

Guidance for prescribing phosphodiesterase type-5 (PDE5) inhibitors for erectile dysfunction in primary care

March 2015



DOCUMENT CONTROL

Document Location

Copies of this document can be obtained from:

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Revision History

The latest and master version of this document is held on the Medicines Management SharePoint:

REVISION DATE	ACTIONED BY	SUMMARY OF CHANGES	VERSION
04/12/2014	L Postlethwaite	Initial draft for review by GMMMG	0.1
04/12/2014	A Pracz	Comments	0.2
29/12/2014	L Postlethwaite	Amended	0.3
03/02/2015	A Pracz	Redrafting	0.4
04/03/2015	L Postlethwaite	Amended	0.5
31/03/2015	S Jacobs	Amended	0.6
13/04/2015	A White	Amended	0.7
10/05/2015	S Jacobs	Amended	1.0

Approvals

This document must be approved by the following before distribution:

NAME	TITLE	DATE OF ISSUE	VERSION
Andrew White	Head of medicines optimisation	13/04/2015	0.7

Distribution

This document has been distributed to:

NAME	TITLE	DATE OF ISSUE	VERSION
NWCSU	Medicines Optimisation Team	04/12/2014	0.1
NWCSU	Medicines Optimisation Team	29/12/2014	0.3
GMMMG	GMMMG members	15/04/2015	0.7
GMMMG	GMMMG members	14/05/2015	1.0

Contents

	Page number
Summary of recommendations	4
Introduction	5
1. The guidance on treatment of erectile dysfunction	5
2. Choice of PDE5 inhibitors – availability and drug characteristics	6
3. Prescribing regulations within the NHS	7
4. Patients suffering from severe distress as a result of erectile dysfunction and specialist service referral	8
5. GMMMG recommendation	9
6. References	9



Summary of recommendations

1. Generic sildenafil is no longer subject to selected list scheme (SLS) restrictions. It is therefore available to be prescribed on NHS by primary care clinicians for all men with erectile dysfunction. This does not apply to prescribing of any other phosphodiesterase type-5 (PDE5) inhibitor.
2. Where drug treatment is indicated for erectile dysfunction, generic sildenafil should be used as a first line PDE5 inhibitor at the lowest effective dose.
3. All NHS prescriptions for sildenafil should be prescribed generically.
4. Branded sildenafil (Viagra[®]) should only be prescribed on a private prescription.
5. It is now possible for patients suffering from severe distress due to erectile dysfunction to be prescribed generic sildenafil from their own GP, rather than attend a specialist service.
6. Patients treated for erectile dysfunction with sildenafil on a private basis are now eligible for an NHS prescription and should be no longer prescribed private prescriptions.
7. General practitioners should review patients, currently treated for erectile dysfunction with other PDE5 inhibitors, and consider the opportunity to switch to generic sildenafil.
8. An alternative PDE5 inhibitor can be prescribed **only** for those patients who have no response to generic sildenafil and who meet the criteria set out in the Department of Health (DH) guidance on treatment for impotence (Health Service Circular (HSC) 1999/148 and 177) and Drug Tariff Part XVIII B section.^{1,2,3}
9. PDE5 inhibitors available on the GMMMG formulary, at the time of writing this guidance (April 2015), are sildenafil and avanafil.
10. All NHS prescriptions should be endorsed “SLS” to confirm prescribing of alternative PDE5 inhibitor is within NHS criteria.
11. For NHS patients not meeting the NHS criteria, a private prescription can be provided.
 - Private prescriptions should be provided by the GP with no prescription writing charge.
 - Patients should be informed they will have to pay to have this prescription dispensed.
12. Prescribing products listed in Schedule 2 of the NHS 2004 Regulations (i.e. in-patient, branded erectile dysfunction treatment PDE5 inhibitors) outside the SLS defined circumstances is in breach of the GP contractual terms of service.



Introduction

The purpose of this guidance is to assist clinicians and other healthcare professionals in prescribing of PDE5 inhibitors for the management of erectile dysfunction in line with the current evidence and generic prescribing opportunity, whilst adhering to the new Department of Health (DH) regulations.

There is an opportunity for significant savings that could be generated by ensuring sildenafil is prescribed generically for new and the existing patients suffering with erectile dysfunction.

