AWMSG Secretariat Assessment Report – Limited submission

Fosaprepitant (IVEMEND®) 150 mg powder for solution for infusion

Company: Merck Sharp & Dohme Ltd

Licensed indication under consideration: Prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in patients aged 6 months to less than 18 years of age. Fosaprepitant is given as part of a combination therapy.

Date of licence extension: 30 April 2018

Comparator(s)

The comparators included in the company submission are:

- aprepitant (EMEND®) in combination with ondansetron with or without dexamethasone, a 5-HT3 antagonist and a corticosteroid respectively
- ondansetron and dexamethasone.

Limited submission details

- A minor licence extension.
- Anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

Clinical effectiveness

- Fosaprepitant has been in use in Wales for adults since 2009. It did not meet the criteria for appraisal by the All Wales Medicines Strategy Group (AWMSG), as its marketing authorisation date for the adult population was granted before 1 October 2010. This submission considers a licence extension for fosaprepitant for the prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in patients aged from 6 months to less than 18 years when used in combination with other antiemetic agents.
- Fosaprepitant is a prodrug which is rapidly converted in 30–60 minutes to aprepitant which is within the period of infusion. In 2016, AWMSG approved aprepitant capsules and oral suspension in patients aged from 6 months to less than 18 years old for the same indication under consideration.
- Fosaprepitant was given a licence extension for paediatric patients based on a number of studies previously submitted to the European Medicines Agency. There are two dosing regimens: 1-day fosaprepitant for single-day chemotherapy regimens and up to three days of fosaprepitant for single or multi-day chemotherapy regimens. The efficacy of the paediatric 1-day fosaprepitant regimen was extrapolated from two phase III studies in adult patients receiving a single-dose of fosaprepitant. The efficacy of the paediatric 3-day fosaprepitant regimen was bridged from one pivotal phase III study in paediatric patients receiving the 3-day oral aprepitant regimen and two supportive studies (phase I and phase III). The fosaprepitant dosing regimens in children were based on

modelling and simulation of paediatric pharmacokinetic data. This approach was supported by the Committee for Medicinal Products for Human Use (CHMP).

- The safety of fosaprepitant in paediatric patients was investigated in three studies and supported by the 3-day oral aprepitant studies referred to above. No new safety concerns were identified for fosaprepitant in paediatric patients. CHMP concluded that the safety profile of fosaprepitant in the paediatric population is consistent with the known safety profile of aprepitant, and fosaprepitant in the adult population.
- Clinical expert opinion sought by AWTTC noted that fosaprepitant would be a useful optional treatment, particularly with highly emetogenic chemotherapy when the oral route is unavailable.
- The company also proposes fosaprepitant may be a useful option when administration to children is affected by factors such as anticipatory chemotherapy-induced nausea and vomiting, and chemotherapy-related odynophagia and mucositis.

Budget impact

- The company estimates that there will be 126 children diagnosed with cancer in Year 1 rising to 129 patients in Year 5; this is based on Welsh Cancer Intelligence and Surveillance Unit data, national population projections for Wales statistics and an estimated 9% annual mortality rate based on the 1-year survival rates for childhood cancer in the UK. Based on clinical expert opinion outside of Wales sought by the company, it is assumed that 75% of paediatric patients in Wales will receive chemotherapy and all newly diagnosed patients will receive moderately or highly emetogenic chemotherapy regimens. This equates to 95 patients in Year 1 increasing to 97 patients in Year 5 eligible to receive fosaprepitant.
- The company estimates that the market uptake (6.8%) will remain the same in Year 1 to Year 5 which equates to six patients in Year 1 rising to seven patients in Year 5. The company's rationale for the fixed annual market share was that not all patients who receive aprepitant will switch to fosaprepitant. Clinical expert opinion sought by AWTTC is supportive of the company's estimates.
- The budget impact model presented by the company assumed all patients receive intravenous dexamethasone and eight chemotherapy cycles. The net medicine acquisition cost for 1-day fosaprepitant regimen is estimated to be £1,989 in Year 1 and £2,321 in Year 5, and the net medicine acquisition cost for the 3-day fosaprepitant regimen is estimated to be £6,542 in Year 1 and £7,632 in Year 5. On days 2 and 3 of the 3-day fosaprepitant regimen patients could be switched to aprepitant, therefore this is likely to be an overestimate.
- The true net medicine acquisition cost will depend on the average number of chemotherapy cycles given to children in Wales. The clinical trials of aprepitant in the paediatric population allowed for up to six cycles of chemotherapy, although not all patients received the six full cycles. It is not clear whether eight cycles of chemotherapy reflect the treatment of paediatric cancer patients in Wales.
- The estimated budget impact is based on medicine acquisition costs and does not consider associated intravenous administration costs.

Additional information

- AWTTC is of the opinion that, if recommended, fosaprepitant (IVEMEND®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

Evidence search

Date of evidence search: 2 August 2018
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 at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Fosaprepitant (IVEMEND®) 150 mg powder for solution for infusion. Reference number: 3789. October 2018.