film coating of the tablet contains lactose. VIAGRA CONNECT should not be administered to men with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per tablet. Patients on low sodium diets can be informed that this medicinal product is essentially 'sodium-free'. 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, 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 VIAGRA CONNECT with ritonavir (a highly potent P450 enzyme inhibitor) is contraindicated (see **Precautions**). 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 **Precautions**). 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. VIAGRA CONNECT should not be used in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease). VIAGRA CONNECT 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 VIAGRA CONNECT is taken with food, the onset of activity may be delayed compared to the fasted state. Patients should be advised that they may need to take VIAGRA CONNECT 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 (≥ 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 < 30 mL/min), individuals previously diagnosed with severe renal impairment must be advised to consult their doctor before taking VIAGRA CONNECT, since a 25 mg tablet may be more suitable for them (see **Precautions**). 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 VIAGRA CONNECT, since a 25 mg tablet may be more suitable for them (see **Precautions**). The safety of sildenafil has not been studied in patients with severe hepatic impairment, and its use is therefore contraindicated (see **Contra-indications**). Paediatric population: VIAGRA CONNECT 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 co-administration with sildenafil is contraindicated (see **Contra-indications**), individuals receiving concomitant treatment with CYP3A4 inhibitors must be advised to consult their doctor before taking VIAGRA CONNECT, since a 25 mg tablet may be more suitable for them (see **Precautions**). In order to minimise the potential of developing postural hypotension in patients receiving alpha blocker treatment (e.g. alfuzosin, doxazosin or tamsulosin), patients should be stabilised on alpha blocker therapy prior to initiating sildenafil treatment. Thus, patients taking alpha blockers must be advised to consult their doctor before taking VIAGRA CONNECT since a 25 mg tablet may be more suitable for them (see **Precautions**). Addition of a single dose of sildenafil to sacubitril/valsartan at steady state in patients with hypertension was associated with a significantly greater blood pressure reduction compared to administration of sacubitril/valsartan alone. Therefore, caution should be exercised when sildenafil is initiated in patients treated with sacubitril/valsartan. **C+D Trade Price (exc VAT):** 2 pack £8.82, 4 pack £16.17 and 8 pack £28.39 **Date of revision:** 04/2023

Please continue to report suspected adverse drug reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme. It is easiest and quickest to report adverse drug reactions online via the Yellow Card Website: <https://yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, you can report via some clinical IT systems (EMIS/SystemsOne/Vision/MiDatabank) or by calling the Commission on Human Medicines (CHM), free phone line: 0800-731-6789. Adverse reactions/events should also be reported to MAH at e-mail address: pvuk@viatris.com.

The SmPC for this product, including adverse reactions, precautions, contra-indications, and method of use can be found at: <http://www.mhra.gov.uk/Safetyinformation/Medicinesinformation/SPCandPILs/index.htm> and from Viatris Medical Information, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshire, AL10 9UL, phone no. 01707 853000, Email: info.uk@viatris.com