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PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: PS144 FINAL
FIRST BOARD DATE: 29 JUL 2015
LAST BOARD DATE: 31 JAN 2018



Pan Mersey
Area Prescribing Committee

NALOXEGOL Tablets (Moventig®▼)

GREEN

The Pan Mersey Area Prescribing Committee recommends the prescribing of NALOXEGOL Tablets (Moventig®▼) as an option for treating opioid induced constipation in adults in accordance with [NICE TA345](#) (22nd July 2015)

Naloxegol is recommended, within its marketing authorisation, as an option for treating opioid induced constipation in adults whose constipation has not adequately responded to laxatives.

An inadequate response is defined as opioid-induced constipation symptoms of at least moderate severity in at least 1 of the 4 stool symptom domains (that is, incomplete bowel movement, hard stools, straining or false alarms) while taking at least 1 laxative class for at least 4 days during the prior 2 weeks.

When naloxegol therapy is initiated, it is recommended that all currently used maintenance laxative therapy should be halted, until clinical effect of naloxegol is determined.

For further information on the treatment of chronic constipation please refer to the Pan Mersey Chronic Constipation Guidelines

<https://www.panmerseyapc.nhs.uk/media/2235/constipation.pdf>

Note: Patients who are not eligible for treatment under this policy may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. If appropriate an exceptional funding request will be required following the usual locally defined process.

NALOXEGOL Tablets (Moventig®▼)

<p>EFFECTIVENESS¹</p> <p>Naloxegol is a form of naloxol which has been pegylated, in this form it selectively antagonises peripheral opioid receptors to relieve constipation. The main clinical evidence for naloxegol came from the pivotal, phase III trials KODIAC 4 (n=649) and KODIAC 5 (n=697). These international, multicentre, randomised, double-blind trials compared naloxegol with placebo in adults with non-cancer pain and opioid-induced constipation.</p> <p>In both KODIAC trials, treatment with naloxegol 25mg resulted in significantly higher response rates than placebo in both the overall population (KODIAC 4: 44.4% vs 29.4%, p=0.001; KODIAC 5: 29.3% vs 39.7%, p=0.021) and the laxative inadequate responder population (KODIAC 4: 48.7% vs 28.8%, p=0.002; KODIAC 5: 46.8% vs 31.4%, p=0.014). In both studies, naloxegol showed consistent improvements in a range of secondary end points, including time to first post-dose spontaneous bowel movement (SBM), total SBMs per week, number of days per week with at least 1 SBM, and use of rescue medication at least once over the treatment period.</p>	<p>SAFETY</p> <p>The most common adverse reactions are abdominal pain and diarrhoea ($\geq 1/10$), nasopharyngitis, headache, flatulence, nausea, vomiting, hyperhidrosis ($\geq 1/100$ to $< 1/10$)². The majority of gastrointestinal (GI) adverse reactions are graded as mild to moderate, occur early in treatment and resolve with continued treatment¹. Opioid withdrawal symptoms are an uncommon adverse effect.</p> <p>Contra-indications²</p> <ul style="list-style-type: none"> - Known or suspected GI obstruction or increased risk of recurrent GI obstruction. - Concomitant use with strong CYP3A4 inhibitors (e.g. clarithromycin, ketoconazole, itraconazole or telithromycin; protease inhibitors such as ritonavir, indinavir or saquinavir; grapefruit juice when consumed in large quantities), - Underlying cancer with heightened risk of GI perforation. <p>Cautions²</p> <ul style="list-style-type: none"> - Any condition which might result in impaired integrity of the GI tract wall. - Clinically important disruptions to blood/brain barrier - CV conditions (MI within 6 months, symptomatic congestive heart failure, overt CV disease, QT interval ≥ 500msec). - Patients taking methadone <p>Refer to SPC for full information.</p>									
<p>COST (On-line BNF & Drug Tariff accessed 9th Oct 2017)</p> <table border="1"> <thead> <tr> <th>Treatment</th> <th>Regimen</th> <th>Annual treatment cost (£)</th> </tr> </thead> <tbody> <tr> <td>Naloxegol</td> <td>25mg once daily (12.5mg for people with renal insufficiency)</td> <td>671.60</td> </tr> <tr> <td>Methylnaltrexone (4 months of treatment)^a</td> <td>Subcutaneous injection, every 2 days</td> <td>1,284.05</td> </tr> </tbody> </table> <p>^a Methylnaltrexone is licensed for the treatment of opioid-induced constipation but is currently restricted by Pan Mersey for palliative care recommendation only.</p> <p>NICE states that although additional drug costs are anticipated where naloxegol is used in place of conventional laxative treatments, there may be cost savings if it is used as an alternative to methylnaltrexone. If a person's condition responds to treatment with naloxegol, there may be further savings to commissioners on treating opioid-induced constipation because of the avoidance of hospital attendances, or treatments such as enemas.³</p>	Treatment	Regimen	Annual treatment cost (£)	Naloxegol	25mg once daily (12.5mg for people with renal insufficiency)	671.60	Methylnaltrexone (4 months of treatment) ^a	Subcutaneous injection, every 2 days	1,284.05	<p>PATIENT FACTORS²</p> <p>No dosage adjustment required in elderly patients, mild renal impairment and mild to moderate hepatic impairment.</p> <p>Use in patients with severe hepatic impairment is not recommended.</p> <p>Use in pregnancy and breast feeding is not recommended.</p> <p>Patients should be advised to promptly report severe, persistent or worsening gastrointestinal symptoms to their physician. Consideration may be given to lowering the dose to 12.5mg in patients experiencing severe gastrointestinal adverse events depending upon the response and tolerability of individual patients.</p>
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<p>PRESCRIBING INFORMATION</p> <p>The recommended dose is 25mg once daily, taken in the morning for patient convenience to avoid bowel movements in the middle of the night. It should be taken on an empty stomach at least 30 minutes prior to the first meal of the day or 2 hours after the first meal of the day. When naloxegol therapy is initiated, it is recommended that all currently used maintenance laxative therapy should be halted, until clinical effect of naloxegol is determined. The starting dose in moderate or severe renal insufficiency and for patients taking moderate CYP3A4 inhibitors (e.g. diltiazem, verapamil) is 12.5mg. The dose can be increased to 25mg if 12.5mg is well tolerated by the patient.²</p> <p>If the opioids are stopped the naloxegol should also be stopped.</p>
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REFERENCES

1. National Institute for Health and Care Excellence. Naloxegol for treating opioid-induced constipation. [NICE Technology Appraisal Guidance 345](#), July 2015. Accessed 22/07/15.
2. Moventig®▼ Summary of Product Characteristics, AstraZeneca UK Ltd. Accessed 09/10/2017 <http://www.medicines.org.uk/emc/medicine/30483>
3. National Institute for Health and Care Excellence. [Costing statement: Naloxegol for treating opioid-induced constipation \(TA345\)](#), July 2015. Accessed 22/07/15.