TEPADINA (thiotepa) 100 mg: possible risk of defective vials in batches n°1709192/1, n°1709192/2 and n°1709192/3 presenting a crimp seal not properly fixed on the vial.

Dear Healthcare Professional,

ADIENNE Srl in agreement with the European Medicines Agency and the <National competent authority> would like to inform you of the following:

Summary

- **There is the possible risk that some defective TEPADINA 100 mg vials present a crimp seal not properly fixed.**
- **This defect can be easily identified when removing the flip-off cap from the aluminium crimp before reconstitution, as during flip-off removal, caps not properly fixed to the vials will be immediately detected.**
- **This issue may affect batches n° 1709192/1, n° 1709192/2 and n° 1709192/3. These three secondary packed batches were manufactured starting from the same bulk batch n° 1709192, expiry 02/2021.**
- **As the sterility and the thiotepa content of defective vials cannot be guaranteed these vials must be discarded and the Marketing authorisation holder, ADIENNE Srl, should be notified (to qualitycomplaint@adienne.com, safety@adienne.com and med-info@adienne.com).**
- **It is reminded to handle the product under safety hood wearing gloves when removing the flip-off in order to avoid the potential risk to be accidentally exposed to the medicinal product.**

Background on the safety concern

There is the possible risk that some defective vials of the above-mentioned batches present a crimp seal not properly fixed on the vial. This defect can be easily identified when removing the flip-off from the aluminium crimp before starting the product reconstitution, as during flip-off removal, caps not properly fixed to the vials will be immediately detected: the cap will easily move and fall off. Should any vials presenting this defect be noted, these vials must be discarded.

As a consequence of this *product container seal issue*, container closure system integrity could potentially not be guaranteed. If this happens patients may be at risk to be administered a non-sterile product and therefore could be at risk of developing infections/sepsis.

In addition, medicinal product from vials which could present this product container seal issue may potentially be affected by a degradation of thiotepa with consequent formation of product related substances. This could result in lack of efficacy caused by a possible decreased content of thiotepa.

Finally, there could be the potential risk for Health Care Professionals to be accidentally exposed to the medicinal product during the drug reconstitution procedure. It is reminded to handle the product under vertical laminar flow safety hood wearing gloves when removing the flip-off before preparing the solution for infusion and to proceed as indicated in the medicinal product labelling/material safety data sheet in case of accidental spillage or exposure.

The described quality defect was detected for another bulk batch 1709191 for which two cases were reported. The bulk batch 1709191 is being recalled. No quality defect reports have been received for bulk batch 1709192 so far. The risk of occurrence of defective packaging is low.

Tepadina is indicated, in combination with other chemotherapy medicinal products:

- with or without total body irradiation (TBI), as conditioning treatment prior to allogeneic or autologous haematopoietic progenitor cell transplantation (HPCT) in haematological diseases in adult and paediatric patients;
- when high dose chemotherapy with HPCT support is appropriate for the treatment of solid tumours in adult and paediatric patients.

Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V

Company contact point

For medical information enquiries please contact med-info@adienne.com.

For notification of side effects for the use of the medicinal product please contact safety@adienne.com

For product complaints, please contact qualitycomplaint@adienne.com.

www.adienne.com

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	TEPADINA 100 mg (thiotepa)
Marketing authorisation holder(s)	ADIENNE Srl
Safety concern and purpose of the communication	TEPADINA (thiotepa) 100 mg: possible risk of defective vials in batches n°1709192/1, n°1709192/2 and n°1709192/3 presenting a crimp seal not properly fixed on the vial. This defect can be easily identified when removing the flip-off from the aluminum crimp seal before starting the product reconstitution. In fact during the procedure of removal of the flip-off, caps not properly fixed to the vials can be immediately detected. Should any vials presenting this defect be noted, these vials must be discarded.
DHPC recipients	Specialists, hospital pharmacists
Member States where the DHPC will be distributed	Czechia, Estonia, Germany, Poland

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP	20 May 2020
Submission of translated DHPCs to the national competent authorities for review	22 May 2020
Agreement of translations by national competent authorities	29 May 2020
Dissemination of DHPC	1 June 2020