



Public Assessment Report

Prescription only medicine to Pharmacy medicine Reclassification

Viagra Connect 50mg film-coated tablets

Sildenafil citrate

PL 00165/0392 – 0001

Pfizer Consumer Healthcare Limited

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1. About Viagra Connect

Viagra Connect (containing sildenafil 50mg) is a treatment for adult men (aged 18 years and older) with erectile dysfunction, also known as impotence. This is when a man cannot get and maintain an erection hard enough for satisfactory sexual activity. Sildenafil is currently a prescription only medicine.

This report relates specifically to the proposal to reclassify Viagra Connect from a prescription to pharmacy medicine. If you want more information on sildenafil as a prescription medicine then please refer to sildenafil Public Assessment Reports available here:

<http://www.mhra.gov.uk/public-assessment-reports/>

What is in Viagra Connect?

Viagra Connect are tablets containing 50 mg sildenafil citrate.

This was the first application for a sildenafil product to be available as a pharmacy medicine.

What is sildenafil citrate used for?

Sildenafil belongs to a group of medicines called phosphodiesterase type 5 (PDE5) inhibitors. It works by blocking the phosphodiesterase enzyme, which normally breaks down a substance known as cyclic guanosine monophosphate (cGMP). During sexual stimulation, cGMP is produced in the penis, where it causes the muscle in the spongy tissue of the penis (the corpora cavernosa) to relax, allowing the flow of blood into the corpora, producing the erection. By blocking the breakdown of cGMP, sildenafil improves erectile function. Sexual stimulation is still needed to produce an erection.

NHS Choices provides health advice about erectile dysfunction:

<http://www.nhs.uk/conditions/Erectile-dysfunction/Pages/Introduction.aspx>

Who has made the proposal?

The licence holder for Viagra Connect tablets (Pfizer Consumer Healthcare Limited) has applied to make this product available as a pharmacy medicine. Pharmacy medicines can be supplied without prescription only from pharmacies, by or under the supervision of a pharmacist.

Pfizer Consumer Healthcare Limited is referred to as 'the applicant' throughout this document.

What is the view of the Commission on Human Medicines?

The Commission on Human Medicines (CHM) has advised that this product can be available as a pharmacy medicine. The CHM advises ministers on the safety, efficacy and quality of medicinal products. CHM is an advisory non-departmental public body, sponsored by the [Department of Health](#).

2. Proposed terms of reclassification

What are the details of this change?

Viagra Connect will be available through pharmacy outlets in the following circumstances:

- For oral use
- Strength: 50 mg sildenafil citrate
- For adult men with erectile dysfunction
- Dose: 50 mg tablet to be taken as needed with water approximately 1 hour before sexual activity
- Maximum dose: 50 mg
- Maximum daily dose: 50 mg
- Maximum pack size: 8 tablets

Medicines containing sildenafil will still also be available to obtain on prescription.

3. How was the proposal assessed for Viagra Connect being available as a pharmacy medicine?

A medicine will be non-prescription unless it fulfils the criteria for prescription control as set out below. Prescription-only status will apply where:

1. A direct or indirect danger exists to human health, even when used correctly, if used without medical supervision
2. There is frequently incorrect use which could lead to direct or indirect danger to human health
3. Further investigation of activity and/or side-effects is required
4. The product is normally prescribed for parenteral administration (by injection)

In the UK, these criteria are laid down in the Human Medicines Regulations 2012, regulation 62(3).¹ The MHRA assessed the application against the criteria for prescription control to assess the suitability for pharmacy availability.

The company has produced pharmacy training and a checklist that pharmacists can choose to use when supplying the medicine. This checklist can be used to determine whether the medicine is suitable for a patient by asking a series of questions around cardiovascular health, other medicines and other conditions. The patient will have the patient information leaflet and packaging to refer to, which contain the key safety messages.

3.1 Criterion 1 – “It is likely to present a direct or indirect danger to human health, even when used correctly, if used without medical supervision”

The main criterion that must be considered in the reclassification of Viagra Connect to pharmacy status is that it does not present a direct or indirect danger to human health if used, even correctly, without the supervision of a doctor. A direct danger may be present if the product causes adverse reactions that are important because of their seriousness, severity, or frequency. A danger may also be present if the reaction is one for which there is no suitable preventative action such as being able to identify the group of patients who are at risk if they use the product without medical supervision so that they can be excluded from using the pharmacy product. Direct danger may arise from drug interactions with commonly used medicines. For the product to be suitable for pharmacy status the drug interactions would need to be preventable.

