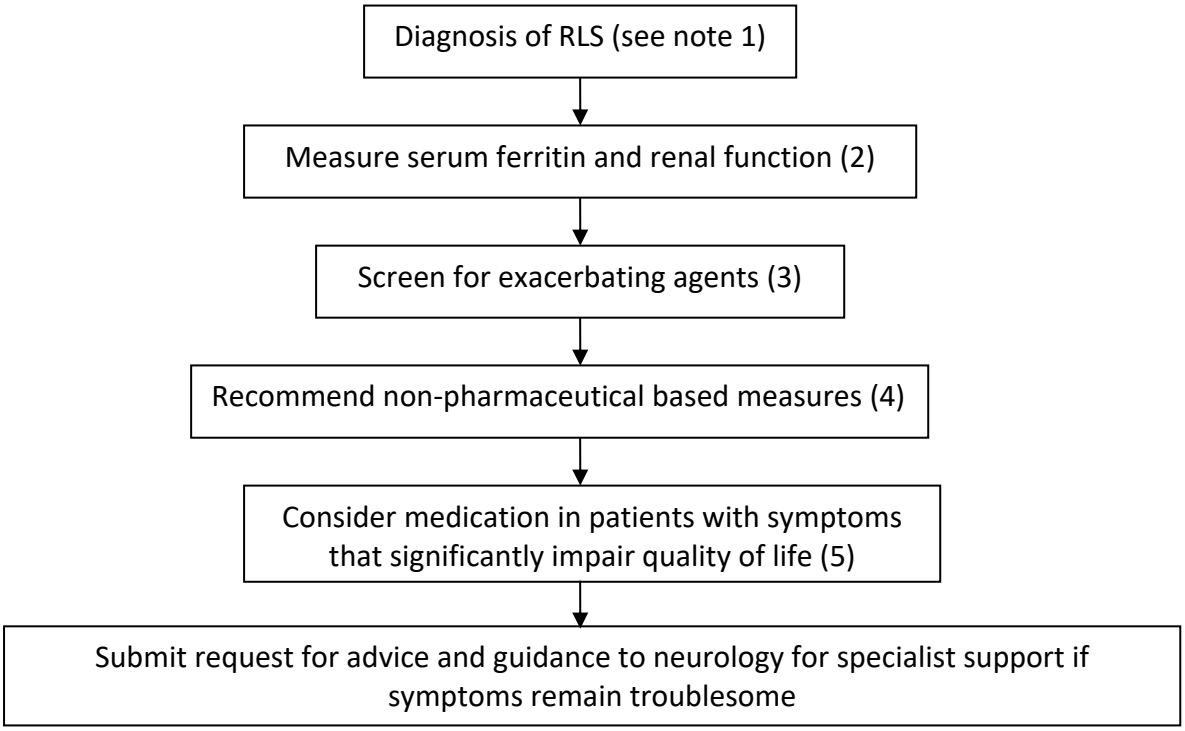
Restless legs treatment algorithm



Notes:

1) Criteria for a diagnosis of restless legs syndrome

Essential diagnostic criteria	Supportive criteria	Associated features
• An urge to move the legs, usually accompanied or caused by uncomfortable or unpleasant sensations in the legs. • Unpleasant sensations or urge to move begin or worsen during periods of rest or inactivity, such as lying or sitting. • Unpleasant sensations or urge to move are partially or totally relieved by movement, at least for as long as the activity continues. **Unpleasant sensations or urge to move are worse during the evening or night than during the day, or they occur only during the evening or night.**	• Positive response to dopaminergic agents. • Periodic limb movements of sleep or during wakefulness. • Positive family history of restless legs syndrome.	• Onset can be at any age, but patients are usually middle aged or older at presentation. • Leg discomfort or the need to move results in insomnia. • Low serum ferritin (<90 µg/L). • Symptoms fluctuate - They can be very severe for a few weeks and then ease off considerably.

2) Measure serum ferritin in all patients with symptoms of restless legs syndrome. Anaemia is not sufficiently sensitive as a marker for iron deficiency. Patients with a serum ferritin of less than 90 µg/L should be started on iron supplements. Renal impairment can also cause restless legs symptoms.

