Omeprazole suspension and product physical consistency issues

Introduction

Omeprazole (Pedippi®) is an gastric acid reducing agent which is concentrated and activated due to the acidy environment in the intracellular canaliculi within the parietal cell, where it inhibits the proton pump. Regardless of the stimulus, omeprazole inhibits the basal acid secretion as well as the stimulated acid secretion [1].

Omeprazole is indicated in adults for treatment and prevention of (recurrent) *ulcus duodeni* and *stomach ulcers* in general, or when associated with NSAID use. In adolescents and children older than 4 years old, omeprazole is also indicated for eradication of Helicobacter pylori in combination with the correct antibiotics in *ulcus duodeni* patients. Furthermore, it is indicated for treatment *of reflux esophagitis* and treatment of *symptomatic gastroesophageal reflux disease* in adults and children older than 1 month, and for long term treatment of adults that have *recovered from reflux esophagitis* [1].

Omeprazole has been registered since November 1988. Omeprazole was not registered for infants for a long time, and was therefore administered off-label. The granules from the omeprazole capsules could be dispersed into a slightly acid liquid (e.g. yoghurt) and coated granules from tablets could be disintegrated in water and subsequently administered by probe [2].This form of administration in some cases led to too rapid dissolution of the coating with reduced effect as result, due to its contact with acidic gastric contents [3-5]. Since November 25th, 2019 an omeprazole suspension has been registered for infants [1]. Lareb has recently received two reports on physical consistency issues in which this suspension was described as too thick and slimy to swallow.

Reports

In the period from June 15th 2021 to Sept 14th 2021 Lareb received 2 reports on product physical consistency issues of omeprazole suspension (Pedippi®).

Case A NL-LRB-00592558 This spontaneous report from a pharmacist concerns a female aged 0-1 years, with product physical consistency issue following administration of omeprazole suspension oral 2mg/ml (Pedippi®). The suspension was thick and slimy and the child almost choked on it. The pharmacist (reporter) mentioned that they had received more complaints about the consistency of omeprazole suspension of the brand Pedippi®. It is unknown who prepared the suspension and how long it was kept before administration.

Case B NL-LRB-00580953 This spontaneous report from a consumer or other non-health professional concerns a female aged 0-1 years, with a product physical consistency issue following drug substitution of omeprazole (Fagron®) into omeprazole (Pedippi®) suspension oral 2mg/ml for regurgitation. The suspension was prepared at the pharmacy, where the mother of the baby collected it during the day. She administered the suspension the same evening after shaking it (like she was used to with omeprazole suspension from Fagron®). The suspension was too thick and sticky to swallow and the child almost choked on it. Administration was tried with the syringe as well as the spoon, but could not be swallowed. She had already planned an appointment for a feeding tube (which was not related to the swallowing problems) through which it could also be administered according to her pharmacist. However, the feeding tube also became obstructed with the suspension and had to be removed. The problem was solved when they returned to omeprazole (Fagron®).

It is unclear from the first report whether the suspension was correctly prepared. In the second report it is described that the suspension was prepared in the pharmacy, hence it is likely that instructions were followed. Also, the suspension was administered the same day it was prepared. Unfortunately, in both cases, batch numbers were unknown, so a difference in viscosity related to the batch could not be excluded.

Other sources of information

SmPC

As this signal concerns a consistency issue of the drug, we only refer to the excipients, storage and user instructions in this paragraph.

Excipients:

Sodium hydrogen carbonate (E500)
Potassium hydrogen carbonate (E501)
Sodium alginate (E401)
Maltitol (E965)
Mannitol (E421)
Sucralose (E955)
Xanthan gum (E415)
Natural vanilla flavor with met maltodextrin (Corn),
Silicon dioxide (E551)
Vegetable oil fats natural mint flavor with arabic gum/acacia gum (E414)
Pulegone titanium dioxide (E171)
Sodium benzoate (E211)
Sodium methyl para-hydroxybenzoate (E219)

Xanthan gum en **Sodium alginate** are thickening agents

Storage
Constituted suspension: 28 days. The constituted suspension should be stored in the fridge (2°C - 8°C). Keep in the original packaging to protect the medicine from light and moisture. Keep the bottle closed. It can be stored outside the fridge below 25°C for a maximum of 2 days [1].

Special instructions for constitution, administration

Merge the powders from the cap and the bottle
- Shake the bottle 10 seconds to loosen the powder
- Turn the red cap against the clock (see arrow on lid) until the seal breaks
- The powder from the red cap will drop into the bottle.
- Turn the red cap back in the original position and tighten it.

Constitution of the powder
- Shake the bottle 10 seconds thoroughly to mix the powders.
- Touch the bottom of the bottle three times on a hard horizontal surface to make sure that all the powder is in the bottle and no longer in the cap.
- Remove the red cap from the bottle
- Add 64 ml water using a suitable measuring cup (until the line on the label).
- Tighten the red cap and shake the bottle 30 seconds thoroughly.

Databases

There were no other cases with product consistency issues for omeprazole described in the WHO database VigiBase [6].

Discussion and conclusion

The Netherlands Pharmacovigilance Centre Lareb has received 2 reports on consistency issues with omeprazole suspension (Pedippi®). For one of the reports it remained unclear, after additional follow-up questions, whether instructions were correctly followed when preparing the suspension and how long it had been stored before it was administered. An extended period between preparation and administration could have led to spontaneous thickening of the suspension or to loss of moisture through the semipermeable bottle, even though it is stated in the product information that the suspension can be stored for 2 days outside the fridge when stored below 25°C. However, considering the young age (from 1 month) included in the indication, and the potential serious consequences the thick consistency has (choking), the cause of the thick consistency should be reported to the market authorization holder and further investigated.

References

1. Dutch SmPC of Omeprazole Pedippi® [cited: 24-09-2021] Available from: https://www.geneesmiddeleninformatiebank.nl/smpc/h123563_smpc.pdf.
2. Kinderformularium (The Dutch National Formulary for Children). NKFK - Nederlands Kenniscentrum Farmacotherapie bij Kinderen. (version date: 2021, access date: 28-09-2021) http://kinderformularium.nl/search/stof.php?id=132.
3. Omeprazole suspension and regurgitated gastric content discoloured (2017) https://databankws.lareb.nl/Downloads/Signals_2017_omeprazole%20and%20gastric%20content%20discoloured.pdf.
4. (Es)Omeprazole and regurgitated gastric content discoloured – an update (2019): https://databankws.lareb.nl/Downloads/Signals_2019_omeprazole_gastic_contents_discolouration_update.pdf.
5. Omeprazole and discolouration of the gastric content (2013): https://databankws.lareb.nl/Downloads/KWB_2013_4_omepr.pdf.
6. WHO Global Individual Case Safety Reports database (Vigilyze). (version date: 2021 , access date: 24-09-2021) https://tools.who-umc.org/webroot/ (access restricted). .

This signal has been raised on December 20, 2021. It is possible that in the meantime other information became available. For the latest information, including the official SmPC's, please refer to website of the MEB www.cbg-meb.nl