3.1.1 Direct danger to human health

The safety profile of sildenafil is favourable and well known when used under medical supervision, especially for the adverse events and interactions. Overall there are no identified concerns related to how it works, interactions with other medicines, and side effects that are not already well documented. The main known or potential adverse effects of sildenafil relate to pharmacological effects arising from the elevation of cGMP in other tissues such as systemic vascular smooth muscle, the retina, platelets, and gastrointestinal smooth muscle. The most commonly reported adverse reactions in clinical studies among sildenafil-treated patients were headache, flushing, dyspepsia (indigestion), nasal (nose) congestion, dizziness, nausea (feeling sick), hot flush, visual disturbance, cyanopsia (vision tinted blue), and blurred vision.

The particular areas that could potentially lead to direct danger are;

- Use with nitrates
- Use with certain other medications (CYP3A4 inhibitors, alpha-blockers, guanylate cyclase stimulators)
- Previous episodes of non-arteritic anterior ischaemic optic neuropathy (NAION)
- Priapism

¹ The Human Medicines Regulations 2012. <http://www.legislation.gov.uk/uksi/2012/1916/contents/made>

Nitrates

Use at the same time with nitrates or nitric oxide donors (such as glyceryl trinitrate, isosorbide mononitrate, nicorandil, or amyl nitrate (also known as “poppers”), which are used for angina (chest pain) or heart failure, can lead to a dangerous fall in blood pressure. Therefore, Viagra Connect must not be used at the same time as nitrates or nitric oxide donors.

CYP3A4 inhibitors, guanylate cyclase stimulators, alpha-blockers

Ritonavir (a CYP3A4 inhibitor) increases the concentration of sildenafil in the blood by four times. Therefore, Viagra Connect must not be used at the same time.

PDE5 inhibitors, including sildenafil, must not be used at the same time with guanylate cyclase stimulators, such as riociguat (used to treat high blood pressure in the lungs), because this may potentially lead to symptomatic hypotension (low blood pressure causing dizziness).

Clinical trial data indicates a reduction in sildenafil clearance when taken with other CYP3A4 inhibitors (with the exception of ritonavir). This means that if sildenafil is taken with these types of medicines it stays longer in the bloodstream. Although no increased incidence of adverse events was observed in these patients, the prescription-only product recommends a starting dose of 25 mg sildenafil for these patients.

Use of sildenafil at the same time as alpha-blocker medicines may lead to symptomatic hypotension in a few susceptible individuals. To minimise the potential of developing postural hypotension (a sudden fall in blood pressure when standing up, which can lead to dizziness or fainting) in patients receiving alpha-blocker treatment, the prescription-only product recommends a starting dose of 25 mg sildenafil.

As it is not practical to reduce the dose to 25 mg in the pharmacy model of supply, and to simplify the supply model Viagra Connect must not be supplied to men taking CYP3A4 inhibitors and alpha-blockers, and these men should be referred to their doctor.

NAION

Non-arteritic anterior ischaemic optic neuropathy (NAION; a loss of vision because of damage to the optic nerve) has been reported rarely post-marketing in temporal association with the use of all PDE5 inhibitors, including sildenafil. Therefore, Viagra Connect must not be used in any patient with a history of vision loss or in anyone with an inherited eye disease (such as retinitis pigmentosa).

Priapism

Prolonged and sometimes painful erections lasting longer than 4 hours (priapism) have been occasionally reported with sildenafil in post-marketing experience. The product information advises patients who have conditions that may expose them to priapism (such as sickle cell anaemia, multiple myeloma, or leukaemia) to consult a doctor before using Viagra Connect, and that after using, if an erection persists longer than 4 hours, the patient should seek immediate medical assistance.

Renal Impairment

No dosage adjustments are required for patients with mild to moderate renal (kidney) 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 not be supplied Viagra Connect and must be advised to consult their doctor before taking this product, since the 25 mg prescription dose may be more suitable for them.

Hepatic Impairment

Sildenafil clearance is reduced in individuals with hepatic (liver) impairment (for example, cirrhosis). Individuals previously diagnosed with hepatic impairment must not be supplied Viagra Connect and must be advised to consult their doctor before taking Viagra Connect tablets, since the 25 mg prescription dose may be more suitable for them.

Can direct risk be minimised as a pharmacy medicine?

