This policy statement is approved by Halton, Knowsley, Liverpool, Southport and Formby, South Sefton, St Helens, Warrington, Wirral, and West Lancashire CCGs

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PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
FIRST APC BOARD DATE: 25 FEB 2015
LAST APC BOARD DATE: 25 JUL 2018

NHS
Pan Mersey
Area Prescribing Committee

PHOSPHODIESTERASE TYPE-5 INHIBITORS for the treatment of erectile dysfunction

GREEN

The Pan Mersey Area Prescribing Committee recommends generic sildenafil as the first-choice phosphodiesterase type-5 inhibitor for the treatment of erectile dysfunction.

Generic sildenafil has been chosen as the first-line phosphodiesterase type-5 (PDE-5) inhibitor for erectile dysfunction (ED). Where sildenafil is not suitable, the second choice of PDE-5 inhibitor should preferably be one with the least acquisition cost, currently "as required" generic tadalafil (10mg or 20mg). Once daily tadalafil (2.5mg or 5mg) should not be initiated, as per NHS England advice, and prescribers should be supported in deprescribing "once daily" tadalafil.

Restrictions described below on prescribing sildenafil for ED on the NHS have been removed* for generic sildenafil. Branded sildenafil (Viagra®) and all other PDE-5 inhibitors for ED must continue to be prescribed in accordance with National Health Service (General Medical Services Contracts) (Prescription of Drugs etc.) Regulations 2004. This means that GPs may only issue NHS prescriptions (endorsed "SLS") to those men who in their clinical judgement are suffering from erectile dysfunction and who:

- have diabetes, multiple sclerosis, Parkinson's disease, poliomyelitis, prostate cancer, severe pelvic injury, single gene neurological disease, spina bifida, or spinal cord injury
- are receiving dialysis for renal failure
- have had radical pelvic surgery, prostatectomy, or kidney transplant
- were receiving alprostadil (Caverject®, MUSE® Viridal®), moxisylyte (Erecnos®), apomorphine (Uprima®) tadalafil (Cialis®), thymoxamine hydrochloride (Erecnos®) or sildenafil (Viagra®) at the expense of the NHS on 14 September 1998.

The Department of Health advises that one treatment a week will be appropriate for most patients treated for erectile dysfunction.

Sildenafil is available for purchase "over the counter" for ED.

* The National Health Service (General Medical Services Contracts) (Prescription of Drugs etc.) (Amendment) Regulations 2014

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Version: 6.3
Review date: Mar 2022
(or earlier if there is significant new evidence relating to this recommendation)

PHOSPHODIESTERASE TYPE-5 INHIBITORS
for the treatment of erectile dysfunction

EFFECTIVENESS

There is substantial evidence from randomized controlled trials (RCTs) that PDE-5 inhibitors are effective in the treatment of erectile dysfunction.[2-4] The four PDE-5 inhibitors marketed in the UK (avanafil, sildenafil, tadalafil, and vardenafil) are likely to be equally effective, although there is a lack of direct head-to-head RCTs to verify this.

SAFETY

Agents for the treatment of erectile dysfunction should not be used in men for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders such as unstable angina or severe cardiac failure). Visual defects and cases of non-arteritic anterior ischaemic optic neuropathy have been reported in connection with the intake of PDE-5 inhibitors. The patient should be advised that in case of sudden visual defect, he should stop taking the medicine and consult a physician immediately. Prescribers should take account of potential interactions with inhibitors / inducers of cytochrome P450-3A4, 3A5 and 2C enzymes. Concomitant treatment with nicorandil or nitrates and alpha blockers should be avoided. For further information see the electronic medicines compendium (eMC) www.medicines.org.uk/emc[5-8]

COST (4 doses/month) Drug Tariff May 2018[(1)]

Avanafil 50mg (4 tabs) £10.94
100mg (4 tabs) £14.08 (initial dose)
200mg tablets (4 tabs) £21.90
Patent expiry: September 2025

Sildenafil (generic) 25mg (4 tabs) £0.37
50mg (4 tabs) £0.42
100mg (4 tabs) £0.59
Patent expired: June 2013

Tadalafil 10mg (4 tabs) £2.13
20mg (4 tabs) £3.17
Patent expired: November 2017

Vardenafil 5mg (4 tabs) £8.32
10mg (4 tabs) £14.78 (initial dose)
20mg (4 tabs) £24.30
Patent expiry: October 2018

Across the Pan Mersey area the annual spend on sildenafil has fallen by £1.041million since the patent expired (currently £142,000).

PATIENT FACTORS

Several measures are described in the literature to salvage patients, clearly identified as non-responders:

- Counsel again on proper use
- Optimise treatment of concurrent diseases and frequently re-evaluate for new risk factors
- Consider treatment of concurrent hypogonadism.

It is well established that testosterone regulates the expression of PDE-5 and the responsiveness of PDE-5 inhibitors in the corpus cavernosum. Several studies have shown that patients can be salvaged by treating low or low-normal levels of testosterone.
N.B. occasionally patients may respond to one drug when another has failed.

PRESCRIBING INFORMATION

In severe renal impairment (creatinine clearance < 30 mL/min) the lowest dose of sildenafil (25mg) should be considered initially. Based on efficacy and tolerability, the dose may be increased. 10mg is the maximum recommended dose of tadalafil. In severe renal impairment (creatinine clearance < 30 ml/min) avanafil is contraindicated, and a starting dose of 5 mg vardenafil should be considered.

Since clearance is reduced in patients with hepatic impairment (e.g. cirrhosis) the lowest dose of sildenafil (25mg) should be considered. Based on efficacy and toleration, the dose may be increased. The maximum dose of vardenafil recommended in patients with moderate hepatic impairment (Child-Pugh B) is 10 mg. There is limited clinical data on the safety of tadalafil in patients with severe hepatic impairment (Child-Pugh class C); if prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician. There are no available data about the administration of doses higher than 10mg of tadalafil to patients with hepatic impairment. Avanafil is contraindicated in patients with severe hepatic impairment (Child Pugh class C). Patients with mild to moderate hepatic impairment (Child-Pugh class A or B) should initiate treatment with avanafil at the minimum efficacious dose and adjust dose based on tolerance.

IMPLEMENTATION NOTES

Prescribers should be supported in deprescribing “once daily” tadalafil.

REFERENCES

1. NHSBS Drug Tariff, (accessed 02/05/2018).
2. NICE Clinical Knowledge Summary - Erectile dysfunction Dec 2017 (accessed 02/05/2018).
3. British Society for Sexual Medicine. Guidelines on the management of erectile dysfunction 2013. (accessed 02/05/2018).
4. NICE Evidence Summary ESNM45, Erectile dysfunction: avanafil. 2014 (accessed 02/05/2018)
5. SPC Cialis 2.5mg, 5mg, 10mg 20mg (accessed 02/05/2018).
6. SPC Levitra 5mg, 10mg, 20mg (accessed 02/05/2018).
7. SPC Viagra 25mg, 50mg, 100mg (accessed 02/05/2018).
8. SPC Spedra 50mg, 100mg, 200mg (accessed 02/05/2018).