South East London Area Prescribing Committee
Formulary recommendation

Reference	**090**
Intervention:	**Specific agents (diazepam/ zopiclone/rotigotine patch/pramipexole/ donepezil) for the third line/last line management of REM behaviour disorder in adults** (Diazepam/zopiclone are sedative hypnotic agents; pramipexole and rotigotine patch are dopamine agonists; donepezil is an anticholinesterase)
Date of Decision	**July 2018**
Date of Issue:	**August 2018**
Recommendation:	**Amber 2 – initiation and minimum 3 months supply by the specialist sleep service**
Further Information	• In line with the local pathway, modified release melatonin is the **first line** treatment option for the management of REM behaviour disorder (administered at a dose of 0.5mg to 6mg at night). • Clonazepam is a **second line** option (dose of 0.25mg to 4mg at night) where there is no significant improvement or there is an adverse reaction to melatonin. Note: There may be circumstances where clonazepam is considered a first line option where parasomnia behaviours place the patient or others at risk of harm. • Diazepam/zopiclone/rotigotine patch/pramipexole are accepted for use in South East London as **third line monotherapy** treatment options for the management of REM behaviour disorder. • Donepezil is accepted for use as a last line treatment option where the above options have failed or are not tolerated. • Refer to the pathway for dosing information and refer to APC recommendation 91 for information on the **hospital only last line** treatment options (sodium oxybate and agomelatine). • The decision on choice of third line/last line agent will be made by the sleep specialist taking into account individual patient factors, such as symptoms. • Treatment will be initiated and monitored by the sleep service. The service will regularly review patients for ongoing effectiveness of treatment. • The sleep service will prescribe ongoing supply of the agents covered by this recommendation for a **minimum of 3 months**. • Prescribing will only be transferred to primary care once the therapy is confirmed as effective, the patient is on a stable dose and has been confirmed to be tolerating the medication. • The sleep service will provide the patient's GP with information for GPs and pharmacists and sleep hygiene information. • 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. • Clonazepam, diazepam and zopiclone are schedule 4 (part 1) controlled drugs. Prescribers should be aware of the risks associated with these agents, including falls, cognitive impairment, dependence and withdrawal symptoms. These risks will be considered by the sleep specialist team before these agents are initiated for REM Behaviour Disorder.
Shared Care/ Transfer of care required:	No - individual management plan to be in place, e.g. detailed clinic letter and supporting resources.
Cost Impact for agreed patient group	• As these treatments are proposed as third line or last line, the formulary submissions estimate that only a small number of patients would be suitable. If 50% of patients were suitable, this would mean 20-25 patients, and 10-12 would be expected to come from SE London.

Cost Impact for agreed patient group	• The formulary submissions suggest an even split of usage between each of the options, which would equate to a cost impact of approximately £2,000 per annum for South East London.
Usage Monitoring & Impact Assessment	• Sleep centre to monitor use and submit usage data/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.