All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

# AWMSG Secretariat Assessment Report – Limited submission

## Aprepitant (EMEND®▼) 80 mg, 125 mg hard capsules and 125 mg powder for oral suspension

**Company:** Merck Sharp & Dohme Ltd.

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

**Marketing authorisation date:** 16 December 2015

## Comparator(s)

The comparators included in the company submission were ondansetron and dexamethasone, a 5-HT3 antagonist and a corticosteroid respectively.

## Limited submission details

AWMSG limited submission criteria were met as this is a minor licence extension for use in patients from the age of 6 months to less than 18 years old, and the anticipated usage of aprepitant is considered to be of minimal budgetary impact. The oral suspension is also considered a significant new formulation.

## Clinical effectiveness

- The key clinical evidence supporting the clinical effectiveness of aprepitant is derived from MK-0869-208, a phase III randomised trial investigating the efficacy and safety of aprepitant for the prevention of chemotherapy-induced nausea and vomiting (CINV) in 302 patients aged 6 months to 17 years. In the 25–120 hour period after initiation of emetogenic chemotherapy, patients who received aprepitant in addition to ondansetron (with or without dexamethasone) were significantly more likely to achieve a complete response (no vomiting, no retching, and no use of rescue medication) than those who received the same regimen but with placebo in place of aprepitant.
- In MK-0869-208, children less than 12 years of age received aprepitant as the oral formulation (powder for oral suspension), while patients aged 12–17yrs received the adult regimen (hard capsules). Subgroup analysis shows that for the primary trial outcome, aprepitant was significantly more effective that placebo in both age groups.
- In clinical practice most patients will receive multiple cycles of chemotherapy. Although the design of the pivotal study allowed for up to six cycles of aprepitant, the main focus of the analyses was on a single double-blind cycle of aprepitant (cycle 1). Use of aprepitant was open-label when given during any subsequent cycles, and only safety outcomes were reported. Twenty seven percent of patients included in cycle 1 completed a further five cycles of treatment.
- The toxicity profile of aprepitant includes anaemia, febrile neutropenia, vomiting, neutropenia, nausea, and decreased neutrophil count, all of which reflect a typical

patient population with cancer receiving chemotherapy.

- The Committee for Medicinal Products for Human Use concluded that in the clinical paediatric studies of aprepitant for the treatment of CINV, the safety and tolerability of aprepitant combined with ondansetron and optional dexamethasone was comparable with that of ondansetron with optional dexamethasone. The Committee concluded in their report that there were no new safety concerns in paediatric subjects.

## Budget impact

- Aprepitant is administered in addition to (rather than instead of) a regimen that includes a 5-HT3 antagonist and a corticosteroid.
- Using Welsh Cancer Intelligence & Surveillance Unit statistics, the company has estimated that on average 100 children and young adults aged 6 months to 18 years are diagnosed with cancer each year in Wales. It is assumed that all paediatric patients in Wales receive moderately or highly emetogenic chemotherapy regimens and would be eligible to receive aprepitant.
- The company estimates the expected uptake of aprepitant among the paediatric population in Wales to be 5% in year 1, 11% in year 2, 22% in year 3, 33% in year 4 and 44% in year 5. Therefore, a total of five paediatric patients are likely to receive aprepitant as part of anti-emetic combination therapy in year 1, increasing to 22 patients in year 3 and 44 in year 5.
- The additional cost per treatment course across all eligible paediatric patients per year of treating paediatric patients with aprepitant in combination with current anti-emetic standard of care therefore ranges from £237 in year 1 to £2,087 in year 5.
- The annual budget impact is calculated for one course per patient per year which is likely to be an underestimate. The true budget impact will depend on the average number of cycles of chemotherapy children receive. Patients in MK-0869-208 were eligible for up to six cycles of chemotherapy, and therefore the most conservative estimate of the budget impact of aprepitant would be up to six times higher than estimated. However, only 27% of patients in the trial received a full six cycles of chemotherapy. Furthermore, it is not clear whether the number of cycles of chemotherapy received by patients in the trial accurately reflects the treatment of paediatric cancer patients in Wales.

## Additional information

- Aprepitant (EMEND®▼) 80 mg and 125 mg hard capsules have been available for prevention of CINV in adults since 2003 and is considered an established medicine.
- AWTTC is of the opinion that, if recommended, aprepitant (EMEND®▼) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company do not anticipate that aprepitant (EMEND®▼) will be supplied by a home healthcare provider.

## Evidence search

**Date of evidence search:** 8 March 2016
**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. Aprepitant (EMEND®▼) 80 mg,125 mg hard capsules and 125 mg powder for oral suspension. Reference number: 2937. June 2016.