It is essential for pharmacists to be aware of the above issues relating to interacting medicines, renal and hepatic impairment, NAION, and priapism. It is considered that pharmacists can question patients on the medicines that they are currently taking and on their medical history, and that pharmacies in England have access to Summary Care Records.² This will assist the pharmacist in identifying patients with renal and hepatic impairment and those on interacting medicines (especially nitrates), and these patients will be signposted to their doctor. The pharmacist will also question patients to identify if they have suffered from any eye problems or any conditions that predispose them to priapism. Additionally, the product information (including the patient information leaflet and label) has been strengthened for pharmacy supply to clearly state that these men should not take Viagra Connect.

The counselling points available on the checklist for pharmacists remind the patient to seek medical attention immediately if they develop an erection that lasts more than 4 hours or experience any sudden visual impairment. These points are also clearly included in the patient information leaflet provided with the product, which the patient can refer to.

The MHRA considers that the direct risks can be minimised to an acceptable level for pharmacy supply of Viagra Connect.

3.1.2 Indirect danger to human health

Medicines may present an indirect danger when particular symptoms are caused by a range of different conditions. If the patient cannot easily self-diagnose the cause of such symptoms it may be inappropriate to provide a product to treat the symptoms without also treating and managing the underlying disease.

An important example of an indirect danger is when treating the symptoms might mask an underlying condition requiring medical attention. Consideration should be given to whether an indirect danger might exist and if so, whether the risk, its frequency and the seriousness of the consequences would make reclassification unacceptable. Additional warnings, such as a recommendation to seek medical advice if symptoms continue beyond a stated time period, may be necessary in such instances.

Erectile dysfunction is a symptom of cardiovascular disease, and may also be caused by psychological factors or alcohol use. If these are not identified by the pharmacist an indirect danger to health may exist.

Cardiovascular disease and risks

Several medical conditions are associated with erectile dysfunction, most notably cardiovascular disease and diabetes mellitus, and there is generally low awareness among both the public and healthcare professionals of these established links. The applicant states that pharmacy availability of Viagra Connect is likely to increase the number of men with erectile dysfunction who seek treatment. This should lead to an increase and/or earlier diagnosis of erectile dysfunction by a healthcare professional, along with earlier diagnosis of potential underlying conditions such as cardiovascular disease or diabetes, by increasing patient awareness of the association of erectile dysfunction with other more chronic conditions and facilitating dialogue with a healthcare professional.

² A summary care record is an electronic record of important patient information, created from GP records. It can be seen and used by authorised staff in other areas of the health and care system involved in the patient's direct care.

For Viagra Connect, it is proposed that patients with certain cardiovascular conditions and risk factors who are not suitable to be supplied this product will be provided with clear instructions to consult a doctor. These patients are those:

- (a) With severe cardiovascular disorders, such as a recent acute myocardial infarction (heart attack) or stroke (within the last 6 months), unstable angina or severe cardiac failure.
- (b) With uncontrolled hypertension (high blood pressure), moderate to severe valvular disease (problems with heart valves), left ventricular dysfunction (problems in heart muscle), hypertrophic obstructive and other cardiomyopathies (inflammation of the heart muscle), or significant arrhythmias (irregular heart beat).
- (c) With increased susceptibility to vasodilators, including those with left ventricular outflow obstruction or aortic narrowing (heart problems causing blood flow issues), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure.
- (d) Who feel very breathless or experience chest pain after light or moderate physical activity, such as walking briskly for 20 minutes or climbing 2 flights of stairs.

The following patients are considered to be at low cardiovascular risk and will be able to use the product, providing they are considered to be fit for sex (in response to questioning on d above):

- (e) patients who have been successfully revascularised (for example, via coronary artery bypass grafting, stenting, or angioplasty), patients with asymptomatic controlled hypertension, and those with mild valvular disease.

The applicant will be supplying a checklist with this product that enables a pharmacist to perform a basic screening for cardiovascular health. It is considered that the patients in categories (a) to (c) can be identified by the pharmacist asking a series of questions about cardiovascular health history and the medicines they are taking. Those patients who are not suitable for supply would be referred to a doctor.

The more nuanced area is category (e) – those patients who are considered at low cardiovascular risk from sexual activity. It is considered that patients who have been successfully vascularised, those with asymptomatic controlled hypertension, and those with mild valvular disease are considered suitable to take the product if they are fit for sex. It is proposed that cardiovascular fitness for sex is assessed by a simple question (can you walk briskly for 20 minutes or climb 2 flights of stairs without getting breathless?). It is considered that, although it is difficult to quantify this question, it is a simple and practical way to determine fitness considering that there is a low risk of cardiovascular events with the use of sildenafil.

