AWMSG Secretariat Assessment Report – Limited submission

Diamorphine hydrochloride (Ayendi®) 720 microgram/actuation and 1600 microgram/actuation Nasal Spray

Company: Wockhardt UK Ltd

Licensed indication under consideration: treatment of acute severe nociceptive pain in children and adolescents 2 to 15 years of age in a hospital setting. Diamorphine hydrochloride (Ayendi®) nasal spray should be administered in the emergency setting by practitioners experienced in the administration of opioids in children and with appropriate monitoring.

Marketing authorisation date: 18 October 2013

Comparator(s)

The comparator included in the company submission is:

- Unlicensed intranasal diamorphine

Limited submission details

- Use of intranasal diamorphine for the indication under consideration is recognised as established practice and is recommended in clinical guidelines. Ayendi® is the first licensed intranasal diamorphine product for the treatment of acute severe nociceptive pain in children and adolescents 2 to 15 years of age in a hospital setting.
- Anticipated usage in NHS Wales considered to be of minimal budgetary impact.

Clinical effectiveness

- Ayendi® is a multi-patient product available as a powder for solution which is reconstituted with diluent and delivered in a non-pressurised metered dose nasal spray. Once reconstituted it must be used within two weeks. The recommended strength and dose (number of nasal sprays) of Ayendi® is based on the age and bodyweight of the patient and no dose calculations are required.
- Ayendi® was granted its license based on a number of studies submitted to the Medicines and Healthcare Products Regulatory Agency (MHRA). The company submission includes results from three of these; one pivotal study, one pharmacokinetic study and one safety study.
- The pivotal study was a randomised, single blind, UK multicentre clinical study designed to compare the effectiveness, acceptability and safety of diamorphine nasal spray (n = 204) with intramuscular morphine (n = 200) in patients aged between 3 and 16 years presenting in an emergency department with acute pain due to a clinical fracture. The diamorphine ampoules used in the study were reconstituted according to patient weight and administered using a nasal dosing device into one nostril. Ayendi® nasal spray is administered in alternate nostrils

but the MHRA considered this difference in delivery would have minimal effect and the study results can be extrapolated to Ayendi®.

- Pain was assessed with the 6-point Wong Baker face pain scale (where 1 = smiling and 6 = crying). Results showed that pain scores improved over time in both groups, although the onset of analgesia was faster in the group receiving diamorphine nasal spray. The distribution of pain scores was significantly lower in the diamorphine nasal spray group than in the intramuscular morphine group at 5 (4.29, p = 0.04), 10 (8.74, p = 0.003) and 20 minutes (9.84, p = 0.002) after treatment. At 30 minutes there was no difference (1.66, p = 0.20). Staff and parent acceptability of the nasal spray treatment was also shown to be significantly greater.
- The pharmacokinetics of Ayendi® were assessed in an open-label, single dose study in patients aged between 1 and 16 years undergoing surgery (n = 50), conducted by the applicant company. The company concludes that the pharmacokinetics of diamorphine metabolites were similar to those reported in previous studies of morphine metabolism in young children.
- The safety of Ayendi® was assessed in the pivotal study and an open-label, single dose study in patients aged between 2 and 16 years in an emergency setting with a fracture or other trauma (n = 226). No severe or serious adverse events were observed in the study. The most common treatment-related adverse event was mild nasal irritation: the majority resolving within an hour of administration. The MHRA concluded Ayendi® has an acceptable level of safety.
- In the absence of a licensed diamorphine nasal spray, an ampoule of diamorphine is diluted according to body weight and the dose is administered using a single use nasal atomiser. This requires dose calculations and staff preparation time.
- The use of diamorphine nasal spray for severe pain in children and adolescents is recommended in the Royal College of Emergency Medicine clinical guidelines and in guidelines produced by the Advanced Paediatric Life Support Group.

Budget impact

- The company estimates 2,002 patients (aged 2 to 15 years) in Wales are eligible for Ayendi® in Year 1, rising to 2,029 in Year 5. Due to limited published data for Wales the applicant company based this on published data on patients (aged 2 to 15 years) attending emergency departments in Scotland for fractures or burns, and applied this to population and A&E attendance data for Wales.
- The budget impact analysis is based on Ayendi® partially displacing unlicensed intranasal diamorphine. The company assumes, given that Ayendi® is a multi-patient product, unlicensed intranasal diamorphine may continue to be used because some hospitals may not see enough patients to warrant using Ayendi®.
- The company estimate [commercial in confidence figure removed] patients will be treated with Ayendi® in Year 1 based on an anticipated uptake of [commercial in confidence figure removed], rising to [commercial in confidence figure removed] patients in Year 5 based on estimated uptake of [commercial in confidence figure removed]. The net medicine acquisition costs of introducing Ayendi® is estimated to be [commercial in confidence figure removed] in Year 1, rising to [commercial in confidence figure removed] in Year 5.
- The estimated budget impact costs for Ayendi® and unlicensed intranasal diamorphine are based on the medicine acquisition and material costs only; associated administration costs have not been considered.

Additional information

- AWTTC is of the opinion that, if recommended, diamorphine hydrochloride (Ayendi®) for the indication under consideration may be appropriate for use within NHS Wales prescribed under specialist recommendation.

Evidence search

Date of evidence search: 15 and 16 July 2019.
Date of range of evidence search: no date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Diamorphine hydrochloride (Ayendi®) 720 microgram/actuation and 1600 microgram/actuation Nasal Spray. Reference number: 2406. October 2019.