**South East London Integrated Medicines Optimisation Committee**
**Formulary recommendation**

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| **Reference** | **138** |
| **Intervention:** | **Pitolisant hydrochloride (Wakix™) for the treatment of cataplexy in adult patients with type 1 narcolepsy**<br>(Pitolisant increases wakefulness and alertness by activating specific neurons in the brain) |
| **Date of Decision** | **August 2022, updated December 2023 following report on outcomes data - time limit to approval removed** |
| **Date of Issue:** | **November 2022 (time limited approval for 12 months), re-issued January 2024** |
| **Recommendation:** | **RED – suitable for prescribing and supply by the specialist Sleep Centre at Guy's and St. Thomas' NHS Foundation Trust (GSTfT) only** |
| **Further Information** | • Narcolepsy is a rare, disabling long-term brain disorder characterised by excessive sleepiness and abnormal rapid eye movement (REM) sleep manifestations. Patients with type 1 narcolepsy additionally suffer from cataplexy which is a sudden muscle weakness or hypotonia that occurs while a person is awake in response to a strong emotion.<br>• Pitolisant is only supported for the treatment of cataplexy in adult patients with type 1 narcolepsy as a **second or third line treatment option** where first or second line treatments have failed or are not well tolerated.<br>• The first line agents used to treat cataplexy associated with type 1 narcolepsy are clomipramine 10-75mg at night or venlafaxine 75mg – 150mg in the morning or in two divided doses for 3 - 6 months.<br>• For patients with a co-morbidity which would benefit from a serotonin selective reuptake inhibitor (SSRI) e.g. neuropathic pain, fluoxetine can be trialed as a second line agent if clomipramine or venlafaxine is not tolerated or effective.<br>• Without the presence of a co-morbidity, pitolisant or sodium oxybate can be trialed if clomipramine or venlafaxine is not tolerated or effective.<br>• The Sleep Centre at GSTfT reviews patients at 3 – 6 months at each step of therapy to assess treatment effectiveness.<br>• The other **second or third line** treatment option on the formulary for the Sleep Centre at GSTfT for the treatment of cataplexy in adult patients with type 1 narcolepsy is sodium oxybate.<br>• Use of pitolisant in this setting should be in line with the local treatment pathway.<br>• Response to treatment is individualised and will include the review of the:<br>- number of cataplexy events per week<br>- cause of cataplexy events - spontaneous or triggered<br>- type of cataplexy event – partial or generalised<br>- personal patient circumstances that might affect cataplexy<br>- safety concerns linked to cataplexy which may justify the indication of trialing alternative treatment<br>• All prescribing and supply of pitolisant will be carried out by the Sleep Centre at GSTfT.<br>• Pitolisant has been designated as a high-cost drug excluded from the national tariff. Treatment with pitolisant is agreed in line with this formulary recommendation.<br>• **December 2023:** A report summarising outcomes with the use of pitolisant in this setting was requested by the Committee after 12 months outlining the total number of patients initiated on treatment, outcomes, and safety data. The outcome data indicated numbers treated were less than expected. Patients treated reported improved quality of life and less cataplexic events with pitolisant, which ultimately led to fewer or no occurrences of cataplexy related injuries. |

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| **Shared Care/ Transfer of care required:** | N/A |
| **Cost Impact for agreed patient group** | • The Sleep Centre at GSTfT estimates 15 to 20 patients will be eligible for treatment with pitolisant in this setting each year. Approximately 25-30% of these patients will be from SEL (up to 6 patients per year in SEL).<br>• Treatment with pitolisant costs ~ £4,000 to £8,000 per patient per year (depending on dosage). For SEL, this equates to ~£40,000 - £60,000 per annum (~ £2,105 - £3,158 per 100,000 population).<br>• As pitolisant has a lower treatment cost vs. the current second line option of sodium oxybate, use of pitolisant may result in an overall lower cost impact in this setting.<br>• A report presented in December 2023 found the numbers treated was less than expected, over the 12 month period, 2 patients in SEL were treated vs. the 6 that were originally estimated for SEL. The cost impact is therefore lower than original estimates. |
| **Usage Monitoring & Impact Assessment** | **Acute Trusts:**<br>• Monitor and audit usage of pitolisant as outlined in the "For information" section and report back to the Committee upon request of the Committee. |
| | **SEL Borough Medicines Teams:**<br>• Monitor exception reports from GPs if inappropriate prescribing requests are made to primary care |
| **Evidence reviewed** | **References (from evidence review)**<br>1. Scammell, T., 2015. Narcolepsy. New England Journal of Medicine, [online] 373(27), pp.2654-2662. Available here [Accessed 15 June 2022]<br>2. Sleepfoundation.org. 2022. Cataplexy: Causes, Symptoms, and Treatment \| Sleep Foundation. Available here [Accessed 17 June 2022]<br>3. Uptodate.com. 2022. Clinical features and diagnosis of narcolepsy in adults. Available here [Accessed 17 June 2022]<br>4. Medicines.org.uk. 2021. Wakix 4.5 mg / 18mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc). Available here [Accessed 15 June 2022]<br>5. Bassetti, C., Kallweit, U., Vignatelli, L., Plazzi, G., Lecendreux, M., Baldin, E., Dolenc-Groselj, L., Jennum, P., Khatami, R., Manconi, M., Mayer, G., Partinen, M., Pollmächer, T., Reading, P., Santamaria, J., Sonka, K., Dauvilliers, Y. and Lammers, G., 2021. European guideline and expert statements on the management of narcolepsy in adults and children. European journal of Neurology. Available here [Accessed 17 June 2022]<br>6. Ema.europa.eu. 2015. Assessment report Wakix. Available here [Accessed 1 August 2022]<br>7. Dauvilliers, Y., Bassetti, C., Lammers, G., Arnulf, I., Mayer, G., Rodenbeck, A., Lehert, P., Ding, C., Lecomte, J. and Schwartz, J.2013. Pitolisant versus placebo or modafinil in patients with narcolepsy: a double-blind, randomised trial. The Lancet Neurology, 12(11), pp.1068-1075.<br>8. Szakacs, Z., Dauvilliers, Y., Lecomte, I., Lecomte, J. and Schwartz, J., 2017. Pitolisant efficacy on cataplexy: a double blind, randomised, placebo controlled trial in patients with narcolepsy (the HARMONY-CTP trial). Sleep Medicine, 40, p.e322.<br>9. European Medicines Agency. 2016. Wakix - European Medicines Agency. Available here [Accessed 17 June 2022]<br>10. Nice.org.uk. 2017. Evidence review \| Narcolepsy with or without cataplexy in adults: pitolisant \| Advice \| NICE. Available here [Accessed 17 June 2022] |

**NOTES:**

a) SEL IMOC recommendations and minutes are available publicly via the website.

b) This SEL IMOC 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**