1. The guidance on treatment of erectile dysfunction

- 1.1. The British Society for Sexual Medicine (BSSM) guidelines on the management of erectile dysfunction state that treatment should involve
 - identifying and treating any curable causes of erectile dysfunction,
 - initiating lifestyle change and risk factor modification and
 - providing education and counseling to patients and their partners.⁴
- 1.2. BSSM guidelines recommend PDE5 inhibitors as first-line pharmacological treatment.⁴
- 1.3. Other treatments such as vacuum erection devices, intracavernous injection therapy, intraurethral or topical alprostadil and penile prosthetics are not discussed in this document.⁴
- 1.4. PDE5 inhibitors have proven efficacy and safety both in non-selected populations of men with erectile dysfunction and in specific sub-groups of patients (e.g. men with diabetes and those who have had a prostatectomy).⁴
- 1.5. NICE has not published a clinical guideline on erectile dysfunction, although several published NICE guidelines do make recommendations around identifying and managing this condition in specific patient groups. See relevant guidance for specific information: <http://www.nice.org.uk>
 - Type 1 diabetes: Diagnosis and management of type 1 diabetes in children, young people and adults (NICE CG15). (N.B. - due to be updated August 2015)
 - Type 2 diabetes: The management of type 2 diabetes (NICE CG87) (N.B.– due to be updated August 2015)
 - MI - Secondary prevention: Secondary prevention in primary and secondary care for patients following a myocardial infarction (NICE CG172).
 - Prostate cancer: diagnosis and treatment (NICE CG175).⁵

2. Choice of PDE5 inhibitors – availability and drug characteristics

2.1. The GMMMG formulary includes sildenafil and avanafil.⁶ Only these two PDE5 inhibitors are compared in this document.

Table 1. Comparison of selected pharmacokinetic and clinical characteristics^{7,8}

	Sildenafil tablets	Avanafil tablets
Maximum frequency	Once daily	Once daily
Time to taken before sexual actual activity	60 minutes	15 – 30 minutes
Time to erection	25 minutes (range 12- 37 minutes)	20 minutes (range 20 – 40 minutes)
Time still able to produce erection post dose	4-5 hours	No data available

2.2. GMMMG only recommends avanafil for those patients who have no response to generic sildenafil and meet 'SLS' criteria, Link: [GMMMG - Avanafil for ED](#)

2.3. The GMMMG Formulary no longer includes tadalafil. The New Therapies subgroup does not recommend the use of tadalafil once daily tablets for erectile dysfunction, Link: [GMMMG - Tadalafil Once Daily for ED](#)

2.4. PDE5 inhibitors have similar side effects, contraindications, precautions in use and drug interactions – see individual SPC for detailed information (<http://www.medicines.org.uk>).

2.5. No data is available from double or triple blind multicentre studies comparing the efficacy of, or men's preference for sildenafil or avanafil.⁹

Table 2. Comparison of cost of treatment of ED with PDE5 inhibitors^{3,10}

PDE5 inhibitor	Price per month based on 4 doses per month
Sildenafil 25mg tablets (generic)	£1.09*
Sildenafil 50mg tablets (generic)	£1.13*
Sildenafil 100mg tablets (generic)	£1.22*
Avanafil 50mg tablets (Spedra®)	£10.49\$
Avanafil 100mg tablets (Spedra®)	£14.08\$
Avanafil 200mg tablets (Spedra®)	£21.90\$
Viagra® 25mg tablets	£16.59*
Viagra® 50mg tablets	£21.27*
Viagra® 100mg tablets	£23.50*
Tadalafil 10mg tablets (Cialis®)	£26.99*
Tadalafil 20mg tablets (Cialis®)	£26.99*
Vardenafil 5mg tablets (Levitra®)	£7.56*
Vardenafil 10mg tablets (Levitra®)	£14.08*
Vardenafil 20mg tablets (Levitra®)	£23.48*

* Drug Tariff, March 2015

\$ BNF 68

PDE5 inhibitor	Price based on once daily dose
Tadalafil 2.5mg tablets (Cialis®)	£54.99*
Tadalafil 5mg tablets (Cialis®)	£54.99*

