NHS
Vale of York
Clinical Commissioning Group

COMMISSIONING POLICY RECOMMENDATION
TREATMENT ADVISORY GROUP
Policy agreed by (Vale of York CCG/date)

Drug, Treatment, Device name		
Tadalafil (Cialis; Eli Lilly)		
Licensed indication		
Treatment of the signs and symptoms of benign prostatic hyperplasia in adult males.		
Cost per patient (at recommended dose)		
Drug	Dose	Cost for 28 days treatment
Tadalafil	5mg daily	£54.99
Tamsulosin MR	400mcg daily	£5.16
Alfuzosin	2.5mg TDS	£10.05
Finasteride	5mg daily	£1.69
Resource impact on population		
Recommendation to Routinely Commission **OR** **Not Routinely Commission** **OR** **Commission under criteria**		
When is funding appropriate?		
Tadalafil is not recommended 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.		
Clinical and cost effectiveness evidence		

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.

NICE Clinical guideline 97: Lower urinary tract symptoms in men. May 2010.

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.
* Review to assess symptoms and the effect of the drugs on the man's quality of life, and to ask about any adverse effects.		

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.

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 randmonised, 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 ≤ 15ml/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 ≤ 15ml. 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 9n=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 tadalaf8il and tamsulosin.
It concluded that monotherapy or tamsulosin resulted in significant and numerically similar improvements versus placeboin LUTs/BPH and Qmax. However only tadalafil improved erectile function.

Tadalafil relieves lower urinary tract symptoms secondary to benign prostatic hyperplasia.
McVary KT et al.
J Urol. 2007 Apr; 177(4):1401-7
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.
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.

Points for consideration

- 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.

Place in therapy relative to available treatments
Health gains
This treatment would have the potential of improving symptoms of benign prostatic hypertrophy and treating erectile dysfunction in appropriate patients.
Patient safety / pharmacovigilance
• Avoid in patients with significant history of cardiovascular disease • When used in combination with nitratesit has been shown to augment the hypotensive effect. • Stop treatment if sudden loss in vision. • Monitor for other adverse effects.
When to stop treatment
Who prescribes?
Stakeholder views
Equity of access

SPECIFICATION DATE, REVIEW DATE, AND LEAD NAME/JOB TITLE	
Origin Date: April 2013	Originator:
TAG Review Date:	Reviewer: Christopher Ranson, Senior Pharmacist
TAG Recommendation Date: 8th April 2013	

Impact on individual clinical commissioning groups

CCG	Population	Cost Impact
York	337,500	
HaRD	160,100	
Scarborough	118000	
H&R	141,600	
East Riding	320,642	
Hull	295,987	
North Lincs	168,400	
North East Lincs	167,200	