In addition to the checklist, the applicant is providing training material that provides background information and covers the management of erectile dysfunction, misconceptions around the condition, and how Viagra Connect should be supplied. The pharmacy training materials and checklist assists pharmacists in identifying these patients appropriately. In addition, the leaflet and label clearly warns patients, using patient-friendly terminology, that they should not take the product if they suffer from certain cardiovascular conditions.

Erectile dysfunction with a psychological cause

Difficulties with erections can sometimes develop because of depression or anxiety. Psychological causes account for 1 in 10 cases of erectile dysfunction. Psychological causes can occur for a wide range of reasons. These include issues such as performance anxiety in relation to erectile dysfunction and the fear this will keep occurring, lack of sexual knowledge, past sexual problems, or life stress.

Erectile dysfunction can often have both physical and psychological causes. For example, erectile dysfunction may be a symptom of depression and/or in men with erectile dysfunction, the emotional stress commonly associated with loss of sexual function may lead to depression. Additionally, antidepressant drugs can also cause erectile dysfunction.

It is important for the pharmacist to look out for signs of untreated depression, which may not have been picked up before. There is no reason why Viagra Connect should not be supplied for those men with erectile dysfunction with a psychological origin. However, lifestyle advice should also be provided in conjunction with supply of the product. This could be generic lifestyle advice and stress-reducing tips, whereas others may need to be referred to the doctor or supported by counselling. Details relating to this are provided in the pharmacy training materials and the checklist advises the pharmacist to check for signs of concern from a psychological perspective and how to guide the patient accordingly.

Alcohol use

Alcohol is a depressant and using it heavily can dampen mood, decrease sexual desire, and make it difficult for a man to achieve erections or reach an orgasm while under the influence. Drinking alcohol to excess in both the short term and the long term can cause erectile dysfunction. As such, there may be patients with erectile dysfunction who wish to take Viagra Connect who may have underlying issues with alcohol use.

It is acceptable for Viagra Connect to be used in these patients, although it would be advisable that the pharmacist advises the patient about moderating alcohol intake and the possible effect excess alcohol may have on sexual performance, even if they are using Viagra Connect. The pharmacist should also look at the consultation as an opportunity to help guide the patient to make lifestyle changes. The pharmacy training guide emphasises the actions patients can take for themselves in relation to erectile dysfunction. This includes reference to the reducing alcohol intake to help to prevent the erectile dysfunction in the first place. Furthermore, if the pharmacist believes that the man has an issue with short or long term alcohol intake, they can refer to him to his doctor or other relevant supportive services.

Can indirect danger be minimised as a pharmacy medicine?

The information provided to the pharmacist (the pharmacy training, and the checklist) and the information for the patient (leaflet, label) help to identify those patients who have certain cardiovascular problems, and help to inform the patient that the product is not suitable for them so they should see their doctor.

The training and checklist also help pharmacists to recognise patients who may be suffering from depression, anxiety, and alcohol use, and to counsel, support, and refer these patients appropriately.

There is a low risk of masking underlying disease (an 'indirect danger' under criterion 1). However, this is considered to be minimised by the supply model provided and also outweighed by the benefits of patients being able to access a legitimate supply from a pharmacist who can provide healthcare advice and signpost the patient to their GP if appropriate.

3.2 Criterion 2 – “It is frequently and to a very wide extent used incorrectly, and as a result is likely to present a direct or indirect danger to human health”

Addiction, dependence, recreational use, and misuse can be considered to be incorrect use.

There is no indication from controlled clinical trial or post-marketing data that patients develop dependence or addiction to sildenafil. There are no underlying pharmacological mechanisms or neural or behavioural signs and symptoms that suggest that sildenafil would induce drug-seeking behaviour. There have been no reports of drug abuse or drug dependence associated with the use of sildenafil in clinical trials.

There is evidence that sildenafil, often obtained illegally, is used with the recreational use of other drugs (for example, methamphetamine, methylenedioxy-N-methylamphetamine, poppers (e.g. amyl nitrate), and opioids) in people who do not normally have erectile dysfunction. This appears to be mainly in healthy men who use erectile dysfunction medicines to counteract effects of recreational drugs. It is unknown whether these users would purchase Viagra Connect from a pharmacy if that option was available, so it is not known whether reclassification would have any effect on this group. However, there appears to be little evidence of harm from this intentional incorrect use that leads to a direct or indirect danger to health and it is considered that the second prescription only medicine criteria is not fulfilled.

