South East London Integrated Medicines Optimisation Committee
Formulary recommendation

Reference:	**142**
Intervention:	**Melatonin modified release, trazodone, mirtazapine and quetiapine for the pharmacological management of co-morbid insomnia in adults** • *Melatonin is a naturally occurring hormone produced by the pineal gland and is structurally related to serotonin* • *Trazodone is a tricyclic-related antidepressant which may have noradrenergic potentiation (exact mechanism of action is not precisely known)* • *Mirtazapine is an antidepressant which increases central noradrenergic and serotonergic neurotransmission* • *Quetiapine is an atypical antipsychotic agent with affinity for brain serotonin and dopamine receptors*
Date of Decision:	**March 2023**
Date of Issue:	**April 2023**
Recommendation:	**Amber 2 – initiation and supply by the specialist Sleep Centre at Guy's and St. Thomas' NHS Foundation Trust (GSTfT) until dose is stable and ongoing treatment is indicated only after which prescribing may be transferred to primary care**
Further Information	• Melatonin modified release (M/R), trazodone, mirtazapine and quetiapine 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, gastro-oesophageal reflux disease (GORD), or physical pain • The use of melatonin M/R, trazodone, mirtazapine and quetiapine 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 melatonin M/R, trazodone, mirtazapine and quetiapine is **restricted** to the specialist Sleep Centre at Guy's and St. Thomas' NHS Foundation Trust team, until a patient's dose is stable and a review determining if ongoing treatment is indicated has occurred. Prescribing can then be continued in primary care under "Amber 2" arrangements. • Melatonin M/R is the **first line** pharmacological treatment for the management of co-morbid insomnia. Melatonin M/R is not licensed for use in this setting (off-label use) • Trazodone, mirtazapine and quetiapine are **second line** pharmacological treatment options for the management of co-morbid insomnia. These agents are 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 melatonin M/R, trazodone, mirtazapine and quetiapine is started • Patients will be reviewed by the specialist sleep centre 3 to 6 months after initiating treatment with melatonin M/R, trazodone, mirtazapine or quetiapine. See the co-morbid insomnia pathway for more information.
Shared Care/ Transfer of care required:	N/A Practices should be signposted to the co-morbid insomnia pathway
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: • **Melatonin M/R**: Based on an average of 4mg daily and approximately 720 patients per annum eligible for treatment, estimated costs for SEL are £95,000 per annum (~£5,000 per 100,000 population) • **Trazodone:** Based on approximately 150 patients per annum eligible for treatment, estimated costs for SEL are £2,000 per annum (~£105 per 100,000 population) • **Mirtazapine:** Based on approximately 150 patients per annum eligible for treatment, estimated costs for SEL are £1,000 per annum (~£53 per 100,000 population) • **Quetiapine:** Based on approximately 50 patients per annum eligible for treatment, estimated costs for SEL are £350 per annum (~£19 per 100,000 population) However it is likely that the majority of the estimated costs are already in baseline as several of these treatments, including melatonin, are likely to be in routine practice for the use in co-morbid insomnia.

Usage Monitoring & Impact Assessment	**Acute Trusts:** • Monitor and audit usage of melatonin M/R, trazodone, mirtazapine and quetiapine as agreed and report back to the Committee (against this recommendation) upon request of the Committee
	SEL Borough Medicines Teams • Monitor ePACT2 data and exception reports from GPs if inappropriate prescribing requests are made to primary care
Evidence reviewed	**References (from evidence review):**

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NOTES:

a) SEL IMOC recommendations and minutes are available 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.