25 September 2014
EMA/CHMP/496850/2014
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Moventig

naloxegol

On 25 September 2014 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Moventig, 12.5 mg and 25 mg, film-coated tablet intended for the treatment of opioid-induced constipation (OIC) in adult patients who have had an inadequate response to laxative(s). The applicant for this medicinal product is AstraZeneca AB. They may request a re-examination of any CHMP opinion, provided they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

The active substance of Moventig is naloxegol, a peripheral opioid receptor antagonist to be used as drug for opioid induced constipation. The ATC Code is A06AH03. Naloxegol functions as a peripherally-acting mu-opioid receptor antagonist in the gastrointestinal tract due to the chemical structure which refers to PEGylated derivative of the mu opioid receptor antagonist naloxone, thereby decreasing the constipating effects of opioids without impacting opioid-mediated analgesic effects on the central nervous system. Indeed, PEGylation reduces naloxegol's passive permeability and also renders the compound a substrate for the P glycoprotein transporter. Due to poorer permeability and increased efflux of naloxegol across the blood brain barrier, related to P-gp substrate properties, the CNS penetration of naloxegol is minimal.

The benefits with Moventig are its ability to decrease the constipating effects of opioids without impacting opioid-mediated analgesic effects on the central nervous system. Moventig demonstrated higher response rates than placebo in the primary efficacy endpoint, defined by >3 Spontaneous Bowel Movements (SBMs) per week and a change from baseline of >1 SBM per week for at least 9 out of the 12 study weeks and 3 out of the last 4 weeks. In the first pivotal study, response rates in the placebo, 12.5 mg and 25 mg groups in laxative inadequate responders (LIR) were 28.8%, 42.6% (p=0.028) and 48.7% (p=0.002). In the second pivotal study, the corresponding response rates were 31.4, 42.4% (p=0.074, not significant under multiplicity testing) and 46.8% (p=0.014). It reduces the time to first SBM in LIR subgroup when compared to placebo with a respective median time to first post dose SBM of 43.4, 20.6, and 5.4 hours, for placebo, 12.5 mg and 25 mg dose respectively in the first

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion.

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pivotal study and the corresponding times to first post dose SBM were 38.2, 12.8, and 18.1 hours, respectively in the second pivotal study. Furthermore, it increases the mean number of days per week with at least one SBM in the LIR subgroup for the 25 mg dose ($p<0.001$) and also for the 12.5 mg dose ($p=0.006$) in both pivotal studies. The 25 mg dose in the LIR subgroup improves rectal straining. The 25 mg dose in the LIR subgroup increases mean days per week compared with placebo with at least 1 complete spontaneous bowel movement (CSBM) in both pivotal studies ($p<0.001$). Naloxegol also reports positive patient reported outcomes (PRO) in terms of constipation symptoms, in patient assessment of constipation symptoms (PAC SYM) rectal domain scores and for the stool domain scores.

The most common side effects are: abdominal pain, diarrhoea, nausea, headache and flatulence. The majority of gastrointestinal adverse reactions were graded as mild to moderate, occurred early in treatment and resolved with continued treatment. They were often reported as having a component of cramping discomfort. Therefore, Naloxegol at doses of 12.5 mg and 25 mg is generally safe and well tolerated as compared with placebo in the treatment of OIC patients with non-cancer related pain.

A pharmacovigilance plan for Moventig will be implemented as part of the marketing authorisation.

The approved indication is: "Moventig is indicated for the treatment of opioid-induced constipation (OIC) in adult patients who have had an inadequate response to laxative(s) ". Moventig is a medicinal product subject to medical prescription

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers there to be a favourable benefit-to-risk balance for Moventig and therefore recommends the granting of the marketing authorisation.