The concurrent use with poppers, including amyl nitrate, causing blood vessel dilation and blood pressure drop leading to myocardial infarction is a well-established concern. Use with amyl nitrate is contraindicated in the product information, and it is considered that this is an acceptable risk minimisation measure.

Viagra Connect cannot be supplied to men without erectile dysfunction, women, and children/adolescents under 18 years old.

3.3 Criterion 3 – “It contains substances or preparations of substances of which the activity requires, or the side effects require, further investigation”

The safety profile of sildenafil is well known. It has been available in the UK as a prescription only medicine for 18 years and it is widely used, therefore this criterion is not considered to be applicable to the non-prescription application. There is no indication that any issue requires further investigation. Therefore, Viagra Connect does not meet the requirements for medical prescription in relation to this criterion.

3.4 Criterion 4 – “It is normally prescribed by a doctor for parenteral administration (that is, by injection).”

This product is a tablet, so this criterion does not apply.

4. Further details on the application

4.1 Risk Management Plan

As is required for all new marketing authorisation applications, the application contained a risk management plan (RMP) which documents the following:

- the known safety profile of the medicine including any important identified and potential risks
- what is not known about the safety profile ('missing information')
- how the safety profile will be monitored after the medicine is licensed, including any plans for further studies to actively gain more knowledge about the safety of the medicine ('additional pharmacovigilance activities')
- how any important risks will be prevented or minimised in patients ('risk minimisation measures') and how the utility and effectiveness of the risk minimisation measures will be assessed

The RMP for this product has detailed the important identified and potential risks based on the known safety profile of sildenafil which has been established through 18 years of use in the POM setting. In addition, the RMP for this product includes the important potential risk “Serious cardiovascular events associated with sexual activity in men with pre-existing or undiagnosed cardiovascular disease and/or risk factors”. This relates specifically to the Pharmacy supply of Viagra Connect and the possibility that men won't be assessed by their GP for underlying cardiovascular (or other) causes of their erectile dysfunction and an opportunity to diagnose and treat underlying cardiovascular disease may be missed. Viagra Connect must not be given to men in whom sexual activity is not advised. To address this potential risk the applicant is providing Pharmacy training materials and a checklist (see

section 4.1.1). This will be supplied in addition to the routine risk minimisation measures (SPC, labelling and patient information leaflet).

In addition, the applicant will be undertaking a survey-based study to assess the utility and effectiveness of the proposed pharmacy risk minimisation material in conveying the key messages to pharmacists and how these impact on self-reported pharmacy practice. (The outcome measure is that Viagra Connect will have been supplied to only men in whom its use is appropriate and/or appropriate advice issued).

The applicant has proposed routine pharmacovigilance activities to take place; no additional safety studies are planned. This is accepted given the well-established safety profile of sildenafil.

4.1.1 Pharmacy support materials

Additional resources will be provided for pharmacists, which cover the following areas:

Essential information for pharmacists – The training guide provides information to pharmacists on the safe use of Viagra Connect.

Pharmacist checklist – The checklist contains a list of yes/no questions to determine the patient's cardiovascular health, interacting medicines, and whether the patient has any conditions that mean Viagra Connect must not be taken. Points for counselling are also included, as are advice cards for those who have and haven't been supplied Viagra Connect. The use of the checklist is not compulsory, as pharmacists can choose to use this as appropriate depending on their experience and the patient's preferences.

5. Consultation on Pharmacy availability

Consultation document ARM94³, which summarises the proposals on the pharmacy only (POM) to pharmacy (P) reclassification of Viagra Connect, was posted on the GOV.UK website on 27 March 2017. The deadline for comments was given as 18 April 2017.

ARM 94 can be accessed via the following link:

<https://www.gov.uk/government/consultations/proposal-to-make-sildenafil-50mg-film-coated-tablets-available-from-pharmacies>

47 responses were received. 33 responses supported the proposal, 13 did not support the proposal, and 1 was unsure about the proposal.

