South East London Integrated Medicines Optimisation Committee
Formulary recommendation

Reference	**143**
Intervention:	**Doxepin, agomelatine and vortioxetine for the pharmacological management of co-morbid insomnia in adults** • *Doxepin is an antidepressant with adrenergic activity* • *Agomelatine is an antidepressant and melatonin receptor agonist* • *Vortioxetine is an antidepressant*
Date of Decision	**March 2023**
Date of Issue:	**April 2023**
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	• Doxepin, agomelatine and vortioxetine are accepted for use in South East London for the pharmacological management of co-morbid insomnia in adults • Co-morbid insomnia is a sleep disorder believed to arise as a result of another condition such as anxiety, depression, sleep apnoea, gastroesophageal reflux disease (GERD), or physical pain • The use of doxepin, agomelatine and vortioxetine for the pharmacological management of co-morbid insomnia in adults should be prescribed in line with the co-morbid insomnia treatment pathway. • The initiation of doxepin, agomelatine and vortioxetine is **restricted** to the specialist Sleep Centre at Guy's and St. Thomas' NHS Foundation Trust team **and** only after a Sleep Centre multidisciplinary team discussion • Melatonin M/R is the **first line** pharmacological treatment for the management of co-morbid insomnia. See formulary recommendation 142 and the co-morbid insomnia treatment pathway for more information. • Doxepin, agomelatine and vortioxetine are **second line** pharmacological treatment options for the management of co-morbid insomnia, the following should be noted before initiation: - Doxepin is not licensed for use in this setting (off-label use) in patients **without** co-morbid depression. Informed consent should be gained from the patient before off-label treatment with doxepin is started. - Agomelatine and vortioxetine should **only** be prescribed in patients with co-morbid depression. This use is in line with the product licence. • Patients should be reviewed by the specialist sleep centre 3 to 6 months after initiating treatment with doxepin, agomelatine and vortioxetine. • Further information can be found in the co-morbid insomnia pathway and formulary recommendation 142.
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	The following cost impact is based on assumptions that 35% of the total patients from the sleep centre are from SEL and that treatment is long term: • **Doxepin**: Based on approximately 15 - 25 patients per annum eligible for treatment, estimated costs for SEL are £10,000 per annum (<£1,000 per 100,000 population) • **Agomelatine:** Based on approximately 15 - 25 patients per annum eligible for treatment, estimated costs for SEL are £4,000 per annum (negligible cost per 100,000 population) • **Vortioxetine:** Based on approximately 15 - 25 patients per annum eligible for treatment, estimated costs for SEL are £3,000 per annum (negligible cost per 100,000 population)

Usage Monitoring & Impact Assessment	**Acute Trusts:** • Monitor and audit usage of doxepin, agomelatine and vortioxetine as agreed and report back to the Committee (against this recommendation) upon request of the Committee
	SEL Borough Medicines Teams: • Monitor exception reports from GPs if inappropriate prescribing requests are made to primary care
Evidence reviewed	**References (from evidence review)** 1. Edmonds C, Swanoski M. A Review of Suvorexant, Doxepin, Ramelteon, and Tasimelteon for the Treatment of Insomnia in Geriatric Patients. The Consultant Pharmacist, March 2017 VOL. 32, NO. 3 p156-160. 2. Silenor (Doxepin), FDA label. Available here online [Accessed 29/06/2021] 3. Yueng W, Chung K, Yung K et al. Doxepin for insomnia: A systematic review of randomized placebo-controlled trials. Sleep Medicine Reviews 19 (2015) p75-83. 4. Krystal A, Durrence H, Scharf M et al. Efficacy and safety of doxepin 1 mg and 3 mg in a 12-week sleep laboratory and outpatient trial of elderly subjects with chronic primary insomnia. Sleep 2010;33(11):1553-61. 5. Krystal A, Lankford A, Durrence H et al. Efficacy and safety of doxepin 3 and 6 mg in a 35-day sleep laboratory trial in adults with chronic primary insomnia. Sleep 2011;34(10):1433-42. 6. Lankford A, Rogowski R, Essink B et al. Efficacy and safety of doxepin 6 mg in a four week outpatient trial of elderly adults with chronic primary insomnia. Sleep Medicine 2012;13(2):133-8. 7. Rios Romenets S, Creti L, Fichten C et al. Doxepin and cognitive behavioural therapy for insomnia in patients with Parkinson's disease: a randomised study. Parkinsonism & Related Disorders 2013;19(7):670-5. 8. Valdoxan (agomelatine). Summary of Product Characteristics. Available here [Accessed 04/07/2021] 9. Mi W, Tabarak S, Wang L et al. Effects of agomelatine and mirtazapine on sleep disturbances in major depressive disorder: evidence from polysomnographic and resting-state functional connectivity analyses. Sleep 2020 doi: 10.1093/sleep/zsaa092 10. Altınyazar V, Kiylioglu N. Insomnia and dementia: is agomelatine treatment helpful? Case report and review of the literature. Ther Adv Psychopharmacol 2016, Vol. 6(4) 263– 268. 11. Brintellix (vortioxetine). Summary of product characteristics. Available here [Accessed 04/07/2021] 12. NICE TA367 - Vortioxetine for treating major depressive episodes 13. Liguori C, Ferini-Strambi L, Izzi F et al. Preliminary evidence that vortioxetine may improve sleep quality in depressed patients with insomnia: a retrospective questionnaire analysis. Br J Clin Pharmacol (2019) 85 240–244.

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.**