Pathway for the pharmacological management of co-morbid insomnia in adults

Note: Melatonin, trazodone, mirtazapine and quetiapine are IMOC Amber 2 category – initiation by the sleep centre followed by maintenance prescribing in primary care. GPs are not expected to initiate these treatments but may be asked to take on prescribing in line with IMOC recommendations. Doxepin, agomelatine and vortioxetine are IMOC RED category (hospital only) – initiation and ongoing prescribing will be by the sleep service.

Initial assessment and management

Screen for associated perpetuating factors and optimise management accordingly (e.g. pain, acid reflux, depression, anxiety).

- Optimise lifestyle factors, such as exercise and sleep routine
- Offer behavioural guidance and CBT-I or digital CBT-I where available and appropriate

For detail, see appendix 2 on page 3.

For Chronic Insomnia

First line pharmacological therapy *(off label)*

- Melatonin M/R tablets 2mg at night (take 1-2 hours before bedtime), increasing up to 6mg if required.

Only licensed for primary insomnia at 2mg daily for up to 13 weeks in those ≥55years

For Acute Insomnia

Only for consideration for transient or expected short-term comorbid insomnia

- Zopiclone 3.75 mg to 7.5 mg at night
- Zolpidem 5 mg to 10 mg at night

>2 weeks use not recommended outside of Sleep Centre patient assessment.

Second line pharmacological therapy options (*off label use*)

- Trazodone 50 mg to 150 mg at night*
- Mirtazapine 7.5 mg to 15 mg at night*

Use permitted only after Sleep Disorder Centre MDT discussion

- Quetiapine 12.5 mg to 50 mg at night*
- Doxepin 3 mg to 10 mg at night**
- Agomelatine 25 mg to 50 mg at night***
- Vortioxetine 5 mg titrated up to 20mg in the morning***
- Trazodone 150 mg to 300 mg at night***

**Use in patients without comorbid depression is off-label*
***Off-label Hospital prescribing only.*
****Used only in patients with insomnia comorbid with depression, so can be considered within product licence. Hospital prescribing only. For detail, see appendix 3*

General principles of patient management in the Sleep Disorder Centre

- Patients are reviewed by the specialist 3 to 6 months after starting a treatment.
  - *Aim for a reduction of >6 in the ISI (Insomnia Severity Index)*
  - InsomniaIndex (ons.org)
  - *Aim for HADs score of <10 (no validated reduction in this scale)*
    Depression and anxiety self-assessment quiz - NHS (www.nhs.uk)
- Follow up consultations with the sleep pharmacist are available when necessary.
- Patients are counselled on initiation, including when to dose titrate, and when to stop treatment if not working or no longer necessary. This detail is clearly communicated to GPs in the clinic letter.
- Provided the patient's dose is stable and ongoing treatment is indicated, primary care prescribing may be requested after initial supplies from the clinic.
- When treatment is no longer required (e.g. insomnia resolved, not tolerated), the GP will be informed via a clinic letter, including any detail of treatment tapering if req

South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: SEL Integrated Care Board (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

Appendix 1 – Understanding the condition

Sleep Foundation

Sleeping problems often have a bidirectional relationship with other health issues.
Co-morbid insomnia or secondary 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.

Acute Insomnia
Acute insomnia otherwise know as short-term insomnia is a brief episode of difficulty sleeping.
It may be caused by a stressful life event such as a bereavement, global pandemic or a major job or relationship change.
Acute insomnia tends to last for less than three months.
However, it can be persistent and become chronic insomnia.

Chronic Insomnia

Chronic insomnia is a long-term pattern of difficulty sleeping.
Insomnia is considered chronic if a person has trouble falling asleep or staying asleep at least three nights per week for three months or longer.
Like acute insomnia, it may be linked to stressful situations, but it may also be related to irregular sleep schedules, poor sleep hygiene, other sleep disorders etc.

Appendix 2 – Non-pharmacological Management

Lifestyle optimisation measures

- **Stimulus control**
  - Bed/bedroom use only for sleep, sex and getting dressed (not reading, resting, phone, watching TV etc.)
  - Get out of bed if not sleeping after 15-20 min (especially if agitated)

- **Sleep scheduling**
  - Limit time in bed to time actual average total sleep time (best achieved via sleep diaries)
  - Avoiding daytime and evening naps
  - Getting into bed only when sleepy tired
  - Getting up at the same time every day, including weekends

- **Additional**
  - Avoid caffeine after 12pm; switch to decaffeinated drinks
  - Avoid alcohol, at the very least in the 2 hours before bed
  - Daily exercise, ideally outside to gain exposure to natural day light
  - Other sleep hygiene advice via the Sleep Foundation

Naps

- Discouraged because they reduce sleep drive.
- If naps cannot be avoided, then try to limit them to 20 minutes (setting an alarm), and ideally not in the 5 hours before the main episode of sleep.

Digital Cognitive Behavioural Therapy for Insomnia (CBT-I) available

- **Sleepio** - Currently available free in some areas in the UK)
- **Sleepstation** – Available free on the NHS. The patient self-refers and then sees the GP who needs to approve the referral

Recommended

- Overcoming Insomnia: A Cognitive-Behavioural Therapy Approach, Workbook (Treatments That Work) by Jack Edinger & Colleen Carney (2014)
- Overcoming Insomnia and Sleep Problems: A Self Help Guide Using Cognitive Behavioural Techniques by Colin Espie (2012)
- Say Goodnight to Insomnia: A Drug-Free Programme Developed at Harvard Medical School by Gregg Jacobs (2011)
- How to Beat Insomnia and Sleep Problems One Step at a Time: Using evidence-based low-intensity CBT by Kirstie Anderson (2018)

Appendix 3
Patient cohorts appropriate for second line pharmacological therapies used in the management of co-morbid insomnia

Drug	Types of patients this is most useful for	Cautions
Trazodone	• Sleep initiation and maintenance difficulties • Co-morbid nightmares • Co-morbid Restless Legs Syndrome	• History of impulsive drug overdose • Prolonged QTc interval
Mirtazapine	• Sleep initiation and maintenance difficulties. • Co-morbid prominent nocturnal anxiety	• Not helpful in nightmares • Can worsen restless legs syndrome
Quetiapine	• Severe insomnia, which has not responded to trazodone nor mirtazapine • Paradoxical insomnia	• Prolonged QTc interval • Can use with other anti-psychotics in dose range for insomnia; total antipsychotic dose load to be calculated
Doxepin	• Sleep initiation and maintenance difficulties. • When a liquid hypnotic is required e.g. PEG fed etc. • In patients with intellectual disabilities • In patients where there is no response to trazodone or mirtazapine, or where these are contraindicated	• Patient or carer needs to be able to make new doxepin solution each evening.
Agomelatine	• Insomnia with co-morbid depression. • If treatment failure on melatonin for REM Sleep Behavioural Disorder. • Consider in Smith Magenis Syndrome if lack of response to melatonin	• Not in patients with hepatic dysfunction.
Vortioxetine	• Depression with insomnia • Depression with REM Sleep Behavioural Disorder • Depression with sleep movement disorders	