IMPORTANT DRUG INFORMATION

August 26, 2016

Subject: **For Intramuscular Administration Only - Newly Released Vials of ERWINAZE® (asparaginase *Erwinia chrysanthemi*) from Batches 174A and 177A**

Dear Health Care Provider:

The purpose of this letter is to alert you that previously unreleased ERWINAZE vials from batches 174 and 177 (see Dear HCP letters dated May and June 2016) are now being made available for use (the "Newly Released Vials") for **intramuscular administration only**. These Newly Released Vials may contain particulate matter on the underside of the stopper, which may appear as a black discoloration. Even if particulate matter is observed on the underside of the stopper, these vials may be reconstituted and administered to the patient intramuscularly as set forth below.

In order to minimize the potential risk of adverse events from the particulate matter, health care providers should administer vials from batches 174A and 177A by intramuscular administration only, not by intravenous administration. Additionally, healthcare providers should continue to 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.

During routine visual inspection of ERWINAZE batches 174 and 177, particulate matter was observed bound to the stopper of some vials. Transference studies demonstrated that the particulate matter bound to the stopper in the vials from these batches is unlikely to transfer to the product during reconstitution. To reduce the length of a potential product shortage, the vials of ERWINAZE from batches 174 and 177 that were previously segregated due to the presence of visible particulate matter on the stopper (the "Newly Released Vials") will now be made available for use. In a study conducted by Jazz Pharmaceuticals, there was no evidence that filtration through a 5-micron filter needle after reconstitution negatively impacts ERWINAZE activity.

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

- **Prior to reconstitution, carefully inspect each vial. If you observe particulate matter anywhere other than on the underside of the stopper (for example, on or in the product), quarantine the vial. If you do not observe particulate matter anywhere other than on the underside of the stopper, reconstitute the product as set forth below.**
- **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 in the reconstituted product, do not administer to the patient and quarantine the vial.**
- **If no visible particulate matter is seen in the reconstituted product, 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. Do not transfer to an IV infusion bag. Administer intramuscularly only.**
- **If you see particulate matter anywhere other than on the underside of the stopper (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 the Newly Released Vials:

FOR INTRAMUSCULAR USE ONLY

REQUIRES 5-MICRON FILTER NEEDLE FOR PREPARATION

SEE INCLUDED IMPORTANT DRUG INFORMATION LETTER

The Newly Released Vials can also be identified by numbering on the individual vial labels. The Newly Released Vials will have one of the following lot numbers: 174AK116, 174AK216, 177AK116, and 177AK216.

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 update in steps #1 and #7 that include observation of particulate matter other than on the underside of the stopper, the use of a 5-micron filter needle to withdraw the reconstituted ERWINAZE, and intramuscular administration only.

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 for intramuscular use: ERWINAZE Batch 174A or 177A Vial

Preparation and Handling Instructions

1. Carefully inspect each vial. If you observe particulate matter anywhere other than on the underside of the stopper (for example, on or in the product), quarantine the vial. If you do not observe particulate matter anywhere other than on the underside of the stopper, reconstitute the product as follows.

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, if you observe particulate matter in the reconstituted product, quarantine the vial.

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.

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 Prescribing Information - How Supplied/Storage and Handling (16)].

10. If you see particulate matter anywhere other on than the underside of the stopper (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 for **ERWINAZE Batch 174A or 177A**

ERWINAZE solution can be administered by intramuscular injection only. Do not administer 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.