Treatment of Restless Legs Syndrome and Periodic Limb Movement Disorder: An American Academy of Sleep Medicine Clinical Practice Guideline

Guidelines at-a-Glance

ADAPTED FROM

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CERTAINTY OF EVIDENCE

⊕⊕⊕⊕	High
⊕⊕⊕⊖	Moderate
⊕⊕⊖⊖	Low
⊕⊖⊖⊖	Very Low

BENEFITS VERSUS HARMS

B>H	Benefits outweigh harms
B=H	Benefits approximately equal harms
B|H	Variability in the estimates of benefit/harm/burden
H>b	Harms outweigh benefits

PATIENT VALUES AND PREFERENCES

	Vast majority of patients would use
	Majority of patients would use
	Variability in patient values/preferences
	Majority of patients would not use
	Vast majority of patients would not use

GOOD PRACTICE STATEMENT

1. In all patients with clinically significant RLS, clinicians should regularly test serum iron studies including ferritin and transferrin saturation (calculated from iron and total iron binding capacity, TIBC). The test should ideally be administered in the morning avoiding all iron-containing supplements and foods at least 24 hours prior to blood draw. Analysis of iron studies greatly influences the decision to use oral or intravenous (IV) iron treatment. Consensus guidelines, which have not been empirically tested, suggest that supplementation of iron in adults with RLS should be instituted with oral or IV iron if serum ferritin ⩽75 ng/mL or transferrin saturation < 20%, and only with IV iron if serum ferritin is between 75 ng/mL and 100 ng/mL. In children, supplementation of iron should be instituted for serum ferritin < 50 ng/mL with oral or IV formulations. These iron supplementation guidelines are different than for the general population.
2. The first step in the management of RLS should be addressing exacerbating factors, such as alcohol, caffeine, antihistaminergic, serotonergic, anti-dopaminergic medications, and untreated obstructive sleep apnea.
3. RLS is common in pregnancy; prescribers should consider the pregnancy-specific safety profile of each treatment being considered.

IMPLICATIONS OF STRONG AND CONDITIONAL RECOMMENDATIONS FOR CLINICIAN USERS

Strong Recommendation (We recommend...): Almost all patients should receive the recommended course of action. Adherence to this recommendation could be used as a quality criterion or performance indicator.

Conditional Recommendation (We suggest...): Most patients should receive the suggested course of action; however, different choices may be appropriate for different patients. The clinician must help each patient determine if the suggested course of action is clinically appropriate and consistent with his or her values and preferences.

The ultimate judgment regarding the suitability of any specific recommendation must be made by the clinician.

TREATMENT OF ADULTS WITH RESTLESS LEGS SYNDROME (RLS)

1.	In adults with RLS, the AASM recommends the use of gabapentin enacarbil over no gabapentin enacarbil. (STRONG)	⊕⊕⊕⊖ B>H
2.	In adults with RLS, the AASM recommends the use of gabapentin over no gabapentin. (STRONG)	⊕⊕⊕⊖ B>H
3.	In adults with RLS, the AASM recommends the use of pregabalin over no pregabalin. (STRONG)	⊕⊕⊕⊖ B>H
4.	In adults with RLS, the AASM recommends the use of IV ferric carboxymaltose over no IV ferric carboxymaltose in patients with appropriate iron status (see good practice statement for iron parameters). (STRONG)	⊕⊕⊕⊖ B>H
5.	In adults with RLS, the AASM suggests the use of IV low molecular weight iron dextran over no IV low molecular weight iron dextran in patients with appropriate iron status (see good practice statement for iron parameters). (CONDITIONAL)	⊕⊖⊖⊖ B>H

REMARKS

[A] Levodopa may be used to treat RLS in patients who place a higher value on the reduction of restless legs symptoms with short-term use and a lower value on adverse effects with long-term use (particularly augmentation).

[B] Pramipexole may be used to treat RLS in patients who place a higher value on the reduction of restless legs symptoms with short-term use and a lower value on adverse effects with long-term use (particularly augmentation).

[C] Transdermal rotigotine may be used to treat RLS in patients who place a higher value on the reduction of restless legs symptoms with short-term use and a lower value on adverse effects with long-term use (particularly augmentation).

[D] Ropinirole may be used to treat RLS in patients who place a higher value on the reduction of restless legs symptoms with short-term use and a lower value on adverse effects with long-term use (particularly augmentation).

