

**South East London Area Prescribing Committee  
Formulary recommendation**

<b>Reference</b>	<b>063</b>
<b>Intervention:</b>	<b>Pitolisant hydrochloride (Wakix<sup>®</sup>) for the treatment of narcolepsy with or without cataplexy in adults</b> (Pitolisant increases wakefulness and alertness by activating specific neurones in the brain)
<b>Date of Decision</b>	<b>February 2017, updated May 2019</b>
<b>Date of Issue:</b>	<b>March 2017, re-issued June 2019</b>
<b>Recommendation:</b>	<b>RED – suitable for prescribing and supply by the specialist Sleep Centre at Guy's and St. Thomas' NHS Foundation Trust (GSTfT) only</b>
<b>Further Information</b>	<ul style="list-style-type: none"> <li>• This recommendation has been updated following presentation of a report by the Sleep Centre summarising outcomes with pitolisant over a year, which was requested by the APC as part of the original formulary approval.</li> <li>• Narcolepsy is a long term disorder where brain is unable to regulate sleeping and waking patterns normally. The main characteristic is overwhelming daytime sleepiness so that the patient is unable to stay awake for &gt;3 hours. The condition may be accompanied by cataplexy, which occurs in approximately 50% of patients.</li> <li>• Medication may be considered in patients with an excessive daytime sleepiness score (ESS) of &gt;12/24.</li> <li>• The first line agent used to treat narcolepsy is modafinil at a dose of 100-400mg daily for 3 months.</li> <li>• If this fails to show improvement, the 2<sup>nd</sup> line treatment options are either methylphenidate <b>or</b> dexamfetamine.</li> <li>• Where 2<sup>nd</sup> line agent fails, the alternative agent may be tried as a 3<sup>rd</sup> line option.</li> <li>• The Sleep Centre at GSTfT reviews patients at 3 months at each step of therapy to assess treatment effectiveness.</li> <li>• Pitolisant is only supported for the treatment of narcolepsy with or without cataplexy as a <b>last line treatment option</b> where the treatment steps outlined above have failed.</li> <li>• The other treatment option on the formulary for the Sleep Centre at GSTfT for the treatment of narcolepsy is sodium oxybate which is a last line option for patients only when cataplexy is also present.</li> <li>• Whilst the evidence base for pitolisant is stronger in the single agent setting, the outcomes report presented demonstrated that some patients will need combination treatment to adequately control their symptoms. In these cases every effort will be made by the Sleep Centre specialists to taper and eventually stop the other agents.</li> <li>• Response to treatment will include measuring improvements in the ESS score. A clinically significant change in ESS is defined as an improvement of at least 3 points.</li> <li>• As of April 2019, pitolisant has been designated as a high cost drug excluded from the national tariff. Treatment for patients in line with this formulary recommendation may be billed to Commissioners. A B* notification form will need to be completed and submitted to commissioners for each patient in order for the cost of the medicine to be reimbursed to the Trust.</li> <li>• All prescribing and supply of pitolisant will be carried out by the Sleep Centre.</li> </ul> <p><b>Note:</b> Pitolisant is a black triangle medicine (▼) i.e. as it is a new medicine, it is under additional monitoring to allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to the MHRA via the Yellow Card scheme.</p>
<b>Shared Care/ Transfer of care required:</b>	N/A