Of the 47 responses received, 12 were from specified pharmacy, medical, trade or charity organisations. These organisations included Community Pharmacy Scotland; Dispensing Doctors' Association; Guild of Healthcare Pharmacists; HEART UK – The Cholesterol Charity; Men's Health Forum; Proprietary Association of Great Britain (PAGB); Prostate Cancer UK; Royal Pharmaceutical Society; National Pharmacy Association; and Self Care Forum. Two organisations wished to remain confidential; both supported the proposal.

Of 12 pharmacists who responded, 7 practised in primary care, 3 in secondary care, and 2 did not specify their area of practice. Responses were also received from 10 doctors and 3 members of the public. Another 10 responses were received from community pharmacy companies, pharmaceutical companies, pharmacy students, and unknown respondents (who did not specify in what capacity they were responding)

³ ARM stands for Application to Reclassify a Medicine. An ARM consultation is a public consultation inviting views from all stakeholders on a proposal to reclassify a medicine from POM to P or from P to GSL

The 33 responses that supported the proposal included all responses from pharmacy, medical, or charity organisations; most GPs; all members of the public; all the community pharmacy companies; and all the pharmaceutical companies.

The 13 responses that did not support the proposal included 8 pharmacists, 3 GPs, 1 student, and 1 unknown respondent.

5.1 Responses agreeing with the proposal to reclassify sildenafil tablets as a pharmacy medicine

A number of organisations, doctors and pharmacists believed that sildenafil fulfils the criteria for a POM to P reclassification. In support of this, the following general themes were raised by many respondents:

- (a) Pharmacists are expert healthcare professionals with the skills and expertise to assess whether a treatment is appropriate and to give advice about a condition, side effects, interactions, contraindications, and cautions, as well as lifestyle and usage advice
- (b) The checklist provided is comprehensive and will adequately support pharmacists to supply this medicine appropriately or advise a person to contact another medical professional
- (c) Making sildenafil available as a pharmacy medicine will increase awareness of erectile dysfunction, and provide an opportunity to make people aware that erectile dysfunction could be a symptom of cardiovascular disease or diabetes.
- (d) Medicines for erectile dysfunction, especially the brand Viagra, are a popular target for counterfeit medicines, particularly when purchased online. Making Viagra Connect available to buy without prescription from pharmacies will provide easier access for men to a legitimate, quality supply, and reduce the risks associated with counterfeit online supplies.
- (e) Empowering people to look after themselves appropriately has many benefits by giving people faster and more convenient access to appropriate medicines. It makes more effective use of GPs' time by reducing the number of consultations for self-treatable conditions and reduces NHS costs.

The following is a summary of the key issues raised:

5.1.1 Interaction with nitrates

Some respondents noted that it was very important to emphasise the risks of taking sildenafil with nitrates, in particular poppers such as amyl nitrate. The Commission on Human Medicines (CHM) considered that taking Viagra Connect with nitrates (nitrate-containing medicine and amyl nitrate or 'poppers') was a potential serious safety concern, but that the product information (leaflet and label) minimised these risks.

The pharmacy checklist includes a question about the use of nitrates, and a warning about taking Viagra Connect with nitrates, including amyl nitrate, is reiterated in the counselling points associated with the checklist.

5.1.2 Erectile dysfunction is a symptom of underlying disease

Responses noted the importance of emphasising that erectile dysfunction is a symptom of underlying disease (such as heart and blood vessel problems, high blood pressure, diabetes, and high cholesterol), and that pharmacists should educate men about this and advise them to go to their GP for a health check.

Two respondents noted that advising patients to consult their doctor within 6 months may result in delay in diagnosis of an underlying condition and that patients should be encouraged to see their doctor as soon as possible.

CHM considered the potential that treatment for erectile dysfunction may mask an underlying disease. It was considered that the proposed contraindications and warnings, alongside the pharmacy checklist and the product information, minimised these risks. 6 months was considered a pragmatic timeframe that balances the challenges of getting men to go to their doctor against the opportunity for early detection of underlying disease. However, because 6 months was considered the maximum timeframe, the applicant was requested to change both the leaflet and checklist to reflect that patients should be advised to see a doctor as soon as possible, within 6 months.

5.1.3 Checklist

The responses relating to the pharmacy checklist were positive, and many responses noted that it was similar to the information requested in a patient group direction (PGD).⁴ The applicant was requested to make a number of minor improvements, as a consequence of some responses received: The checklist now:

- Clearly states that it is an optional tool, and pharmacists should use their professional judgement to decide when/how/how much of the checklist to use, because checklists can be seen as a barrier to supply by both pharmacists and patients
- Includes a prompt that the pharmacist can also check the Summary Care Record/Patient Medication Record to check some aspects of medical history/interacting medicines
- Includes that men currently prescribed the product can be supplied the product if they meet the criteria for pharmacy supply
- Has been rephrased in parts to ensure the questions are easily understood by patients

5.1.4 Patient information leaflet

Multiple comments were received that stated that the patient information leaflet was useful and comprehensive.

