NOTICE OF SPECIAL HANDLING INSTRUCTIONS
VIALS of ERWINASE® from BATCH 186G* should be used with a 5-micron filter needle

Dear Healthcare Professional

Jazz Pharmaceuticals UK Limited would like to inform you of the following:

Summary

- Small amounts of particulate matter have been observed bound to the stopper and/or present on the lyophilized cake of some vials of ERWINASE from BATCH 186G
- Vials of ERWINASE with visible particulate matter must not be administered. Please notify and retain the vial for collection. Follow all the recommended steps for the reconstitution of ERWINASE in accordance with the Summary of Product Characteristics
- Carefully inspect the reconstituted product. If you discover particulate matter after reconstitution, do not administer the product and retain for collection.
- If there is no visible particulate matter after reconstitution, **use a standard 5-micron filter needle to withdraw the reconstituted product from the vial prior to administration as an additional precaution.**
- Vials from BATCH 186G can be identified by the following label, attached to the carton:

USE 5 MICRON FILTER NEEDLE **SEE NOTICE OF SPECIAL INSTRUCTIONS**

Recommendations for Preparation

ERWINASE is used in combination with other anti-neoplastic agents to treat acute lymphoblastic leukaemia. It may also be used in other neoplastic conditions where depletion of asparagine might be expected to have a useful effect. Patients receiving treatment with L-asparaginase from *Escherichia coli* and who develop hypersensitivity to that enzyme may be able to continue treatment with ERWINASE as the enzymes are immunologically distinct.

During routine inspection of BATCH 186G, particulate matter was observed bound to the stopper and/or present on the lyophilized cake of some vials of ERWINASE. These affected vials were segregated. There is a possibility that some remaining vials may contain particulate matter bound to the stopper and/or on the lyophilized cake, which if transferred to reconstituted ERWINASE, may pose a safety risk to patients. Section 6.6 *(Special precautions for disposal and other handling)* instructs health care providers that "If there are any visible particles or protein aggregates present the reconstituted solution should be rejected." In the event that you discover particulate matter, pre- or post- reconstitution, please notify the Customer Services department[1] and retain the vial for collection.

In order to minimise the potential risk of exposure to sub-visible particulate matter, **use a standard 5-micron filter needle to withdraw the reconstituted product from the vial**

prior to administration as an additional precaution. A study has demonstrated that filtration through a 5-micron filter needle after reconstitution has no effect on ERWINASE activity.

Jazz Pharmaceuticals has assessed the overall benefit to risk ratio of administering ERWINASE for the treatment of acute lymphoblastic leukaemia as positive, particularly with the additional precaution of using a 5-micron filter needle to withdraw the reconstituted product from the vial.

In the event that you should need to retain a vial of ERWINASE for collection, please contact the Customer Services department for replacement.

[1]Tel +44 (0)1865405019 Fax +44 (0)1865594353

Customerservices.uk@jazzpharma.com

Adverse Event Reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.

- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Cards website - https://yellowcard.mhra.gov.uk/ .
Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.'

Company contact point

If you have any questions about this letter or any other enquiry, please contact Medical Information at the following address:

Tel +44 (0)845 0305089

Medinfo-uk@jazzpharma.com

This information is being sent to you with the agreement of the Medicines & Healthcare Products Regulatory Agency (MHRA).

Yours sincerely,

Dr Kelvin Tan
Vice President Medical Affairs
Jazz Pharmaceuticals

*BATCH 186G may consist of packaged sub-lots: 186G118, 186G218, 186G318, 186G418 or 186G518

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(Additions to the current Summary of Product Characteristics in **bold + italics**)

Vials from BATCH 186G can be identified by the following label, attached to the carton:

USE 5 MICRON FILTER NEEDLE
SEE NOTICE OF SPECIAL INSTRUCTIONS

The contents of each vial should be reconstituted in 1 ml to 2 ml of sodium chloride (0.9%) solution for injection. Slowly add the reconstitution solution against the inner vial wall, do not squirt directly onto or into the powder. Allow the contents to dissolve by gentle mixing or swirling maintaining the vial in an upright position. Avoid froth formation due to excessive or vigorous shaking.

The solution should be clear without any visible particles. Fine crystalline or thread-like wisps of protein aggregates may be visible if shaking is excessive. If there are any visible particles or protein aggregates present the reconstituted solution should be rejected and the vial and content should be retained for collection

A standard 5-micron filter needle should be used to withdraw the reconstituted product from the vial prior to administration as an additional precaution.

The solution should be administered within 15 minutes of reconstitution. If a delay of more than 15 minutes between reconstitution and administration is unavoidable, the solution should be withdrawn into a glass or polypropylene syringe for the period of the delay. The solution should be used within 8 hours.