

General Commissioning Policy

Treatment	Tadalafil (Cialis®; Eli Lilly)																
For the treatment of	The signs and symptoms of benign prostatic hyperplasia in adult males.																
Background	Tadalafil is a phosphodiesterase type-5 inhibitor licensed for treatment of erectile dysfunction and also for the management of the signs and symptoms of benign hyperplasia in adult males. It can be prescribed in primary care for erectile dysfunction under restrictive criteria.																
Commissioning position	Tadalafil is not commissioned for the treatment of signs and symptoms of benign prostatic hyperplasia in adult males. There is no evidence to show it to be more effective than the standard treatment for this condition.																
Effective from	September 2016																
Summary of evidence / rationale	<p>NICE TA 273: Tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia. NICE is unable to recommend the use in the NHS of tadalafil for the treatment of symptoms associated with benign prostatic hyperplasia because no evidence submission was received from the manufacturer.</p> <p>NICE Clinical guideline 97: Lower urinary tract symptoms in men. May 2010, updated June 2015.</p> <table border="1"> <thead> <tr> <th>Indication</th> <th>Treatment</th> <th>Review*</th> </tr> </thead> <tbody> <tr> <td>Moderate to severe LUTS</td> <td>Offer an alpha blocker (alfuzosin, doxazosin, tamsulosin or terazosin)</td> <td>● At 4–6 weeks, then every 6-12 months.</td> </tr> <tr> <td>OAB</td> <td>Offer an anticholinergic</td> <td>● At 4–6 weeks until stable, then every 6-12 months</td> </tr> <tr> <td>LUTS and a prostate estimated to be larger than 30 g or PSA greater than 1.4 ng/ml</td> <td>Consider an alpha blocker plus a 5-alpha reductase inhibitor</td> <td>● At 4–6 weeks, then every 6–12 months for the alpha blocker ● At 3–6 months, then every 6–12 months for the 5-alpha reductase inhibitor</td> </tr> <tr> <td>Storage symptoms despite treatment with an alpha blocker alone</td> <td>Consider adding an anticholinergic</td> <td>● At 4–6 weeks until stable, then every 6-12 months.</td> </tr> </tbody> </table> <p>* Review to assess symptoms and the effect of the drugs on the man's quality of life, and to ask about any adverse effects.</p> <p>SMC: tadalafil 5mg film coated tablets; December 2012 In the absence of a submission from the manufacturer, tadalafil is not recommended for use within NHS Scotland.</p>		Indication	Treatment	Review*	Moderate to severe LUTS	Offer an alpha blocker (alfuzosin, doxazosin, tamsulosin or terazosin)	● At 4–6 weeks, then every 6-12 months.	OAB	Offer an anticholinergic	● At 4–6 weeks until stable, then every 6-12 months	LUTS and a prostate estimated to be larger than 30 g or PSA greater than 1.4 ng/ml	Consider an alpha blocker plus a 5-alpha reductase inhibitor	● At 4–6 weeks, then every 6–12 months for the alpha blocker ● At 3–6 months, then every 6–12 months for the 5-alpha reductase inhibitor	Storage symptoms despite treatment with an alpha blocker alone	Consider adding an anticholinergic	● At 4–6 weeks until stable, then every 6-12 months.
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Notes

1. This Policy will be reviewed in the light of new evidence, or guidance from NICE.
2. General Commissioning Policies are agreed by the Planning and Commissioning Committee on behalf of NHS Hull CCG.

Clinical Evidence

Efficacy and safety of tadalafil once daily in the treatment of men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: results of an international randomised, double-blind, placebo-controlled trial

**Eur Urol.2011 Nov; 60(5): 1105-13
Porst H et al.**

This was a randomised, double blind, placebo-controlled trial to assess the efficacy and safety of tadalafil on treatment of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (BPH-LUTs). Patients were randomised to either tadalafil 5mg (n=161) or placebo (n=164) once daily and continued for 12 weeks. Men were aged ≥ 45 years of age with BPH-LUTS for more than 6 months, International prostate symptom score (IPSS) ≥ 13 , and maximum urine flow rate ≥ 4 to ≤ 15 ml/s.

Tadalafil improved IPSS results, from baseline to endpoint, compared to placebo (-5.6 vs -3.6; p=0.004). The BPH impact index improvement was apparent at 4 weeks and continued at 12 weeks (tadalafil -1.8 vs placebo -1.3; p=0.057). The main adverse events reported for tadalafil were headache (3.7%) and back pain (3.1%).

