Cherubino Ltd.
Since 1906
YOUR HEALTH AT HEART

NOTICE OF SPECIAL HANDLING INSTRUCTIONS
VIALS of ERWINASE® from BATCH 174G* should be used with a 5-micron filter needle

Dear Healthcare Professional

Cherubino Ltd would like to inform you of the following:

Summary

- Small amounts of particulate matter have been observed bound to the stopper of some vials of ERWINASE from BATCH 174G
- Vials of ERWINASE with visible particulate matter should be discarded
- 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, discard the vial
- 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 174G 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 174G, particulate matter was observed bound to the stopper of some vials of ERWINASE. These affected vials were discarded. There is a possibility that some remaining vials may contain particulate matter bound to the stopper, which if transferred to reconstituted ERWINASE, may pose a safety risk to patients. In a small study,

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particulate matter was not transferred from the stopper during reconstitution. 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, discard the vial.

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 discard a vial of ERWINASE, please contact the Customer Services department for replacement.

Tel: +356 21343270 Fax: +356 21330916

care@cherubino.com.mt

Call for Reporting

In the event of any adverse reaction to ERWINASE, please report side effects directly to:

Malta Medicines Authority,
Sir Temi Zammit Building,
Malta Life Sciences Park,
San Gwann SGN 3000
OR
www.medicinesauthority.gov.mt/adrportal

Company contact point

If you have any questions about this letter or any other enquiry, please contact the below:

Mr David Cherubino
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Delf Building,
Sliema Road,
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(additions to the current Summary of Product Characteristics in **bold + italics**)

Vials from BATCH 174G can be identified by the following label, attached to the carton:

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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.

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.

*BATCH 174G may consist of packaged sub-lots: 174G116, 174G216, 174G316, 174G416, 174G516

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Batch 174G has been approved under a Batch Specific Variation for release in the UK by the Medicines & Healthcare Products Regulatory Agency (MHRA.

Yours sincerely,

Mrs. Luisa De'Piro O'Connell B.Pharm (Hons)
Pharmacy Council Reg. No:984
R.P. Cherubino Ltd. Gzira. Malta

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