South East London Area Prescribing Committee
Formulary recommendation

Reference	**091**
Intervention:	**Sodium oxybate and agomelatine as last line options for the management of REM behaviour disorder in adults** (Sodium oxybate is a central nervous system depressant and agomelatine is a melatonin receptor agonist and a selective serotonin-receptor antagonist)
Date of Decision	**July 2018**
Date of Issue:	**August 2018**
Recommendation:	**RED – Prescribing and supply by hospital only**
Further Information	• Sodium oxybate and agomelatine are accepted as **last line monotherapy treatment options** for the management of REM behaviour disorder in adults where other treatments (as outlined in the local pathway have failed/are not tolerated. • The decision on choice of agent will be made by the sleep specialist taking into account individual patient factors, such as symptoms. • Treatment will be initiated, monitored and prescribed by the sleep service. The service will regularly review patients for ongoing effectiveness of treatment. • It should be noted that these agents are not licensed for use in REM Behaviour Disorder. Informed consent should be gained from the patient before treatment is started. • Sodium oxybate is a tariff excluded, CCG commissioned medicine for this indication and will be classified as a B* medicine locally. • A B* notification form will need to be completed and submitted to commissioners for each adult patient treated with sodium oxybate for REM behaviour disorder in order for the cost of the medicine to be reimbursed to the Trust. • Educational risk minimisation materials are in place to help reduce risks associated with using agomelatine. These should be implemented by the specialist sleep service. The materials provided by the company are: (i) a liver monitoring schedule (ii) a patient alert card and (iii) a prescriber guide.
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group **Cost Impact for agreed patient group**	• As these treatments are proposed as last line, the formulary submissions estimate that only a small number of patients would be suitable for treatment with these agents. If 50% of patients were suitable for a third line treatment it would mean 20-25 patients, and 10-12 would be expected to come from SE London. • If 20% require last line options (~2 patients), the most significant additional cost impact would be from sodium oxybate. Assuming the higher dose range, the additional cost impact would be around £24,000 per year for SEL.
Usage Monitoring & Impact Assessment	• Sleep centre to monitor use and submit usage data and audit reports (against this recommendation and the treatment pathway) upon request to the APC.
	• CCGs to monitor ePACT data and exception reports from GPs if inappropriate prescribing requests are made to primary care.

Evidence reviewed	References (from evidence evaluation)
	1. Aurora R, Zak R, Maganti R et al. Best Practice Guide for the Treatment of REM Sleep Behaviour Disorder. Journal of Clinical Sleep Medicine 2010 6 (1) p85-95 2. Bonakis A, Howard RS, Williams A. Narcolepsy presenting as REM sleep behaviour disorder. *Clin Neurol Neurosurg* 2008;110:518-20. 3. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. *Brain* 2000;123:331-9. 4. Schenck CH, Mahowald MW. Long-term, nightly benzodiazepine treatment of injurious parasomnias and other disorders of disrupted nocturnal sleep in 170 adults. *Am J Med* 1996;100:333-7. 5. Diazepam tablets. Summary of Product Characteristics. Available here (accessed 06/04/2018) 6. Clonazepam liquid. Summary of product characteristics. Available here (accessed 06/04/2018) 7. Ringman JM, Simmons JH. Treatment of REM sleep behaviour disorder with donepezil: A report of three cases. *Neurology* 2000;55:870-1. 8. Massironi G, Galluzzi S, Frisoni GB. Drug treatment of REM sleep behaviour disorders in dementia with Lewy bodies. *Int Psychogeriatr* 2003;15:377-83. 9. Holsboer-Trachsler E et al. Effects of the novel acetylcholinesterase inhibitor SDZ ENA 713 on sleep in man. Neuropsychopharmacology. 1993;8(1):87–92. 10. Wang Y, Yang Y, Wu H. Effect of rotigotine on REM sleep behaviour disorder in Parkinson's disease. Journal of Clinical Sleep Medicine 2016 **12** (10) p1403-1409 11. Fantini ML, Gagnon JF, Filipini D, Montplaisir J. The effects of pramipexole in REM sleep behaviour disorder. Neurology 2003;61:1418-20. 12. Schmidt MH, Koshal VB, Schmidt HS. Use of pramipexole in REM sleep behaviour disorder: results from a case series. Sleep Med 2006;7:418-23. 13. Sasai T.; Inoue Y.; Matsuura M. Effectiveness of pramipexole, a dopamine agonist, on rapid eye movement sleep behaviour disorder. Tohoku Journal of Experimental Medicine; 2012; vol. 226 (no. 3); p. 178-181 14. Sasai T.; Inoue Y.; Matsuura M. Factors associated with the effect of pramipexole on symptoms of idiopathic REM sleep behaviour disorder. Parkinsonism and Related Disorders; Feb 2013; vol. 19 (no. 2); p. 153-157 15. Kumru H, Iranzo A, Carrasco E, et al. Lack of effects of pramipexole on REM sleep behaviour disorder in Parkinson disease. Sleep 2008;31:1418-21. 16. Anderson KN, Shneerson JM. Drug treatment of REM sleep behaviour disorder: the use of drug therapies other than clonazepam. J Clin Sleep Med 2009;5:235-9. 17. Bonakis A, Howard RS, Williams A. Narcolepsy presenting as REM sleep behaviour disorder. Clin Neurol Neurosurg 2008;110:518-20. 18. Bonakis A et al. Agomelatine may improve REM sleep behaviour disorder symptoms. J Clin Psychopharmacol. 2012;32(5):732–4. 19. Pagel J, Parnes B. Medications for the treatment of sleep disorders: an overview. The Primary Care Companion to The Journal of Clinical Psychiatry 2001 3(3) p118-125 20. Drug Tariff, April 2018. Available here (accessed 08/04/2018)

NOTES:

a) Area Prescribing Committee recommendations and minutes are available publicly on member CCG websites.

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.