

An exit strategy from dopamine agonists in restless legs syndrome

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Article Summary: Recent guidelines in the treatment of restless legs syndrome continue to recommend the use of gabapentin but *no longer* recommend the use of dopamine agonists such as pramipexole and ropinirole. This article describes a method for down titration of dopamine agonists and up titration of alternative medications.

The current pharmaceutical landscape

Until recently the dopamine agonists (DAs) pramipexole and ropinirole were first line treatments for restless legs syndrome (Aurora et al., 2012). Unfortunately, the DAs have been shown to worsen the symptoms of RLS after many years of use, a phenomenon called 'augmentation' (Silber MH, 2021). For this reason, guidelines have shifted completely away from DAs. Alpha₂delta ligands (A2Ds) such as gabapentin, gabapentin enacarbil, and pregabalin are now considered first line (Garcia-Borreguero D, 2016), (Winkelman JW, 2025). Other medications sometimes used include levodopa, benzodiazepines, and opioids.

How to recognize augmentation

Typical symptoms of augmentation include a gradual worsening of RLS symptoms. This may include symptoms earlier in the day, faster onset and increased intensity. Symptoms may even move from the legs to the arms. Augmentation



can occur after months or years of use and is associated with higher doses.

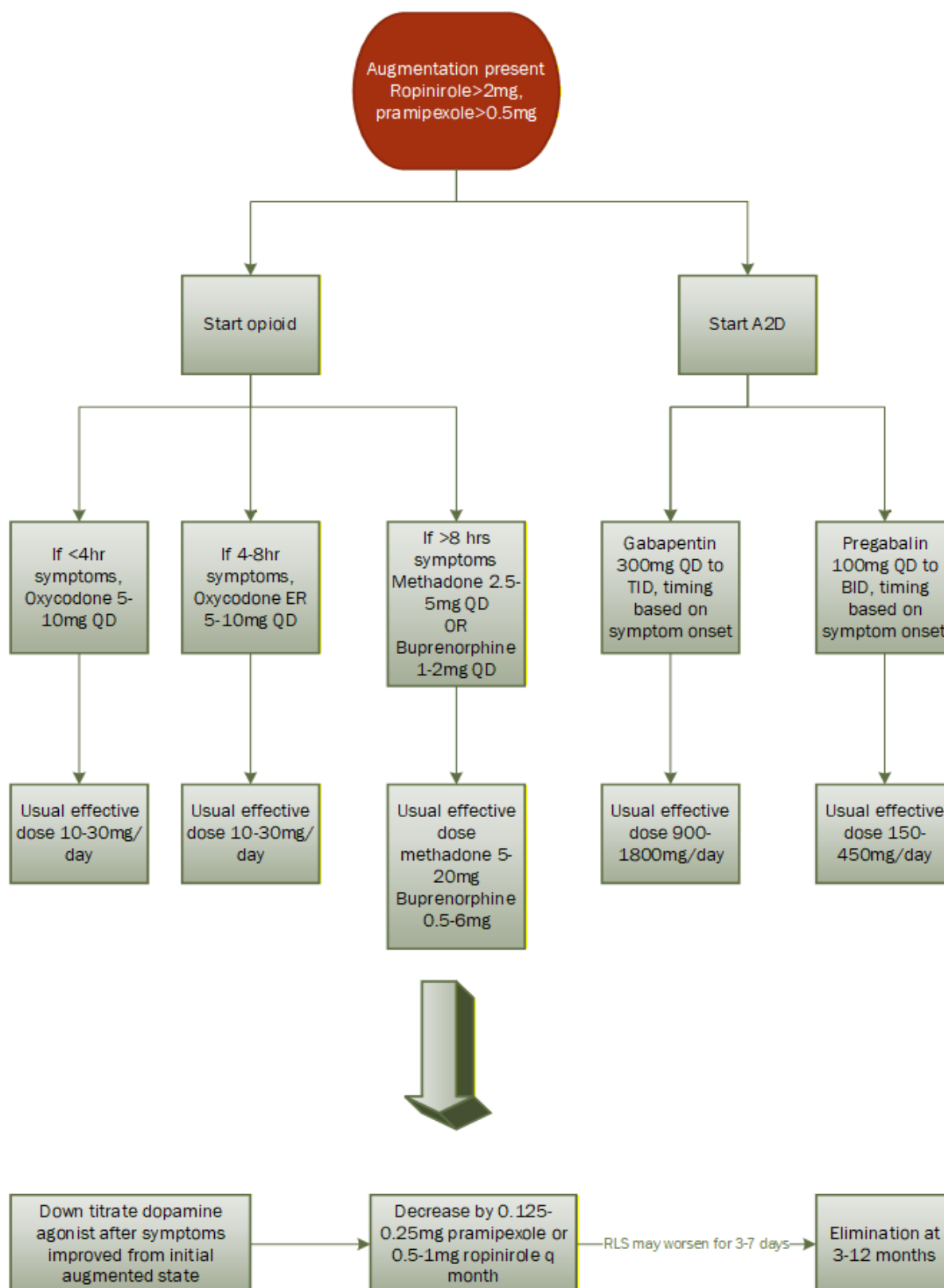
Cross titration of dopamine agonists with alternative agents

Unfortunately, there are no controlled studies that compare cross titration strategies. The goal should be to lower the DA to minimal doses or even off. A 2022 article discusses the intricacies of this process (Winkelman, 2022). A second medication such as buprenorphine or gabapentin should be started as shown in Diagram 1. When the augmented symptoms have improved, the DA can start to be tapered off, monitoring for rebound symptoms and mood. This is a slow process, taking months to a year. There is evidence that being on DAs makes the transition to A2Ds more difficult than for patients not previously taking DAs; as such extreme patience is required (Garcia-Borreguero et al., 2019).

Prevention of Augmentation

Ideally augmentation strategies are used from the beginning, and the latest guidelines support this. For patients currently taking dopamine agonists, but not experiencing augmentation, a proactive approach must still be used. Counseling should reinforce the fact that augmentation is very common. In trials of patients taking pramipexole, augmentation occurred in 1/3 of patients at 2 years (Silber et al., 2003), and may be even more common when used longer. Shared decision making and use of the strategies in this article can be used to help the patient prevent future augmentation.

Diagram 1



Aurora RN, K. D. (2012). The treatment of restless legs syndrome and periodic limb movement disorder in adults-an update for 2012; practice parameters with an evidence-based systematic review and meta-analysis: an American Academy of Sleep Medicine clinical practice guideline. *Sleep*, 1039-1062.

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