<b>Cost Impact for agreed patient group</b>	<ul style="list-style-type: none"> <li>• The Sleep Centre at GSTfT estimates 20 to 25 people will be eligible for treatment with pitolisant each year. Approximately a third of these will be from SEL.</li> <li>• Treatment with pitolisant costs ~ £3,720 to £7,440 per patient per year (depending on dosage).</li> <li>• The outcomes report presented to the Committee suggests a 50% response rate at 3 months.</li> <li>• If it is estimated there may be ~9 people eligible for treatment with pitolisant per year in SEL and 50% stop after 3 months, this equates to medicines related cost across SEL of up to ~£42,000 per year.</li> </ul>
<b>Usage Monitoring &amp; Impact Assessment</b>	<p><b>Acute Trusts:</b></p> <ul style="list-style-type: none"> <li>• Monitor use and report back to APC when required.</li> <li>• Audit use upon request to ensure use is in line with this recommendation.</li> </ul> <p><b>CCGs:</b></p> <ul style="list-style-type: none"> <li>• Monitor E pact 2 data and monthly high cost drugs invoicing submitted to the CSU.</li> <li>• Monitor reports from GP practices where transfer of prescribing to primary care is requested.</li> </ul>
<b>Evidence reviewed</b>	<p><b>References (from evidence review)</b></p> <ol style="list-style-type: none"> <li>1. American Academy of Sleep Medicine 2014. International classification of sleep disorders: diagnostic and coding manual 3rd edition.</li> <li>2. Ohayon M, Priest R, Zulley J et al. Prevalence of narcolepsy symptomology and diagnosis in the European general population. <i>Neurology</i> 2002, 58 (12) p1826-1833</li> <li>3. Unmet needs of patients with narcolepsy: perspectives on emerging treatment options.</li> <li>4. Overeem S, Mignot E, van Dijk JG, Lammers GJ, Narcolepsy: clinical feature, new pathophysiologic insights, and future perspectives. <i>J Clin Neurophysiol</i>, 2001;18(2):78-105</li> <li>5. Nishino S, Sakurai E, Nevsimalova S, et al. Decreased CSF histamine in narcolepsy with and without low CSF hypocretin-1 in comparison to healthy controls. <i>Sleep</i>. 2009;32(2):175-180</li> <li>6. Dr M Johns, The official website of the Epworth Sleepiness scale (ESS), <a href="http://epworthsleepinessscale.com/about-the-ess/">http://epworthsleepinessscale.com/about-the-ess/</a></li> <li>7. Summary of Product Characteristics, Wakix 4.5 mg / 18mg film-coated tablets (last updated on eMC 30-Sep-2016) Lincoln Medical Limited. Accessed via <a href="http://www.medicines.org.uk/emc">www.medicines.org.uk/emc</a> on 21/11/16</li> <li>8. Morgenthaler T, Kapur V, Brown T et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin – and American Academy of Sleep Medicine Report. <i>Sleep</i> 2007 30 (12) p1705-1711.</li> <li>9. Golicki D, Bala M, Niewada M et al. Modafinil for narcolepsy: systematic review and meta-analysis. <i>Medical Science Monitor</i> 2010 16 (8) p177-186</li> <li>10. Summary of product characteristic, Modafinil 100 mg Tablets (last updated on eMC 02-Nov-2016) Generics UK T/A Mylan, accessed via <a href="http://www.medicines.org.uk/emc">www.medicines.org.uk/emc</a> on 21/11/16</li> <li>11. European Medicines Agency, Wakix Assessment report, 2015</li> <li>12. Y Dauvilliers, C Bassetti, GJ Lammers et al, Pitolisant versus placebo or modafinil in patients with narcolepsy: a double-blind, randomised trial, <i>Lancet Neurol</i> 2013; 12:1068-75.</li> <li>13. Dauvilliers Y.; Arnulf I.; Szakacs Z et al, Long term use of pitolisant to treat narcolepsy: HARMONY III study <i>Journal of Sleep Research</i>; 2016; 25:275</li> <li>14. Dauvilliers Y.; Szakacs Z.; Lehert P et al, Efficacy of pitolisant on cataplexy: A double blind, randomised, placebo controlled trial in patients with narcolepsy (the HARMONY-CTP trial), <i>Journal of Sleep Research</i>; 2016; 25:255</li> </ol>

**NOTES:**

- a) Area Prescribing Committee recommendations and minutes are available publicly on the APC website.
- b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
- c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS.**