Pharmacological Management of Restless Legs Syndrome (RLS) or Periodic Limb Movement Disorder (PLMD)

Note: Except for intravenous iron (which is hospital only), treatments noted in this pathway are **IMOC Amber2 category** – initiation and minimum 3 months supply by the sleep centre and neurology team (specialising in RLS/PLMD). GPs are **not** expected to initiate these treatments but may be asked to take on prescribing in line with IMOC recommendations (patients will have individual management plans in place).

Diagnosis of RLS or PLMD

Screen all patients for underlying causative factors. Measure:
- ➤ Serum ferritin, vitamin B_{12}, folate, haemoglobin and thyroid function tests
- ➤ Initiate, vitamin B_{12}, folate, or thyroid replacement therapy as indicated.
- ➤ If ferritin ≤75 mcg/L and transferrin sat < 45%, then prescribe ferrous sulphate 200 mg once daily or ferrous fumarate 210mg once daily.
- ➤ If ferritin remains ≤75 mcg/L despite oral iron, or if the patient is intolerant of oral iron, IV iron (ferric carboxymaltose) may be appropriate (hospital only). This may be referred for at any stage in the pathway. Refer to [formulary recommendation](#) and internal Trust protocols for use.

First Line Therapies

Dopamine Agonists (DA)
- ➤ Ropinirole* 0.25 - 4mg nocte or
- ➤ Pramipexole 0.088 – 0.54mg nocte

If augmentation occurs or predominant presence of daytime symptoms or previous suspected augmentation to shorter acting dopamine agonist:
- ➤ Rotigotine (patch) 1 – 3mg daily**

Review by specialist in 3 months

If intolerant of DA, or has a history of insomnia or compulsive behaviours: Alpha-2-delta ligands
- ➤ Gabapentin 300 – 1200mg nocte (preferred agent) or
- ➤ Pregabalin 25 – 300mg nocte (if intolerant to gabapentin or significant drug interactions

Review by specialist in 3 months

[Recommendation 060 gabapentin/pregabalin in RLS/PLMD](#)

Improvement but residual symptoms:
- ➤ Continue first line therapy
- ➤ Add an additional first line agent i.e. Gabapentin or Pregabalin for painful/neuropathic RLS

Review by specialist in 3 months

If patient is receiving a DA, monitor for Impulse Control Disorders

Second Line Therapies

No significant improvement***, Stop first line therapy and **initiate**:Benzodiazepines/BZRA
- ➤ Clonazepam** **0.25 – 2mg nocte**

(data available is for the use of Clonazepam only)

For insomnia management in RLS****
- ➤ Zolpidem** 5 – 10mg nocte or
- ➤ Zopiclone** 3.75mg – 15mg nocte

Or, Management of pain associated with RLS:
Opioids: First line therapy
- ➤ Codeine** 30 – 90mg nocte
- ➤ Then consider:
- ➤ Oxycodone/Naloxone 5/2.5mg – 20/10mg twice daily (licensed use in RLS) may be used nocturnally only depending on timing of symptoms and/or to limit side effects in individual cases

Review by specialist in 3 months

[Recommendation 061 clonazepam/zopiclone/zolpidem in RLS/PLMD](#)
[Recommendation 062 opioids in RLS /PLMD](#)

- BZRA= Benzodiazepine receptor agonists (Benzodiazepines, Z-Drugs)
- *Immediate release ropinirole recommended only.
- **Off label use; Rotigotine dose may be increased to 4mg daily in treatment resistant cases where an incomplete response observed- this option should be used before considering escalation to clonazepam or opioids
- ***Defined as Significant change in Epworth Sleepiness Scale (ESS)
- ****Opioids and z-drugs/benzodiazepines are not to be used simultaneously.
- When a patient moves to an opioid, consideration should be given to stopping dopamine agonist particularly in those at risk of sedation/falls/dependence.
- For Alpha-2-delta ligands, opioids and benzodiazepines treatment: to check/monitor AHI if pre-existing OSA, or if OSA is diagnosed whilst on treatment; OSA= Obstructive Sleep Apnoea, AHI = Apnea Hypopnea Index
- http://www.med.navy.mil/sites/NMCP2/PatientServices/SleepClinicLab/Documents/EPWORTH-SLEEPINESS-SCALE.pdf **or**
- Restless Legs Syndrome Rating Scale (RLSRS) http://www.medicine.ox.ac.uk/bandolier/booth/RLS/RLSratingscale.pdf http://www.aasmnet.org/Resources/PracticeParameters/TreatmentRLS.pdf
- https://www.guidelines.co.uk/rlsuk/restless-legs