IMPORTANT DRUG INFORMATION

June 17, 2016

Subject: **Notice of Special Handling Instructions**
Use a 5-micron filter needle for preparation of vials of ERWINAZE®
(asparaginase *Erwinia chrysanthemi*) from Batch 177K

Dear Health Care Provider:

The purpose of this letter is to alert you that you should use a 5-micron filter needle to withdraw the reconstituted ERWINAZE (asparaginase *Erwinia chrysanthemi*) product from the vials of Batch 177K, because particulate matter was observed to be bound to the stopper of some vials from this batch. To prevent an immediate shortage of ERWINAZE in the U.S. market, Jazz Pharmaceuticals is asking health care providers to take this necessary step for patient safety.

During routine visual inspection of ERWINAZE Batch 177K, particulate matter was observed bound to the stopper of some vials of ERWINAZE. These affected vials were quarantined. However, there is a possibility that some of the remaining vials may contain particulate matter bound to the stopper, which, if transferred to reconstituted ERWINAZE, may pose a safety risk to patients. In a study conducted by Jazz Pharmaceuticals, no transfer of stopper particulate matter to product was observed.

In order to minimize the potential risk of exposure to sub-visible particulate matter, health care providers should use a standard 5-micron filter needle to withdraw the reconstituted ERWINAZE product from the vial, and then discard the filter needle and replace it with an appropriate needle prior to administration or transfer to an IV infusion bag. There is no evidence based on a study conducted by Jazz Pharmaceuticals that filtration through a 5-micron filter needle after reconstitution negatively impacts ERWINAZE activity.

Please follow the instructions below prior to withdrawing the reconstituted ERWINAZE product from the vials and administering it to patients.

- **Visually inspect and quarantine any vials of ERWINAZE with visible particulate matter.**
- **Follow all recommended steps for reconstitution of ERWINAZE in accordance with the Prescribing Information.**
- **Carefully inspect reconstituted product. In the event that you discover visible**

particulate matter, do not administer to the patient and quarantine the vial.

- **If no visible particulate matter is seen, use a standard 5-micron filter needle to withdraw the reconstituted product from the vial. See filter needle manufacturer's instructions or usage guidelines for proper use of filter needle.**
- **Discard the filter needle and replace with an appropriate needle prior to patient administration or transfer to an IV infusion bag.**
- **If you see particulate matter (pre- or post- reconstitution), do not administer to the patient and quarantine the vial. Contact Jazz Pharmaceuticals Medical Information at 1-800-520-5568 to report the issue and to discuss appropriate resolution.**

The following label, attached to the carton, can identify vials from ERWINAZE Batch 177K:

REQUIRES 5-MICRON FILTER NEEDLE FOR PREPARATION

SEE INCLUDED IMPORTANT DRUG INFORMATION LETTER

Vials from ERWINAZE Batch 177K can also be identified by numbering on the individual vial labels. Vials from the affected batch will have one of the following lot numbers: 177K116, 177K216, 177K316, 177K416, or 177K516.

Please ensure your staff and any provider in your institution who may be involved in the reconstitution and administration of ERWINAZE receives a copy of this letter and specifically reviews the Updated Instructions for Preparation appended to this letter. Please pay special attention to the updates in step #7 that includes the use of 5-micron filter needle to withdraw the reconstituted ERWINAZE.

Further Information

Please see accompanying Full Prescribing Information for ERWINAZE.

For more information, visit www.erwinaze.com or call 1-800-520-5568.

Call for reporting

Healthcare providers should report product quality problems and all suspected adverse events associated with the use of ERWINAZE. If you become aware of a patient experiencing an adverse event while taking ERWINAZE or product quality problems with ERWINAZE, please contact Jazz Pharmaceuticals, Inc. at 1-800-520-5568. Adverse events or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting Program either online, or regular mail, or by fax:

- Complete and submit the report **Online**: www.fda.gov/medwatch/report.htm
- Regular mail or Fax: Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

Sincerely,

Karen Smith, MD, PhD, MBA, LLM
Chief Medical Officer
Jazz Pharmaceuticals, Inc.

Updated Instructions for Preparation: ERWINAZE Batch 177 Vial

Preparation and Handling Instructions

1. Visually inspect the ERWINAZE vial (including powder) for any particulate matter and discoloration prior to reconstitution.

2. Reconstitute the contents of each vial by slowly injecting 1 or 2 mL of preservative free sterile sodium chloride (0.9%) injection (USP) against the inner vial wall.

3. Do not forcefully inject solution for reconstitution directly onto or into the powder. When reconstituted with 1 mL the resultant concentration is 10,000 International Units per mL. When reconstituted with 2 mL the resultant concentration is 5,000 International Units per mL.

4. Dissolve contents by gentle mixing or swirling. **Do not shake or invert vial.**

5. When reconstituted, ERWINAZE should be a clear, colorless solution. Inspect the solution after reconstitution for any visible particles or protein aggregates.

6. Calculate the dose needed and the volume needed to obtain the calculated dose.

7. Withdraw the volume containing the calculated dose from the vial **using a 5-micron filter needle** (according to the filter needle manufacturer's instructions) into a polypropylene syringe within 15 minutes of reconstitution. Discard the filter needle and replace with an appropriate needle prior to administration or transfer of the reconstituted product to an IV infusion bag. For intravenous use, slowly inject the reconstituted ERWINAZE into an IV infusion bag containing 100 mL of normal saline acclimatized to room temperature. Do not shake or squeeze the IV bag.

8. If a partial vial is used, do not save or reuse the unused drug for later administration. Discard unused portions.

9. Do not freeze or refrigerate reconstituted solution and administer within 4 hours or discard [see How Supplied/Storage and Handling (16)].

10. If you see particulate matter (pre- or post- reconstitution), do not administer to the patient and quarantine the vial. Contact Jazz Pharmaceuticals Medical Information at 1-800-520-5568 to report the issue and to discuss appropriate resolution.

Administration Instructions

ERWINAZE solution can be administered by intramuscular injection or by intravenous infusion.

- For intramuscular use, limit the volume of reconstituted ERWINAZE at a single injection site to 2 mL; if reconstituted dose to be administered is greater than 2 mL, use multiple injection sites.

- For intravenous use, infuse ERWINAZE in 100 mL of normal saline over 1 to 2 hours. Do not infuse other intravenous drugs through the same intravenous line while infusing ERWINAZE.