5.1.5 Label

A comment was received that the labelling could be more discrete, especially because the explicit “Helps you get and keep an erection” could cause issues with patient privacy and should be removed. It is noted that the indication and usage instructions are on the back of the pack.

The Viagra name is well recognised so the statement on the label about what the medicine is used for is likely to make little difference with regards to making the product more discrete. Although it is not required by law for the label and/or patient leaflet to contain a statement saying what the product is used for, this is normal for medicines that can be sold without prescription. On balance, it is recommended that the statement about what the medicine is used for remains on the front of the pack to aid in the supply of the product and in patient understanding.

5.1.6 Communications

One organisation stated that the communications to the public and healthcare professionals will need to be carefully considered. They must be clear on what the medication can and cannot be supplied for, and must publicly empower the pharmacist and their team to safely sell this product.

The pharmacy checklist and training material have been assessed for appropriateness. The advertising and promotional material will be pre-vetted by the MHRA before the product is launched.

⁴ Patient group directions (PGDs) are written instructions to help supply or administer medicines to patients, usually in planned circumstances. They are put together by a multi-disciplinary group including a doctor, a pharmacist and a representative of any professional group expected to supply the medicines under the PGD.

5.1.7 Training materials

A number of respondents referred to the training materials and welcomed their availability.

One respondent (an academic) suggested that it should be compulsory for pharmacists to undertake the training before selling the P product. From a regulatory perspective, a condition of this reclassification is that the applicant is required to ensure that the checklist and training materials are made available for all pharmacists. However, whether the pharmacist uses this training material or not is a professional decision.

5.1.8 Other

Comments were received on prescribing restrictions, price, and reclassifying by substance rather than by specific product. These areas fall outside the scope of a reclassification application.

5.2 Responses disagreeing with the proposal to reclassify sildenafil tablets as a pharmacy medicine

5.2.1 Insufficient access to Summary Care Records/patients not disclosing medical history

Some respondents who did not support the reclassification stated that Summary Care Records are not widely used so pharmacists and their staff could not check a man's medical history or check whether he was taking any medicines that should not be taken at the same time as sildenafil. Also, they raised concerns that patients may not respond truthfully or reliably to questions about their medical history or medicines currently being taken.

As of January 2016, in England, 96% of patients have had their Summary Care Record uploaded, and pharmacists have access to these records. The Summary Care Record can support community pharmacists to deliver patient centred services by providing information on a patient's medical conditions and concurrent medication. Summary Care Record access in community pharmacy has shown benefits to patients by enabling access to more information so pharmacists and pharmacy technicians can provide a safer, more efficient, and better-informed service for those patients who require it.⁵ However, it is not the only tool that pharmacists can use to establish whether the patient is on any interacting medicines or has contraindicated/cautioned conditions; the pharmacist can either use the patient medication record (a record of previously prescribed medicines at that pharmacy) or question the patient appropriately. CHM previously considered this issue and felt that the pharmacy checklist, patient leaflet, and label minimised the risks of drug interactions and inappropriate supply under the proposed pharmacy circumstances for use.

5.2.2 Matters relating to professional standards for pharmacists

A few objections were raised about matters relating to professional standards for pharmacists and pharmacy staff. These included the following issues:

- pharmacists may be coerced into supplying the product by patients and the possible threat of complaints to head office, regulators, and local news
- there may be a breach of patient confidentiality
- patients may not wish to discuss their symptoms with the pharmacist

These all fall outside the legal criteria on which reclassification of a medicine is based. Also, some of these arguments could be equally applied to many prescription and over-the-counter medicines. These are a professional standards issue, and cannot be considered as part of the assessment of a reclassification application, as these are not part of the criteria for prescription control laid down in the Human Medicines Regulations 2012, regulation 62(3).

⁵ Health and Social Care Information Centre. [Community pharmacy access to Summary Care Records: proof of concept report v1.1](#). Health and Social Care Information Centre. 2015.

5.2.3 Pharmacists have limited time resource

An objection was raised that pharmacists would not have time to ascertain whether the medicine is suitable, especially considering the cardiac risks.

