South East London Area Prescribing Committee
Formulary recommendation

Reference	**106**
Intervention:	**Melatonin (2mg modified release) for the management of specific headache disorders (all off-label use)** (Melatonin is a naturally occurring hormone produced by the pineal gland and is structurally related to serotonin)
Date of Decision	**June 2019**
Date of Issue:	**July 2019**
Recommendation:	**RED – Prescribing and supply by hospital only**
Further Information	• Melatonin 2mg modified release tablets are accepted for use in SEL for the management of the following headache disorders: - Cluster headache - Migraine - Hypnic headache - Hemicrania continua - Tension-type headache - Primary stabbing headache - Secondary short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) • The use of melatonin is restricted to a **last line** option after all other treatments have been trialled or considered but are not effective, not tolerated or contra-indicated. Patient factors (such as co-morbidities and other medicines the patient is taking) will also be considered by the initiating specialist. • The dose range for melatonin in this setting is 2mg-10mg per day depending on the type of headache disorder. In general, lower doses (2mg per day) are used in migraine and tension-type headache. The higher doses are reserved for cluster headache. • For migraine, in line with the available evidence, the use of melatonin is only supported as **monotherapy**. • Patients will be reviewed by the service at 6 months, which will include assessment of the severity, frequency and duration of attacks (using headache diaries and quality of life scores), symptom control and tolerability. • Melatonin is **not licensed** for use in these headache disorders. Informed consent should be gained from the patient before treatment is started. • A pathway for the management of headache disorders will be developed to outline the place in therapy of the various treatment options. Until the pathway is agreed, melatonin will be categorised as red across SEL. Funding will need to be confirmed at individual Trust level as melatonin in this setting will be prescribed and supplied by the hospital.
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	• The formulary application estimates that 70 patients would be suitable for treatment across KCH and GSTT. • If 50 of those were from SE London, this would equate to additional costs of between £9,250 to £46,500 per annum for SE London depending on the dose. • These costs are likely to be an overestimate as there is already some prescribing of melatonin occurring in this setting.
Usage Monitoring & Impact Assessment	**Acute Trusts:** • Monitor use and report back to APC when required. • Audit use upon request to ensure use is in line with this recommendation.

Usage Monitoring & Impact Assessment (cont'd)	**CCGs:** • Monitor Epact 2 data. • Monitor exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	**References (from evidence evaluation)** 1. International Classification of Headache Disorders – 3rd Edition. Available here (accessed 29/10/2018) 2. Fischera M, Marziniak M, Gralow I. The incidence and prevalence of cluster headache: a meta-analysis of population-based studies. Cephalalgia. 2008 Jun;28(6):614-8 3. Diagnosis and management of headache in adults. SIGN 107, Nov 2008. 4. Headaches in over 12's: diagnosis and management. NICE CG150, Nov 2015 update. 5. Liang J, Wang S. Hypnic headache: a review of clinical features, therapeutic options and outcomes. Cephalalgia. 2014; 34 (10):795. 6. Prakash S, Patel R. Hemicrania continua: clinical review, diagnosis and management. J Pain Res 2017, 10 p1493-1509 7. Guerrero A, Herrero S, Peñas M, Incidence and influence on referral of primary stabbing headache in an outpatient headache clinic. J Headache Pain. 2011 Jun; 12(3): 311–313. 8. Circadin. SPC. Available online here (accessed 29/10/2018) 9. Gelfand A, Goadsby P. The role of melatonin in the treatment of primary headache disorders. Headache 2016 doi 10.1111/head.12862 10. Pringsheim T, Magnoux E, Dobson C et al. Melatonin as adjunctive therapy in the prophylaxis of cluster headache: a pilot study. Headache 2002 42 p787-792 11. Leone M, D'Amico D, Moschiano F et al. Melatonin versus placebo in the prophylaxis of cluster headache: a double-blind pilot study with parallel groups. Cephalagia 1996 16 p494-496 12. Peres M, Rozen T. Melatonin in the preventive treatment of chronic cluster headache. Cephalagia 2001 21 p993-995 13. Altstadhaug K, Odeh F, Salvesen R et al. Prophylaxis of migraine with melatonin: a randomised controlled trial. Neurology 2010 75 p1527-1532 14. Goncalves A, Ferreira A, Riberio R et al. Randomised clinical trial comparing melatonin 3 mg, amitriptyline 25 mg and placebo for migraine prevention. J Neurol Neurosurg Psychiatry 2016 87 p1127-1132 15. Bougea A, Spantideas N, Lyras V et al. Melatonin 4 mg as prophylactic therapy for primary headaches: a pilot study. Functional Neurology 2016 31 (1) p33-37 16. Peres M, Zukerman E, da Cunha Tanuri F et al. Melatonin 3mg is effective for migraine prevention. Neurology 2004 63 p757 17. Karadas O, Gul H. The efficacy of melatonin in migraine prophylaxis (abstract only). Cephalalgia 2011 31(Suppl. 1) 1–216 18. Holle D, Naegel S, Krebs S et al. Clinical characteristics and therapeutic options in hypnic headache. Cephalagia 30 (12) p1435-1442 19. Dodick D. Polysomnograhpy in hypnic headache syndrome. Headache 2000 40 p748-752 20. Rozen T. How effective is melatonin as a preventive treatment for hemicranias continua? A clinic based study. Headache 2015 55 p430-436 21. Rozen T. Melatonin responsive hemicranias continua. Headache 2006 46 p1203-1209 22. Spears R. Hemicrania continua: a case in which a patient experienced complete relief with melatonin. Headache 2006 p524-525 23. Hollingworth M, Young T et al. Melatonin responsive hemicranias continua in which indomethacin was associated with contralateral headache. Headache 2014 54 p916-919 24. Karadas O, Gul H, Sutcugil L et al. Efficacy of melatonin in chronic tension type headache type headache patients and effects on anxiety and depression. Cephalalgia 2011 31(Suppl. 1) 1–216 25. Rozen t. Melatonin as treatment for idiopathic stabbing headache. Neurology 2003 61 p865-866 26. Rojas-Ramirez M, Bertoli E, Smith J et al. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing secondary to head and neck trauma: literature review and case report. Journal of oral & Facial Pain and Headache 2016 30 (1) p68-72

NOTES:

a) Area Prescribing Committee recommendations and minutes are available publicly via 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.