* Drug Tariff, March 2015

3. Prescribing regulations within NHS

- 3.1. The 1999 DH guidance^{1,11} for treatment of impotence restricted the prescribing to patients meeting specific SLS criteria. In the light of those regulations the prescriber must ensure that patients:
- have diabetes, multiple sclerosis, Parkinson's disease, poliomyelitis, or
 - have had severe pelvic injury, single gene neurological disease, spinal cord injury or spina bifida, or
 - have had prostatectomy, radical pelvic surgery and/or have been treated for prostate cancer (surgery and other treatment), or
 - have renal failure treated by transplant or dialysis, or
 - were receiving Caverject[®], Erecnos[®], MUSE[®], Viagra[®] or Viridal[®], at the expense of the NHS for ED before 14 September 1998 regardless of whether they have one of the above medical conditions or not.
- 3.2. The changes in DH regulations on prescribing for erectile dysfunction were triggered by expiry of the UK Viagra[®] patent in 2013 and availability of cheaper generic sildenafil products. A response to consultation¹² on "[Proposed changes to NHS availability of erectile dysfunction treatments: changing prescribing restrictions for Sildenafil](#)" was published by DH in August 2014. As a result, an amendment to the NHS 2004 regulations on prescribing of drugs¹³ was issued. It removed the statutory prescribing restriction (SLS) for generic sildenafil for the treatment of erectile dysfunction.
- 3.3. The SLS criteria have not changed for branded sildenafil (Viagra[®]), and other PDE5 inhibitors (e.g. avanafil, tadalafil and vardenafil). NHS prescriptions for these items must be endorsed as SLS and patients must meet criteria stipulated in 3.1. NHS prescriptions not marked with SLS will not be dispensed.
- 3.4. For NHS patients not meeting the criteria set out in 3.1 (excluding those prescribed generic sildenafil), a private prescription can be provided. GPs should not charge the patient for writing the private prescription. Repeats can be provided on the form. When a private prescription is written the cost of the medication will be determined by the pharmacy at which it is dispensed. Patients should be informed at point of prescribing that they will have to pay for the drug (retail charge not NHS charge).¹
- 3.5. The DH guidance (HSC 1999/148) previously recommended that one treatment per week (4 doses per month) was appropriate for most patients with erectile dysfunction (based on the research evidence in the 40-60 year age group).⁴ This recommendation can be considered out-dated in light of the new regulations in that it does not apply to generic sildenafil.
- 3.6. GPs are allowed to use their clinical judgement to prescribe more than one treatment per week based on individual patient circumstances.

4. Patients suffering from severe distress as a result of erectile dysfunction and specialist service referral.

- 4.1. The 1999 DH guidance² stated that men suffering severe distress as a result of their erectile dysfunction, who are not eligible for NHS prescriptions from their GP, can receive treatment from specialist services (commissioned and operated under local agreement).
- 4.2. The amendment to the 2004 Regulations overrules the above guidance. In effect, it is now possible for patients suffering from severe distress due to erectile dysfunction to be prescribed generic sildenafil from their own GP, rather than attend a specialist service.
- 4.3. The Royal College of General Practitioners (RCGP) responded to the government consultation¹² to say that most GPs know their patients better than hospital doctors, and are better at assessing their holistic needs. Provision of both appropriate and adequate specialist services has always been problematic. Lifting the restrictions and allowing GPs to prescribe generic sildenafil for men suffering with severe distress caused by impotence will allow primary care clinicians to use their clinical judgement and improve care for many people.
- 4.4. The DH recommends that when determining whether a patient is suffering from severe distress the following criteria should be taken into account.²
 - significant disruption to normal social and occupational activity,
 - marked effect on mood, behaviour, social and environmental awareness,
 - marked effect on interpersonal relationships.
- 4.5. If clinically appropriate, NHS patients previously treated at hospital-based clinics with sildenafil (including those with severe distress as a result of their erectile dysfunction) will be now able to receive treatment from their own GP.
- 4.6. The decision about referral of individual patients for specialist services is a matter for the clinical judgement of the clinician. Referrals to specialist services should not be made purely for the purpose of accessing erectile dysfunction treatment as this may be considered low priority and inappropriate on current pressures around NHS budgets/services.²
- 4.7. If a GP believes a patient may be suffering from erectile dysfunction with complications and considered inappropriate to be managed in primary care, they should refer the patient for assessment and advice as per local specialist service. Reasons for specialist referral may include:⁴
 - Priapism (patients to seek urgent medical advice if erection lasting longer than 4 hours).
 - Lack of response to medical therapies and potential requirement for surgical treatment.
 - Patients diagnosed with erectile dysfunction causing severe psychological distress, who are considered inappropriate for management in primary care or with generic sildenafil.

- Young patients who have always had difficulty in obtaining and/or sustaining an erection.
- Abnormality of the testes or penis is found on examination (including Peyronie's disease).
- History of trauma/surgery (e.g. to genital area, pelvis, or spine).
- Underlying cause of erectile dysfunction suspected to be psychogenic.
- Hypogonadism (abnormal testosterone, follicle-stimulating hormone, luteinizing hormone, or prolactin levels).
- Severe cardiovascular disease that would make sexual activity unsafe or contraindicates PDE5 inhibitor use.

5. GMMMG recommendation

- 5.1. As a result of above discussion GMMMG recommends generic sildenafil first line PDE5 inhibitor for treatment of erectile dysfunction.
- 5.2. Treatment should be initiated with 50mg as a single dose and adjust subsequent doses according to response to 25-100mg as a single dose as needed. The lowest effective dose should be used thereafter.¹⁰
- 5.3. Avanafil can be considered as an option for those patients who have no response to generic sildenafil and meet the 'SLS' requirements.

6. References

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11. Department of Health, NHS Executive Health Service Circular 1999/115, May 1999
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