CHM were satisfied that the pharmacy materials would help to ensure that patients were appropriately identified, and that men with high cardiovascular risk were excluded from supply. However, pharmacy workload is, again, a professional issue and does not fall within the reclassification assessment process.

5.2.4 Risk of abuse

The risk of abuse was raised as an objection – there was a concern that sildenafil would be misused for recreational sexual enhancement to compensate for the use of other drugs that may cause erectile dysfunction.

CHM has previously considered this risk of abuse and accepted that there is no suggestion from the controlled clinical trial or post-marketing data that patients develop dependence or addiction to Viagra Connect.

There is some published evidence of intentional incorrect use of sildenafil, outside the prescription setting, particularly through illicit routes of supply and when used at the same time as recreational drugs. However, there appears to be little evidence of harm from this intentional incorrect use that leads to a direct or indirect danger to health and it is considered that the second prescription only medicine criteria relating to the risk of abuse (see section 3.2) is not fulfilled.

5.2.5 Erectile dysfunction with a psychological cause

An objection was raised that pharmacists do not have the clinical competence, medical history, sensitivity, and skill to supply sildenafil to patients who have erectile dysfunction with a psychological cause.

It was considered by the ad hoc stakeholder group, and subsequently by CHM, that the availability of Viagra Connect to men who had erectile dysfunction with a psychological cause would be beneficial as this was an important group to bring into the healthcare system. Pharmacists are experienced at dealing with a variety of sensitive issues and will consider possible causes of erectile dysfunction such as undiagnosed depression, anxiety, and excessive alcohol use, and will provide lifestyle advice or advise men to seek medical advice if appropriate.

In contrast, a consultation response from a GP supported the use of this medicine in the short term for younger men who require a confidence boost.

5.2.6 Sildenafil is available free of charge on prescription

A comment was raised that as sildenafil is available on prescription free of charge to a large number of patients, the pharmacy medicine would only be requested by men who have been unable to obtain this medicine from their doctor.

It is considered that the risks of men intentionally using the product inappropriately are outweighed by the benefits that the pharmacy route of supply can bring – by providing a more convenient way to obtain sildenafil, thus bringing a hard-to-reach group into healthcare earlier with the potential to increase identification of cardiovascular disease and also reducing the risks of men obtaining counterfeits via the internet.

5.2.7 Patients may purchase a larger quantity

Comments raised a concern that patients may buy more than one pack, especially as records are not made of pharmacy sales.

The possibility of multiple purchases exists with every pharmacy medicine, and it is only a significant issue if the product is likely to be abused and, as a result, cause harm. CHM has previously advised that the risk of abuse does not apply to the proposed product. Additionally, the opportunity for multiple purchases already exists (for example via different online prescribers or different online or traditional pharmacies through a Patient Group Direction).

6. Advice from the Commission on Human Medicines

CHM considered the reclassification application and the responses to the public consultation and advised in favour of Pharmacy availability of Viagra Connect under the circumstances outlined above — for adult men with erectile dysfunction with a maximum dose of one tablet each day, and a maximum pack size of 8 tablets.

7. Conclusion

Assessment of the responses to consultation on the application for Viagra Connect has revealed no new issues of concern in addition to those considered by CHM and on which CHM were reassured. Considering the advice from CHM before and after consultation, the MHRA has taken the decision to approve pharmacy (P) legal status for Viagra Connect.

Pharmacy availability of Viagra Connect tablets will be of value to men who suffer from erectile dysfunction. Patients can be assessed for suitability by a pharmacist and made aware of the risks, situations where supply is not appropriate, and potential interactions with other drugs.

The risks of indirect danger arising from missed diagnosis of underlying disease are minimised through the pharmacist using their professional judgement and the checklist to identify men for whom the product is not suitable and referring them to a doctor.

It is also considered that there is a low risk of direct danger and of intentional abuse that will lead to a danger to human health. Furthermore, these low risks are outweighed by the benefits that this route of supply can bring – by bringing a hard-to-reach group into a healthcare environment with the potential to increase early identification of heart disease and also reduce the risks associated with use of counterfeits obtained via the internet.

8. Further information

The summary of product characteristics and the patient information leaflet are available on the MHRA website: <http://www.mhra.gov.uk/spc-pil/>

The responses to the consultation are published here: <https://www.gov.uk/government/consultations/proposal-to-make-sildenafil-50mg-film-coated-tablets-available-from-pharmacies>
