

Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	6 th June 2017
Appraisal & Details	The Northern (NHS) Treatment Advisory Group considered an appraisal of Pitolisant (Wakix®) for the treatment of narcolepsy with or without cataplexy in adults.
Recommendation	The Northern (NHS) Treatment Advisory Group <u>does not</u> recommend the use of Pitolisant. The group was concerned about the following limitations to the clinical trial data: <ul style="list-style-type: none"> • Small patient numbers in clinical trials (n=95 and n=106) • Short duration (7 or 8 weeks only) thereby limiting findings related to long term efficacy and safety in particular. • Limited generalisability of the findings because children, those with unstable comorbidities and those who declined to participate were excluded. • In both studies patients could remain on existing therapies such as sodium oxybate or antidepressants for treating cataplexy, therefore the findings may not be generalizable to patients who are not taking any other medicines for narcolepsy or cataplexy. • A high placebo effect was found on cataplexy rate which may reflect subjective and emotional triggers. • One of the clinical trials (HARMONY Ibis) which was considered pivotal for the license, hasn't yet been fully published so cannot be assessed.
Clinical evidence summary	Two small randomised controlled trials (RCT s) of pitolisant 5–40 mg per day in adults with narcolepsy with or without cataplexy showed that compared with placebo, Pitolisant improved excessive daytime sleepiness, improved time awake in a darkened room and reduced the weekly cataplexy rate. Pitolisant was also compared with modafinil in a non-inferiority analysis. Non-inferiority to modafinil was not shown. The long-term safety and efficacy data for pitolisant are limited. There are no data showing how pitolisant compares to other treatments for narcolepsy or how effective it is in patients who cannot tolerate or do not respond to current treatment options.
Safety	The most common adverse events in the pitolisant groups were insomnia headache, nausea, anxiety, irritability, dizziness, depression, tremor, sleep disorders, fatigue, vomiting, vertigo, dyspepsia, weight increase and upper abdominal pain. The most serious adverse drug reactions are abnormal weight

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	<p>decrease and spontaneous abortion. No participants in the pitolisant groups had withdrawal syndrome during the withdrawal phase. The EPAR states that some uncertainties remain with regard to the effects of pitolisant on depression, weight and appetite, ulcer formation, and more generally on adverse events that might occur after long-term exposure.</p>
Patient Perspective	<p>Narcolepsy is a disabling sleep disorder characterised by excessive daytime sleepiness. Patients are often unable to stay awake or asleep for long periods of time. Around 70% of people with narcolepsy also have cataplexy, which is a sudden loss of muscle tone triggered by strong emotions. Episodes can last from seconds to minutes and occur with varying frequency.</p> <p>Patients will be pleased that there is another treatment option available for a difficult to treat condition. However they will also want to know that pitolisant will be of benefit in the long term and that there are no long term adverse effects; there is insufficient information available to confirm this. It is also not clear how pitolisant compares to other treatments for narcolepsy.</p>
Cost analysis summary	<p>The company anticipate that pitolisant will be used initially for people with narcolepsy who either cannot tolerate current treatments or have not responded to these. It is estimated that narcolepsy affects 0.05% of the population with approx. 31,000 cases in the UK. About 5,000 of these are thought to receive treatment. Of the treated population, it is estimated that about 50% of patients may not tolerate or not respond to their existing medicines and therefore may be eligible for treatment with pitolisant.</p> <p>Using the estimates provided above, approximately 270 patients across the North East and Cumbria receive treatment for their narcolepsy with 50% of these (135) potentially eligible for treatment with pitolisant. The cost of 30 days treatment with pitolisant at a dose of 4.5 mg to 36 mg once daily is £310.00 to £620.00 excluding VAT.</p> <p>The potential cost impact of Pitolisant in the NE&C region for 135 patients is therefore £508,850 pa to £1,018,035 pa.</p> <p>The annual cost for sodium oxybate is £874,800 to £1,749,600 or £9817 to £515,549 pa for other treatments.</p>
Financial impact PbR: likely In-tariff.	<p>No financial impact is considered applicable as the group does not recommend this treatment.</p>