South East London Area Prescribing Committee
Formulary recommendation

Reference	**060**
Intervention:	**Gabapentin and pregabalin for the management of restless legs syndrome (RLS)** (Gabapentin and pregabalin are medicines primarily used to treat epilepsy and neuropathic pain)
Date of Decision	**February 2017**
Date of Issue:	**March 2017**
Recommendation:	**Amber 2 – initiation and minimum 3 months supply by the neurology specialist team (specialising in RLS)**
Further Information	Gabapentin and pregabalin are supported for use in line with the local pathway • for the management restless legs syndrome (RLS). • Restless legs syndrome is often accompanied by unpleasant sensations, which may be painful in 30-50% of cases. • Dopamine agonists (such as ropinerole, pramipexole and rotigotine) should be considered first line for the management of RLS. • Gabapentin (300mg – 1200mg at night) may be considered where the patient: – Is intolerant of dopamine agonists or – Has a history of insomnia or compulsive behaviours • Pregabalin (25mg – 300mg at night) may only be considered after gabapentin if the patient is intolerant to gabapentin or there is a risk of significant drug interactions with gabapentin. • Gabapentin may also be considered as a 3rd line agent for refractory, painful/neuropathic RLS where there are residual symptoms despite 2nd line therapy (e.g. with hypnotics or opioids). As per previous bullet point, pregabalin may only be considered after gabapentin in this setting. • Gabapentin and pregabalin are not licensed for the management of RLS. This is an off label indication and patients should be made aware of this at time of initiation. • Treatment will be initiated and monitored by the neurology team (specialising in RLS). The neurology specialist team will regularly review patients for ongoing effectiveness of treatment. • The neurology specialist team will prescribe treatment for a **minimum of 3 months**. Prescribing will only be transferred to primary care when the therapy is confirmed as effective*, the patient is on a stable dose and has been confirmed to not be experiencing troublesome side-effects. • The neurology specialist team should provide the patient's GP with the South East London APC fact sheet about RLS and the medicines used to treat it and general information for the patient. • .Note: Public Health England and NHS England issued advice for prescribers on the risk of the misuse of pregabalin and gabapentin. Healthcare professionals should prescribe pregabalin and gabapentin appropriately to minimise the risks of misuse and dependence and should be able to identify and manage problems of misuse if they arise. These risks will be considered by the neurology specialist team before gabapentin or pregabalin are initiated for RLS. *Effectiveness will be measured through the Epworth Sleepiness Scale (ESS) and the Restless Legs Syndrome Rating Scale (RLSRS).
Shared Care/ Transfer of care required:	No, however general information about RLS and the drugs used to treat it should be shared with the GP as part of the patients individual management plan.
Cost Impact for agreed patient group	• If the prevalence is 3%, that 50% of patients present to primary care for management and 15% of those require drug therapy to treat symptoms this equates to 225 patients per 100,000 population. • If gabapentin and pregabalin were reserved for use in patients that were

Cost Impact for agreed patient group cont'd	intolerant to dopamine agonists, or had a history of compulsive disorders an estimate would be 40 and 10 patients per 100,000 population suitable for these agents respectively (if pregabalin was reserved for use in patients with intolerance or significant adverse reactions to gabapentin). • This equates to treatment costs of £2,000 and £4,000 per 100,000 population per annum respectively. • For SEL this would result in a cost of between £36,000 to £72,000 per year. However, some of this will be a substitution for the dopamine agonists.
Usage Monitoring & Impact Assessment	• Providers to monitor use and submit usage data and audit reports (against this recommendation and the RLS management pathway) upon request to the APC.
	• CCGs to monitor ePACT data. • Exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	**References (from evidence evaluation)** 1. Garcia-Borreguero, D. and Williams, A. An update on restless legs syndrome (Willis-Ekbom disease): clinical features, pathogenesis and treatment. Current Opinions in Neurology 2014 27(4), 493-501. 2. Allen, R., Picchietti, D., Garcia-Borreguero, D. et al. (2014a) Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria-history, rationale, description, and significance. Sleep Medicine 15 (8), 860-873. 3. Nagandla, K. and De, S. (2013) Restless legs syndrome: pathophysiology and modern management. Postgraduate Medical Journal 89 (1053), 402-410. 4. Leschziner, G. and Gringas, P. (2012) Restless legs syndrome. BMJ 344 (), e3056. 5. Garcia-Borreguero, D., et al. (2012a) European guidelines on management of restless legs syndrome: report of a joint task force by the European Federation of Neurological Societies, the European Neurological Society and the European Sleep Research Society. European Journal of Neurology: The Official Journal of the European Federation of Neurological Societies 19 (11), 1385-96. 6. Hening W, Walters A, Allen R et al. Impact, diagnosis and treatment of restless legs syndrome (RLS) in a primary care population: the REST (RLS epidemiology, symptoms, and treatment) primary care study. Sleep Medicine 2004 p5237-5246 7. Stevens M. Restless legs syndrome/Willis-Ekborn disease morbidity: burden, quality of life, cardiovascular aspects, and sleep> Sleep Medicine Clinics 2015 10 p369-373 8. Neurontin caps Summary of product characteristics. Available here (accessed 23/08/2016) 9. Lyrica caps, Summary of product characteristics. Available here (accessed 23/08/2016) 10. Bogan R, Cramer Bornemann M, Kushida C. Long-term maintenance treatment of restless legs syndrome with gabapentin enacarbil: A RCT. Mayo Clinic Proceedings 2010 85 (6) p512-521 11. Cundy K Sastry S, Luo W et al. Clinical pharmacokinetics of XP13512, a novel transported prodrug of gabapentin. Journal of Clinical Pharmacology 2008 48 (12) p1378-1388 12. Garcia-Borreguero D, Larrosa O, de la Llave Y et al. Treatment of restless leg syndrome with gabapentin: a double-blind, cross-over study. Neurology 2002; 59: 1573-1579 13. Lee D, Ziman R, Perkins A et al. A randomized, double-blind, placebo-controlled study to assess the efficacy and tolerability of gabapentin enacarbil in subjects with Restless Legs Syndrome. Journal of the Canadian Society of Medicine 2011 7 p282-292 14. Kushida CA, et al. Randomized, double-blind, placebo-controlled study of XP13512/ GSK1838262 in patients with RLS. Neurology 2009; 72: 439–446. 15. Ellenbogen AL, Thein SG, Winslow DH, et al. A 52-week study of gabapentin enacarbil in restless legs syndrome. Clin Neuropharmacol 2011; 34: 8–16. 16. Allen R, Chen C, Garcia-Borreguero D et al. Comparison of pregabalin with pramipexole for Restless Legs Syndrome. New England Journal of Medicine 2014 370 (7) p621-631 17. Public Health England and NHS England December 2014. Advice for prescribers on the risk of the misuse of pregabalin and gabapentin

NOTES:

a) Area Prescribing Committee recommendations and minutes are available publicly on member CCG websites.

b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.

c) Not to be used for commercial or marketing purposes. Strictly for use within the NHS.