Kaletra (lopinavir/ritonavir) oral solution, 2 bottle pack containing 2-ml oral dosing syringes: Presence of amide particles in 2-ml oral dosing syringes

Dear Healthcare Professional,

AbbVie, in agreement with the European Medicines Agency (EMA), and the <national competent authority> would like to inform you of the following:

Summary of an identified quality defect

- **Small visible particles/flakes were observed in empty 2-ml oral dosing syringes for use with Kaletra oral solution in November 2020.**
- **The material was identified as erucamide, which is classified and certified as a food additive and was assessed during a toxicology evaluation. These recommendations aim to remove these particles as complete as possible.**
- **The observed particles/flakes are loose in the syringes and could potentially be dispersed into the oral solution.**
- **The particles/flakes are too small to block the syringe and to cause physical injury or internal obstruction even if ingested by very small children.**
- **The risk of harm from ingesting the particles/flakes with the solution is negligible, therefore the product is safe to use by oral administration.**
- **This quality defect only concerns the 2-ml oral dosing syringes; the quality and safety of Kaletra oral solution itself are not affected.**
- **AbbVie recommends washing the syringe before the first use. The information in the package leaflet and the boxed instructions below recommend washing after each use. The same instruction should be followed to wash the syringe before the first use.**

  It is important to let the syringe dry completely before you use that syringe for dosing.

After each dose of Kaletra separate the plunger and the syringe. Wash the plunger and the syringe with washing up liquid and warm water as soon as you can; you may soak both in soapy water for up to 15 minutes. Rinse the syringe and plunger with clean water. Put the syringe back together and draw up and expel tap water a few times to rinse. Let the syringe dry completely before you use that syringe for dosing.

Background on the safety concern

- Kaletra is an HIV-1 protease inhibitor indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and paediatric patients (14 days and older).
- Flakes have recently been identified in the 2 ml oral dosing syringes in some batches of Kaletra oral solution 2 bottle pack. The syringes are only included in this Kaletra oral pack size.

- The particles were identified as erucamide. Erucamide is a biologically and chemically inert approved indirect food additive, and is naturally occurring in vegetable oils such as canola and rapeseed oils.[1,2] In addition, erucamide is an endogenous substance in the human body and plays a role in inhibiting intestinal diarrhea by regulating fluid volume. [3]Based on a review of available toxicology databases (CAS No. 112-84-5) erucamide has very low oral route systemic toxicity potential with no significant adverse events being reported, no genotoxicity and carcinogenicity is not expected to be a concern.

The potential safety risk of the use of the impacted product and ingestion of the particles/flakes with Kaletra oral solution is negligible and there is no reasonable possibility of adverse health consequences with the use or exposure to the impacted product and no impact to the known safety profile of Kaletra oral solution.

Interruption of HIV treatment, while awaiting replacement product, may result in HIV viral rebound and potential development of HIV resistance. This resistance may cause the HIV infection to no longer respond to Kaletra after therapy is restarted, which is categorized as a medium potential safety risk to patients on Kaletra therapy.

For a full prescribing information, see the Summary of Product Characteristics.

Invitation to report side effects

Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continuous monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are encouraged to report any suspected adverse reactions to > national spontaneous reporting system, including the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system>

Company contact point

If you have any questions or need more information on the use of Kaletra, please contact:
>national contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address<

Best regards

Abbvie >Country<
References

1. Erexson G. Extraneous Matter Toxicology Risk Assessment of Polyamide Particles [Erucamide] in Syringes for Kaletra Oral Solution (KOS). AbbVie Report Number: R&D/20/1552 Preclinical Safety, Genetic, Environmental and Occupational Toxicology. 24 November 2020
2. PAFA – Priority-Based Assessment of Food Additives. Erucamide. CAS Registry No.: 112-84-5. ToxPlanet.com/2020.
3. Hamberger, A., Stenhagen, G. Erucamide as a Modulator of Water Balance: New Function of a Fatty Acid Amide. Neurochem Res 28, 177–185 (2003). https://doi.org/10.1023/A:1022364830421

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Kaletra (lopinavir/ritonavir) oral solution
Marketing authorisation holder(s)	AbbVie GmbH & Co.KG, Germany Knollstrasse, 67061 Ludwigshafen
Safety concern and purpose of the communication	Kaletra (lopinavir/ritonavir) oral solution, 2 bottle pack containing 2-ml oral dosing syringes: Presence of amide particles in 2-ml oral dosing syringes
DHPC recipients	Community pharmacists Hospital pharmacists
Member States where the DHPC will be distributed	Austria, Belgium, Estonia, France, Germany, Italy, Latvia, Lithuania, Poland, Sweden, United Kingdom[1] [1]As of 1.2.2020, the UK is no longer an EU Member State. However, EU law still applies to the UK during the transition period

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP/CMDh	21 Dec 2020
Submission of translated DHPCs to the national competent authorities for review	22 Dec 2020
Agreement of translations by national competent authorities	22 Dec 2020
Dissemination of DHPC	23 Dec. 2020