

## Northern (NHS) Treatment Advisory Group

### Treatment Appraisal: Decision Summary

<b>Date</b>	7 <sup>th</sup> September 2021
<b>Appraisal &amp; Details</b>	<p>The Northern (NHS) Treatment Advisory Group considered an re-appraisal of <b>Daily vs on-demand phosphodiesterase-5 (PDE-5) inhibitors for the management of erectile dysfunction following treatment for prostate cancer.</b></p>
<b>Recommendation</b>	<p><b>The Northern (NHS) Treatment Advisory Group recommends that once daily oral 5mg tadalafil may be considered as an option for the management of erectile dysfunction following treatment for prostate cancer.</b></p> <p><b>Oral 2.5mg tadalafil is not recommended by NTAG for this indication on the basis of cost.</b></p> <p>This recommendation was made due to fall in price in tadalafil 5mg tablets since the NTAG last reviewed this in March 2018, and since the use of once daily tadalafil was included in 2017 by NHSE in their Items which should not routinely be prescribed in primary care: Guidance for CCGs.</p> <p>NICE guidelines for prostate cancer recommend that men should have early and ongoing access to specialist erectile dysfunction (ED) services. The guidelines recommend that men with prostate cancer who experience ED (after radical treatment including radical prostatectomy) should be offered a PDE5-i as the first line treatment to improve the chance of a spontaneous erection. However, NICE do not suggest which PDE5-i to choose, which dosing regimen(s) to use or when to start the PDE5-i after surgery.</p>
<b>Clinical evidence summary</b>	<p>There are four oral PDE5 inhibitors licensed for treatment of ED in the UK; sildenafil, tadalafil, vardenafil, or avanafil. Sildenafil, tadalafil and vardenafil are available as generics, while avanafil (Spedra®, Menarini) is still under patent. All four PDE5I's have been used as supportive therapy to rehabilitate erectile function (EF) successfully post-radical prostatectomy.</p> <p>There is limited and conflicting evidence to demonstrate improved outcomes with daily dosing compared to on-demand treatment regimens. Six systematic reviews (with extensive overlap in included trials) and one additional double-blind RCT provide evidence in men who have undergone radical prostatectomy.</p> <p>Both regular (daily or three-times a week) and on-demand (prior to sexual activity) doses were effective but the studies are not designed well enough to draw firm conclusions which regimens offer the best treatment outcomes. There are no specific recommendations within available guidelines on which regimen(s) to choose.</p> <p>A Q&amp;A prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals was published in May 2019 entitled "What rationale, guidance and evidence is there for the use of phosphodiesterase-5 inhibitors as supportive therapy to rehabilitate Erectile Function after nerve sparing radical prostatectomy?"</p>

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<b>Safety</b>	<p>Adverse effects reported in this patient population were in line with the known adverse drug reaction profile of the PDE5 inhibitors, and included flushing, headache, nasal congestion and dyspepsia. No new safety concerns were identified.</p>
<b>Patient Perspective</b>	<p>Erectile dysfunction (ED) is extremely common following treatment for prostate cancer, since the available treatments (radical prostatectomy, androgen deprivation therapy, radiotherapy) can cause physical trauma, vascular changes and endocrine changes, all of which can have a negative impact on erectile function.</p> <p>Standard management for ED involves prescription of PDE5 inhibitors such as sildenafil or tadalafil. These treatments are effective in men with ED due to treatment for prostate cancer, but there is some debate as to the most appropriate treatment regimen. UK clinical practice guidelines recommend either once daily or on-demand PDE5 inhibitors, or some combination of the two. There is limited evidence comparing daily and on-demand treatment regimens.</p>
<b>Cost analysis summary</b>	<p>Since generics of once daily 5mg tadalafil became available the cost has fallen from £715 per patient per annum in 2017 to £50.57 per patient per annum currently based on August 2021 Drug Tariff. (Note: 2.5mg daily tadalafil = £253 per patient per annum currently)</p> <p>For comparison:</p> <p>Sildenafil 25mg to 100mg weekly = £13 to £15 per patient per annum  Sildenafil 25mg to 100mg twice weekly = £25 to £30 per patient per annum  Sildenafil 25mg to 100mg daily = £89 to £106 per patient per annum  Tadalafil (generic) 10mg to 20mg weekly = £16 to £20 per patient per annum  Tadalafil (generic) 10mg to 20mg twice weekly = £33 to £40 per patient per annum  Tadalafil (generic) 10mg to 20mg three x week = £49 to £60 per patient per annum</p> <p>So tadalafil 5mg daily is cost-effective if using tadalafil prn dosing three times a week or more (12 x a month) and because cost effective against sildenafil if using sildenafil 25mg – 100mg four times a a week or more (16 x a month).</p> <p>Generic tadalafil 5 mg now costs approximately £3.89 per month based on August 2021 NHS Drug Tariff.</p>
<b>Financial impact</b>  <b>PbR: NA</b>	<p>Tadalafil 5mg once daily is now comparable in price to sildenafil alternate days, which is currently used post-prostatectomy by some consultants in NENC. (£3.89 per month vs £3.50 to £4.06 per month).</p> <p>Estimates for the number of men treated in the NTAG region each year are not available. Cancer Research UK estimates that the crude rate of prostate cancer in the UK is 149.2 per 100,000. The NTAG region has a population of around 1.45 million men, so around 2165 new cases of prostate cancer would be expected each year. Cancer Research UK further estimates that around 15% of patients have surgery to remove prostate tumours, while a further 32% have radiotherapy as part of their primary treatment.</p>