South East London Integrated Medicines Optimisation Committee
Formulary recommendation

Reference	**126**
Intervention:	**Pitolisant hydrochloride to improve wakefulness and reduce excessive daytime sleepiness in adult patients with idiopathic hypersomnia** (Pitolisant increases wakefulness and alertness by activating specific neurones in the brain)
Date of Decision	**June 2021. Updated September 2022 following report on outcome data and removal of time limit**
Date of Issue:	**July 2021. Re-issued September 2022**
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:	• Idiopathic hypersomnia is a primary disorder of hypersomnolence that is distinguished from narcolepsy by virtue of the absence of electrophysiologic and other features of rapid eye-movement sleep disturbance. • It has a prevalence of 20 to 50 per million population, which makes it about 10 times less common than narcolepsy. • The treatment pathway is similar to that for narcolepsy. Medication may be considered in patients with an excessive daytime sleepiness score (ESS) of >12/24 • Pitolisant is accepted for use in SEL as a **last line** treatment option in patients with idiopathic hypersomnia under the specialist sleep centre service at GSTfT. • Pitolisant may be considered where: i. patients with idiopathic hypersomnia remain symptomatic despite optimisation of the following existing approved formulary options: modafinil, methylphenidate and dexamfetamine, or ii. in patients in whom these formulary approved options are not tolerated or contraindicated. • The first line agent used to treat idiopathic hypersomnia is modafinil at a dose of 100-400mg daily for 3 months. • If this fails to show improvement, the 2nd line treatment options are either methylphenidate **or** dexamfetamine. • Where 2nd line agent fails, the alternative agent may be tried as a 3rd line option. • The Sleep Centre at GSTfT reviews patients at 3 months at each step of therapy to assess treatment effectiveness. • Response to treatment with pitolisant will be measured through the following outcomes: - Reduction in Epworth Sleepiness Scale (ESS) – a clinically significant improvement is an improvement in ESS of 3 points or more. - Improvement in EuroQol-5D-3L - Improvement in EQ-VAS score - Reported 24-hour sleep duration through sleep diary/actigraphy and ESS • All prescribing and supply of pitolisant will be carried out by the Sleep Centre at GSTfT. • Pitolisant has been designated as a high-cost drug excluded from the national tariff. Treatment with pitolisant is commissioned in line with this formulary recommendation • **September 2022:** In line with the original formulary recommendation issued in July 2021, a report back to the Committee was requested after 12 months of use outlining the number of patients who continued treatment and the outcomes and safety data. This was reported back in August 2022, the outcomes data available indicated improvements in Epworth Sleepiness Scale and no safety concerns. • It should be noted that pitolisant is **not licensed** for use in this setting. Informed consent should be gained from the patient before treatment is started.

Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	• The evidence review estimates that idiopathic hypersomnia has a significantly lower prevalence than narcolepsy. • Original estimates during the application stage suggested a maximum of 20 patients might be suitable for treatment per annum, with 25% coming from SE London (5 patients). • However, experts from the Sleep Centre expect that in reality the patient number will be much lower – around 5 patients per year (1 patient per year for SEL). • Based on this estimate, it is anticipated that after 3 years costs would be £12,500 to £17,500 per annum for SE London (or up to ~£1,000 per 100,000 population).
Usage Monitoring & Impact Assessment	**Acute Trusts:** • Monitor use and report back on the information requested as part of the 1-year time limited approval no later than **July 2022**. • The service may be requested by the SEL IMOC to provide clinical audit data to demonstrate outcomes from pitolisant and compliance with the criteria in this recommendation.
	SEL Borough Medicines Optimisation Teams: • Monitor exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	**References (from evidence evaluation)** 1. Ali M, Auger R, Slocumb N et al. Idiopathic Hypersomnia: clinical features and response to treatment. Journal of Clinical Sleep Medicine 2009 5 p562-568 2. Khan Z, Trotti L. Central Disorders of Hypersomnolence – focus on the narcolepsies and idiopathic hypersomnia. Chest July 2015 148 (1) p262-273. 3. Idiopathic Hypersomnia. Uptodate clinical resource. Available online at: https://www.uptodate.com/contents/idiopathic-hypersomnia#H2521197907 (accessed 04/06/2021). 4. Ohayon M, Priest R, Zulley J et al. Prevalence of narcolepsy symptomatology and diagnosis in the European general population. Neurology 2002, 58 (12) p1826-1833 5. European Medicines Agency 2011: Assessment report for modafinil containing medicinal products. Available online at: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Modafinil_31/WC500105597.pdf <accessed 01.06.2021> 6. Morgenthalter T, Kapur V, Brown T et al. Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of Central Origin. Sleep 2007 30 (12) p1705-1711. 7. Wakix (pitolisant), Summary of Product Characteristics. Available online at: https://www.medicines.org.uk/emc/product/7402 (accessed 04/06/2021). 8. Leu-Semenescu S, Nittur N, Golmard J et al. Effects of pitolisant, a histamine H3 inverse agonist, in drug-resistant idiopathic and symptomatic hypersomnia: a chart review. Sleep Medicine 2014 15 (6) p681–7. 9. Schinkelshoek M, Fronczek R, Lammers G et al. Update on the treatment of idiopathic hypersomnia. Current Sleep Medicine reports 2019 5 p207-214. 10. Pitolisant for narcolepsy. Drug and Therapeutics Bulletin 2017 55 (1) 6-8.

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.