[E] Rotigotine may be used to treat RLS in patients who place a higher value on the reduction of restless legs symptoms with short-term use and a lower value on adverse effects with long-term use (particularly augmentation).

6.	In adults with RLS, the AASM suggests the use of IV ferumoxytol over no IV ferumoxytol in patients with appropriate iron status (see good practice statement for iron parameters). (CONDITIONAL)	⊕⊖⊖⊖ B>H
7.	In adults with RLS, the AASM suggests the use of ferrous sulfate over no ferrous sulfate in patients with appropriate iron status (see good practice statement for iron parameters). (CONDITIONAL)	⊕⊕⊕⊖ B>H
8.	In adults with RLS, the AASM suggests the use of dipyridamole over no dipyridamole (CONDITIONAL)	⊕⊕⊖⊖ B>H
9.	In adults with RLS, the AASM suggests the use of extended-release oxycodone and other opioids over no opioids. (CONDITIONAL)	⊕⊕⊕⊖ B>H
10.	In adults with RLS, the AASM suggests the use of bilateral high-frequency peroneal nerve stimulation over no peroneal nerve stimulation. (CONDITIONAL)	⊕⊕⊕⊖ B>H
11.	In adults with RLS, the AASM suggests against the standard use of levodopa.[A] (CONDITIONAL)	⊕⊖⊖⊖ H>b
12.	In adults with RLS, the AASM suggests against the standard use of pramipexole.[B] (CONDITIONAL)	⊕⊕⊕⊖ H>b
13.	In adults with RLS, the AASM suggests against the standard use of transdermal rotigotine.[C] (CONDITIONAL)	⊕⊕⊖⊖ H>b
14.	In adults with RLS, the AASM suggests against the standard use of ropinirole.[D] (CONDITIONAL)	⊕⊕⊕⊖ H>b
15.	In adults with RLS, the AASM suggests against the use of bupropion for the treatment of RLS. (CONDITIONAL)	⊕⊕⊕⊖ B=H
16.	In adults with RLS, the AASM suggests against the use of carbamazepine. (CONDITIONAL)	⊕⊕⊖⊖ H>b
17.	In adults with RLS, the AASM suggests against the use of clonazepam. (CONDITIONAL)	⊕⊖⊖⊖ H>b
18.	In adults with RLS, the AASM suggests against the use of valerian. (CONDITIONAL)	⊕⊖⊖⊖ H>b
19.	In adults with RLS, the AASM suggests against the use of valproic acid. (CONDITIONAL)	⊕⊕⊖⊖ H>b

20. In adults with RLS, the AASM recommends against the use of cabergoline. (STRONG)

» **NO RECOMMENDATIONS WERE MADE FOR THE FOLLOWING TREATMENTS (due to insufficient and/or inconclusive evidence):** Acupuncture, botulinum toxin, cognitive and behavioral therapy, clonidine, IV iron sucrose, near infrared light therapy, perampanel, tramadol, transcranial magnetic stimulation, transcutaneous spinal direct current stimulation, vitamin D, and yoga.

TREATMENT OF ADULTS WITH RLS AND END-STAGE RENAL DISEASE (ESRD)

21. In adults with RLS and ESRD, the AASM suggests the use of gabapentin over no gabapentin. (CONDITIONAL)

22. In adults with RLS and ESRD, the AASM suggests the use of IV iron sucrose over no IV iron sucrose in patients with ferritin < 200 ng/mL and transferrin saturation < 20%. (CONDITIONAL)

23. In adults with RLS and ESRD, the AASM suggests the use of vitamin C over no vitamin C. (CONDITIONAL)

24. In adults with RLS and ESRD, the AASM suggests against the standard use of levodopa. (CONDITIONAL) [A]

25. In adults with RLS and ESRD, the AASM suggests against the standard use of rotigotine. (CONDITIONAL) [E]

» **NO RECOMMENDATIONS WERE MADE FOR THE FOLLOWING TREATMENTS (due to insufficient and/or inconclusive evidence):** vitamin E, and vitamin C + vitamin E.

TREATMENT OF ADULTS WITH PERIODIC LIMB MOVEMENT DISORDER (PLMD)

26. In adults with PLMD, the AASM suggests against the use of triazolam. (CONDITIONAL)

27. In adults with PLMD, the AASM suggests against the use of valproic acid. (CONDITIONAL)

TREATMENT OF CHILDREN WITH RLS

28. In children with RLS, the AASM suggests the use of ferrous sulfate over no ferrous sulfate in patients with appropriate iron status (see good practice statement for iron parameters.