Ecalta 100mg Powder for Concentrate for Solution for Infusion (Anidulafungin): Solution for infusion must no longer be frozen

Dear Healthcare Professional,

Pfizer Europe MA EEIG in agreement with the European Medicines Agency (EMA) and <Name of National Competent Authority>, would like to inform you of the following:

Summary

- The current product information for Ecalta (anidulafungin) allows freezing of the (reconstituted) infusion solution, but a recent study by the manufacturer indicated that this storage condition requires revision. Freezing the product may lead to the formation of visible particles due to the lack of solubility of the Ecalta drug substance (anidulafungin) in the infusion solution following storage at freezer conditions and subsequently thawed.

- **Instructions to health care professionals:** In contrast to what is stated in the current version of the product information, **the (reconstituted) infusion solution should <u>not</u> be frozen. The infusion solution may be stored at 25ºC for 48 hours.**

- The product information of Ecalta will be updated shortly to include the correct instructions.

Further information on the safety concern and the recommendations

The revised storage recommendation is based on an infusion study that was initiated for Ecalta to evaluate in-use stability for Ecalta solutions across labelled storage conditions. The study found the infusion solutions were Out of Limit (OOL) for Completeness & Clarity

USP testing, a test for the presence of visible particles (note that this test is equivalent to the EP Particulate Matter Visible test). In the case of these failures, the infusion solution contained numerous, white, amorphous particles that were very visible after the solution was removed from freezer conditions and brought to room temperature. The visible particles were identified in the infusion solutions at a low rate and only for IV bags that had been frozen. The particulates observed were determined to be anidulafungin, the active substance for Ecalta. There were no other failures for any other testing conducted for this infusion study.

The **current** Section 6.3 of the Summary of Product Characteristics in the Product Information **incorrectly** states that the infusion solution **can be frozen for up to 72 hrs**. **This advice should not be followed** based on aforementioned reasons.

The Summary of Product Characteristics also includes the following statement (**which still is correct**): "The solution should be inspected visually for particulate matter and discolouration prior to administration. If either particulate matter or discolouration are identified, discard the solution".

A search of the post-marketing safety database as for the period 21 February 2017 to 02 December 2019 for anidulafungin identified no safety issues related to OOL for Completeness and Clarity USP testing or presence of visible particulates in anidulafungin IV infusion bags.

A 5-year complaints history from 27 September 2014 to 27 September 2019 was reviewed and no complaints related to this issue were found.

Further information

<Link/reference to other available relevant information, such as information on the website of a competent authority>

<Therapeutic indication of the medicinal product, if not mentioned above>

Call for reporting

Call for reporting - to be completed nationally
Please continue to report any suspect adverse drug reactions to the <Name of National Competent Authority>
<A reminder of the need and how to report adverse reactions in accordance with the national spontaneous reporting system>
<Mention if product is subject to additional monitoring and the reason why>
<Details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system>

Company contact point

Company contact point - to be completed nationally
Alternatively, suspected adverse reaction may also be reported to the marketing authorisation holders using the details provided below. If you have further questions or require additional information, please contact:

Company	Product name	Email	Phone	Fax

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>

ANNEXES

<Relevant sections of the Product Information that have been revised (with changes made visible)>

<Detailed scientific information, if necessary>

<List of literature references, if applicable>

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Ecalta (anidulafungin)
Marketing authorisation holder(s)	Pfizer Europe MA EEIG Boulevard de la Plaine 17 1050 Bruxelles Belgium
Safety concern and purpose of the communication	**Update to storage conditions of the infusion solution to state that it must not be frozen**
DHPC recipients	Hospital pharmacists
Member States where the DHPC will be distributed	Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the UK

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP	10 January 2020
Submission of translated DHPCs to the national competent authorities for review	17 January 2020
Agreement of translations by national competent authorities	To be decided at national level
Dissemination of DHPC	To be decided at national level