Film Coating for Taste-masking of Pediatric Oral Solid Dosage Forms

Case Study

Use of Surelease® and Opadry® in the Development of a Paediatric Form of Raltegravir for the European Union

Raltegravir is anti-retroviral drug, developed by Merck Sharp & Dome (MSD) for the treatment of human immunodeficiency virus (HIV-1) and marketed under the trade name ISENTRESS. The product was first presented as a 400 mg film coated tablet and granted a marketing authorization, valid throughout the European Union in December 2007 for the treatment of HIV-1 infection in adults.

Subsequently MSD decided to develop a paediatric formulation of the drug designed to be suitable for children from the age of two years, for whom the 400mg tablet was not appropriate. For clinical reasons it was decided that two strengths were needed, 25mg and 100mg.

The active substance, raltegravir, has an intense bitter taste and hence the taste masking of this material was seen as an essential part of the development program. Several taste-masking options were evaluated by coating the raltegravir granules prior to processing into the final dosage form. The chosen option was to use a coating comprised of Surelease® (E-7-19040), aqueous ethylcellulose dispersion, in combination with a hypromellose based Opadry® product. Insoluble in water, ethylcellulose acts as the taste-masking agent by delaying the release of the drug in the mouth, while Opadry is used as a pore-former in the coating, which allows immediate release of the drug once in the stomach.

MSD considered a range of different dosage forms for the finished medicinal product including orally disintegrating tablets and chewable tablets. Based on dissolution data and patient questionnaires the decision was made to go forward with a chewable tablet. The final chewable tablet also contains a flavour system in case chewing causes some breakdown of the taste-mask coating.

In the EU, the paediatric form of Isentress gained a positive opinion from the Committee for Medicinal Products for Human use in October 2012, for use in children from the age of 2 years.

Note: In the US, there is also a version of Isentress for oral suspension, which also includes Surelease. This product is licenced for patients at least 4 weeks of age and weighing over 3kg.

Further information on the use of Film Coating for Taste-masking applications can be found at:
http://www.colorcon.com/products-formulation/all-products/film-coatings/sustained-release/surelease

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