Monotherapy with tadalafil or tamsulosin similarly improved lower urinary tract symptoms suggestive of benign prostatic hyperplasia in an international, randomised, parallel, placebo-controlled clinical trial.

**Eur Urol. 2012 May; 61 (5): 917-25.
Oelke M et al.**

This was a randomised, double blind, placebo-controlled, parallel-group study that evaluated tadalafil or tamsulosin versus placebo in the treatment of LUTS/BPH. Eligible men were ≥ 45 years of age who had LUTS/BPH > 6 months and with IPSS ≥ 13 and maximum urinary flow rate (Qmax) ≥ 4 to ≤ 15 ml. The efficacy measures included were IPSS (Primary measure), BPH impact index and international index of erectile function-erectile function domain. Following a 4 week placebo run-in, patients were randomised to placebo (172), tadalafil 5mg (n=171), or tamsulosin 0.4mg (n=168) once daily for 12 weeks.

IPSS was significantly improved versus placebo at week 12 with tadalafil (-2.1+/-0.6; CI -3.3 to -0.8; p=0.001) and tamsulosin (-1.5 +/-0.6; CI -2.8 to -0.2; p=0.023). BPH impact index significantly improved versus placebo at week 12 (tadalafil -0.8; CI -1.3 to -0.3; p=0.003, and tamsulosin -0.6; CI -1.1 to -0.1; p=0.026). The international index of erectile function-erectile function domain improved versus placebo with tadalafil (4; p<0.001) but not tamsulosin 9-0.4; p=0.699). Adverse events were similar between the groups with the most common with tadalafil being headache, nasopharyngitis, back pain and dizziness.

It should be noted that this study was not powered to assess noninferiority or superiority between tadalafil and tamsulosin. It concluded that monotherapy or tamsulosin resulted in significant and numerically similar improvements versus placebo in LUTs/BPH and Qmax. However only tadalafil improved erectile function.

Tadalafil relieves lower urinary tract symptoms secondary to benign prostatic hyperplasia.

	<p>McVary KT et al. J Urol. 2007 Apr; 177(4):1401-7</p> <p>This study was to assess the efficacy and safety of tadalafil once daily for urinary tract symptoms secondary prostatic hyperplasia. Following a 4 week, single blind, placebo run-in 281 men were randomly assigned (1:1) to 5mg tadalafil for 6 weeks, followed by dose escalation to 20mg for 6 weeks or 12 weeks of placebo.</p> <p>Tadalafil significantly improved the mean change from baseline in IPSS at 6 weeks (5mg tadalafil -2.8 vs placebo -1.2) and at 12 weeks (5/20mg tadalafil -3.8 vs placebo -1.7). Significant improvements were also seen in the IPSS irritative and obstructive domains, the IPSS quality of life index, a question about urinary symptom improvement and the benign Prostatic hyperplasia impact index (significant at 12 weeks) vs placebo. International Prostate symptom score and international index of erectile function domain scores significantly improved in the 56% of men with lower urinary tract symptoms/ benign prostatic hyperplasia who were sexually active and had erectile dysfunction. Changes in uroflowmetry parameters were similar in the placebo and tadalafil groups. Commonly reported side effects were dyspepsia, back pain, headache, nasopharyngitis and upper respiratory tract infections. No change in post-void residual volume was seen with tadalafil.</p> <p>Points for consideration</p> <ul style="list-style-type: none"> • Evidence shows that tadalafil may improve lower urinary tract symptoms associated with benign prostatic hyperplasia but is no more effective than the standard treatments recommended by NICE for this indication. • It is unlikely that this treatment would be shown to be cost effective compared to standard treatment such as alpha blockers and 5-alpha reductase inhibitors. • Tadalafil may be beneficial in patients who suffer from both benign prostatic hypertrophy and erectile dysfunction. • Drug treatments for the management of erectile dysfunction can be provided on the NHS for the following conditions: diabetes, multiple sclerosis, Parkinson's disease, poliomyelitis, prostate cancer, prostatectomy, radical pelvic surgery, renal failure treated by dialysis or transplant, severe pelvic injury, single gene neurological disease, spinal cord injury, spina bifida (Ref HSC 1999/148. <p>NICE CG97 (2015) Management of lower urinary tract symptoms in men states "Do not offer phosphodiesterase 5 inhibitors solely for the purpose of treating lower urinary tract symptoms in men, except as part of a randomised controlled trial."</p>
Date	May 2017
Policy to be reviewed by	May 2019
Contact for this policy	Karen Billany, Head of Acute Care, NHS Hull CCG karen.billany@nhs.net