Pan Mersey
Area Prescribing Committee

NALDEMEDINE tablets (Rizmoic® ▼) for the treatment of opioid-induced constipation

The Pan Mersey Area Prescribing Committee recommends the prescribing of NALDEMEDINE tablets (Rizmoic® ▼) for the treatment of opioid-induced constipation in accordance with NICE TA651.

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Naldemedine is recommended as an option for treating opioid-induced constipation in adults who have had laxative treatment.[1]

The treatment of opioid-induced constipation depends on whether the opioid is the only cause of the constipation (pure opioid-induced constipation) or if there are other contributing factors (mixed aetiology constipation). Treatment may include a peripherally acting mu-opioid receptor antagonist (PAMORA) alone. But, commonly a PAMORA and a conventional laxative are used together. Naldemedine is an oral PAMORA for adults who have had laxative treatment. [1]

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

NICE do not expect this guidance to have a significant impact on resources; that is, the resource impact of implementing the recommendations in England will be less than £5 million per year in England (or £9,000 per 100,000 population). This is because naldemedine is a further treatment option and the overall cost of treatment will be similar to the current treatment options available.[1]

Note: Patients who are not eligible for treatment under this statement 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. In this situation, follow locally defined processes.

NALDEMEDINE 200 microgram tablets (Rizmoic® ▼) for the treatment of opioid-induced constipation

Effectiveness

Naldemedine is clinically effective compared with placebo and there are more clinical benefits for patients than considered in the trials.[1] The clinical evidence shows that naldemedine increases the frequency of bowel movements compared with no treatment and other PAMORAs.[1]

The company submission included 4 pivotal randomised trials (COMPOSE-1, -2 -3 and -4) and 3 supportive open-label safety studies (COMPOSE-5, -6 and -7). The primary outcome for COMPOSE-1, -2 and -4 was the proportion of people who had spontaneous bowel movements.

- COMPOSE-1: naldemedine 48%, placebo 35%, percentage change 13.0% (95% confidence interval [CI] 4.8 to 21.2).
- COMPOSE -2: naldemedine 53%, placebo 34%, percentage change 18.9% (95% CI 10.8 to 27.0).
- COMPOSE-4: naldemedine 71%, placebo 34%, percentage change 36.8% (95% CI 23.7 to 49.9).

Because the response rates in the COMPOSE trials were not 100%, this suggests that patients having naldemedine had mixed aetiology constipation.[1]

Naldemedine is an antagonist of opioid binding at the mu-, delta-, and kappa-opioid receptors. Naldemedine functions as a peripherally-acting mu-opioid receptor antagonist in tissues such as the gastrointestinal tract, thereby decreasing the constipating effects of opioids without reversing the central nervous system (CNS)-mediated opioid effects.[2]

Safety

The most commonly reported adverse reactions in patients with chronic non-cancer pain and opioid-induced constipation (OIC) included: Abdominal pain (7.8%), diarrhoea (5.9%), nausea (3.6%), and vomiting (1.1%).

The most commonly reported adverse reactions in patients with cancer and OIC included: Diarrhoea (24.5%) and abdominal pain (3.9%).[2]

Contraindications include hypersensitivity to the active substance or to any of the excipients and patients with known or suspected gastrointestinal obstruction or perforation or patients at increased risk of recurrent obstruction.[2] Full list of side effects can be found in the Summary of Product Characteristics.

Special warnings include:

Gastrointestinal adverse reactions, opioid withdrawal syndrome, patients with cardiovascular conditions, severe hepatic impairment, concomitant use with strong CYP3A inhibitors and inducers.[2]

Cost NHS BSA dm + d browser accessed 13th October 2020

Treatment	Regimen	Annual Treatment Cost (£)
Naloxegol	25mg once daily (12.5mg for people with renal insufficiency)	671.60
Methylnaltrexone (4 months treatment)[a]	Subcutaneous injection, every 2 days	1,263.00
Naldemedine	200 micrograms (one tablet) daily.	543.85

[a] Methylnaltrexone is licensed for the treatment of opioid-induced constipation but is currently restricted by Pan Mersey for palliative care recommendation only.

Patient factors

There is limited experience in patients treated with opioid pain medicinal product(s) at daily doses of more than the equivalent of 400 mg of morphine. There is no experience in patients treated for constipation induced by partial opioid mu-agonists (e.g. buprenorphine).[2]

Prescribing information

The recommended dose of naldemedine is 200 micrograms (one tablet) daily.

Naldemedine may be used with or without laxative(s). It may be taken at any time of the day but it is recommended to be taken at the same time every day.[2] Naldemedine therapy should be discontinued if opioid therapy is stopped.

References

1. National Institute for Health and Care Excellence. Technology Appraisal Guidance TA651: Naldemedine for treating opioid-induced constipation; 30 September 2020. Accessed 13th October 2020.
2. Shionogi. Summary of Product Characteristics - Rizmoic 200 micrograms film-coated tablets; 30 January 2020. Accessed 13th October 2020.