
Clinical Pharmacology Review Addendum

NDA	21549/S-025; 207865
Submission Date	03/04/2014
Drug	Emend (aprepitant)
Submission Type; Code	Pediatric Supplement
Indication	Prevention of CINV in children 6 months to 12 years (NDA 21549/S-025 Emend Capsules for children 12-17 years/ NDA 207865 Emend Powder for Suspension for children 6 months to 12 years)
Applicant	Merck Sharp & Dohme
OCP-Pharmacometrics Review Team	Jian Wang, Ph.D., Nitin Mehrotra, Ph.D.

The clinical pharmacology review team provides the following summary in support of the approval of weight based dosing for oral suspension formulation in pediatric patients 6 month – 12 years old. The dose of 3 mg/kg on day 1 and 2 mg/kg on day 2 & 3 (3/2/2 mg/kg) in 6 month to 12 year old pediatric patients is acceptable. This was the dosing regimen utilized the registration trial. Please refer to the clinical pharmacology review by Dr. Elizabeth Shang in DAARTS dated 07/20/2015 for more details.

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- The sponsor proposed a nomogram based on different weight tiers for ease of dosing in clinical practice to reduce potential dosing errors. In the clinical pharmacology review dated 07/20/2015, the OCP review team concluded that the nomogram based dosing is acceptable. However, since the clinical team considers that the weight based dosing with 3/2/2 mg/kg can be administered accurately in clinical practice, the OCP review team agrees to go without a nomogram.
- The nomogram as developed by the sponsor was based on the 3/2/2 mg/kg regimen applied to the highest weight in each weight tier. It should be pointed out that this was done to avoid underdosing in any patient because efficacy of doses lower than 3/2/2 mg/kg has not been determined. Based on the proposed weight tiered nomogram, the mean simulated systemic exposure was 30% higher than the weight based dosing (3/2/2 mg/kg), which the sponsor considers acceptable based on the overall safety data for aprepitant in adults. There appears to be significant overlap in the distribution of exposures between nomogram-based dosing compared to weight-based dosing. In addition, the mean exposure in adult cancer patients is ~2- fold higher than pediatric exposures.

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/s/

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12/02/2015

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12/02/2015