

**South East London Integrated Medicines Optimisation Committee
Formulary recommendation**

Reference	062
Intervention:	Specific opioids (codeine phosphate or oxycodone/ naloxone) for the management of restless legs syndrome (RLS) (Opioids are medicines used to control moderate to severe pain)
Date of Decision	February 2017, updated March 2024 following RLS pathway update
Date of Issue:	March 2017, re-issued March 2024
Recommendation:	Amber 2 – initiation and minimum 3 months supply by the neurology specialist team (specialising in RLS)
Further Information	<ul style="list-style-type: none"> • Codeine, and oxycodone/naloxone (Targinact®) are accepted for use in line with the local pathway as 2nd line treatment options for the management of pain associated with severe refractory restless legs syndrome (RLS). • Restless legs syndrome is often accompanied by unpleasant sensations, which may be painful in 30-50% of cases. • Codeine phosphate (30 – 90mg at night) should be considered first. • Oxycodone/naloxone (5mg/2.5mg –20mg/10mg twice a day) may be considered after codeine phosphate. • The patient’s first line therapy will be stopped before initiation of an opioid. • Whilst codeine is not licensed for the treatment of RLS, it is licensed for the management of pain. Opioids would generally be used for treatment of patients where pain is a significant symptom. It should however be noted that a single dose of codeine >60mg is outside of the product licence for use in analgesia. Oxycodone/naloxone is licensed as a 2nd line treatment for the symptomatic treatment of patients with severe to very severe idiopathic RLS after failure of dopamine agonists. • 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 SEL IMOC GP fact sheet about RLS and the medicines used to treat it and general information for the patient. • Oxycodone is a Schedule 2 controlled drug. • Prescribers should be aware of the risks associated with these agents, including misuse and dependence. These risks will be considered by the neurology specialist team before these agents are initiated for RLS. The product information for oxycodone/naloxone recommends that treatment should be reviewed every 3 months to evaluate whether benefits outweigh the risks. <p><small>*Effectiveness will be measured through the Epworth Sleepiness Scale (ESS) and the Restless Legs Syndrome Rating Scale (RLSRS).</small></p>
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 patient’s individual management plan.
Cost Impact for agreed patient group	<ul style="list-style-type: none"> • If the prevalence is 3%, that 50% of patients present to healthcare systems for management and that 15% of those require drug therapy to treat symptoms this equates to 225 per 100,000 population. • If 20% of these patients do not respond adequately to dopamine agonists or alpha-2-delta ligands and if 50% of these are deemed suitable for opioids (the other 50% being suitable for benzodiazepines or hypnotics this equates to 23 patients per 100,000 population.

	<ul style="list-style-type: none"> • Costs would be <£1000 per 100,000 if codeine was used instead for this patient population. • If it is assumed 25% (6 patients per 100,000 population) go on to require oxycodone/naloxone at an average dose of 20mg/10mg, this would equate to a cost of £6,600 per 100,000 population per year. • For SEL this would result in a cost of up to £137,000 per year. However, some of this will be a substitution for the dopamine agonists/gabapentin/pregabalin.
Usage Monitoring & Impact Assessment	Acute Trusts: <ul style="list-style-type: none"> • Monitor use and submit usage data and audit reports (against this recommendation and the pathway) upon request to the SEL IMOC
	SEL Borough Medicines Optimisation Teams: <ul style="list-style-type: none"> • Monitor ePACT2 data and exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	References (from evidence evaluation) <ol style="list-style-type: none"> 1. Garcia-Borreguero, D. and Williams, A. An update on restless legs syndrome (Willis-Ekbom disease): clinical features, pathogenesis and treatment. <i>Current Opinions in Neurology</i> 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. <i>Sleep Medicine</i> 15 (8), 860-873. 3. Nagandla, K. and De, S. (2013) Restless legs syndrome: pathophysiology and modern management. <i>Postgraduate Medical Journal</i> 89 (1053), 402-410. 4. Leschziner, G. and Gringas, P. (2012) Restless legs syndrome. <i>BMJ</i> 344 (), e3056. 5. Garcia-Borreguero, D., Ferini-Strambi, L., Kohnen, R. 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. <i>European Journal of Neurology: The Official Journal of The European Federation of Neurological Societies</i> 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. <i>Sleep Medicine</i> 2004 p5237-5246 7. Stevens M. Restless legs syndrome/Willis-Ekbom disease morbidity: burden, quality of life, cardiovascular aspects, and sleep> <i>Sleep Medicine Clinics</i> 2015 10 p369-373 8. Codeine, summary of product characteristics. Available online at: http://www.medicines.org.uk/emc/medicine/23910 (accessed on 04/09/2016) 9. Targinact, summary of product characteristics. Available online at: http://www.medicines.org.uk/emc/medicine/22908 (accessed on 04/09/2016) 10. de Oliveira C, Carvalho L, Carlos K et al. Opioids for restless legs syndrome (Review). <i>Cochrane Library</i> April 2016 11. Trenkwalder C, Benes H, Grote L et al. Prolonged release oxycodone-naloxone for treatment of severe restless legs syndrome after failure of previous treatment: a double-blind, randomised, placebo-controlled trial with an open label extension. <i>Lancet Neurology</i> 2013 12 p1141-1150. 12. Walters A, Wagner M, Hening W et al. Successful treatment of the idiopathic restless legs syndrome in a randomized double-blind trial of oxycodone versus placebo. <i>Sleep</i> 1993 16(4) p327-332 13. Walters A, Winklemann J, Trenkwalder C et al. Long-Term follow-up on restless legs syndrome patients treated with opioids. <i>Movement disorders</i> 2001 16(6) p1105-1109

NOTES:

- a) SEL IMOC recommendations and minutes are available publicly via the [website](#)
- b) This SEL IMOC 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**