3) Take a drug history to screen for exacerbating agents, such as antipsychotics, antidepressants (especially selective serotonin reuptake inhibitors and serotonin noradrenaline reuptake inhibitors), antihistamines, dopamine receptor blocking agents such as metoclopramide and prochlorperazine, and diphenhydramine.

4) Not all patients need treatment, and only about 20% require medicines. Non-pharmaceutical based measures include avoidance of alcohol, caffeine, and smoking; good sleep hygiene; moderate regular exercise; avoidance of overexertion, stress, or sleep deprivation; and brief walking or other motor activities, hot baths, or leg massage before bedtime.

5) Consider medicines in patients with symptoms that seriously impair quality of life, sleep, or daytime functioning:

- There is good evidence for GABAergic and dopamine agonist medications, and both may be considered first line. Pregabalin and gabapentin are both options, as are low dose dopamine agonists. Dopamine agonists can cause augmentation (drug induced worsening) of symptoms in some patients and are therefore sometimes a cause for escalating symptoms. Dopamine agonists may be a preferred choice in the obese or in those with type II diabetes. **Dopamine agonists should not be titrated above the licensed dose for RLS in the BNF**, and all patients need to be counselled on the risk of impulse control disorders. **Do not use Parkinsons disease doses of agonists in patients with RLS**.
- Second line opiate medications such as codeine or oxycodone may be considered, as may clonazepam, although addition, tolerance and driving restriction should all be discussed.
- Rotation of medicines may be helpful for patients who experience augmentation or waning of effect with time with certain classes of medications.

Medicines	Doses as per NICE CKS Restless legs syndrome guidance
Pregabalin	The use of pregabalin for restless legs syndrome (RLS) is off-label. Initial dose: 75 mg in people aged under 65 years and 50 mg in people aged over 65 years. Titration: maximum recommended daily dose for RLS is 450 mg. CKS did not identify any specific guidance on dose titration and the requirement for divided daily doses. However, for another indication (neuropathic pain), divided doses are advised, and it is recommended that initial pregabalin dose can be doubled after 3–7 days, and then increased incrementally on a weekly basis to the maximum dose if required.
Gabapentin	The use of gabapentin for restless legs syndrome (RLS) is off-label. Initial dose: 300 mg if the person is under 65 years old and 100 mg if the person is over 65 years old. Titration: maximum recommended dose for RLS is 2700 mg. CKS did not identify any specific guidance on dose titration for use in RLS. However, for other indications it is recommended that gabapentin therapy is initiated at 300 mg once daily on day one, twice daily on day two, and three times daily on day three, followed by further increases in 300 mg/day increments every 2–3 days to the maximum dose if required.
Pramipexole	Initial dose: 88 micrograms pramipexole base (125 micrograms pramipexole salt) 1–2 hours before bedtime (or anticipated onset of symptoms). Titration: increase if needed by 88 micrograms pramipexole base (125 micrograms pramipexole salt) after every 4–7 days. Maximum recommended dose: 540 micrograms pramipexole base (750 micrograms pramipexole salt) daily. The manufacturer advises that prescribers should avoid abrupt discontinuation of pramipexole. They recommend slow withdrawal of this dopaminergic therapy to avoid neuroleptic malignant syndrome or dopamine agonist withdrawal syndrome.
Ropinirole	Initial dose: 250 micrograms 1–2 hours before bedtime (or anticipated onset of symptoms). Titration: if needed and tolerated, after 2 days increase to 500 micrograms for 5 days, then increase to 1 mg for 7 days, then increase weekly in steps of 500 micrograms. Maximum recommended dose: 4 mg daily.
Rotigotine	Initial dose: rotigotine patch 1 mg/24 hours. Titration: increase if needed by 1 mg/24 hours weekly if required. Maximum recommended dose: 3 mg/24 hours.

See also NICE CKS Restless legs syndrome – July 22
Original reference: Restless legs syndrome review. BMJ 23 May 2012 BMJ 2012;344:e3056.

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Version	Author(s)	Date	Changes
2.0	Original Authors: Steve Haigh, Medicines Information Centre, SFH Dr Gillian Sare, Consultant Neurologist, NUH Update facilitated by Irina Varlan, Interface & Meds Op Pharmacist, NNICB	March 2023	Both DA and GABAergic medicines as option for first line. In line with NICE CKS Restless legs syndrome – July 22;