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Jazz Pharmaceuticals

IMPORTANT DRUG INFORMATION

9 February, 2018

Subject: **ERWINAZE® Batch 185aK**
Notice of *New* Special Handling Instructions
Use a 0.2-micron, low protein binding, in-line filter for IV administration of ERWINAZE® (asparaginase *Erwinia chrysanthemi*) from BATCH 185aK.

Dear Health Care Provider:

The purpose of this letter is to alert you that ERWINAZE (asparaginase Erwinia chrysanthemi) from Batch 185aK may be administered either intramuscularly (IM) or intravenously (IV) according to the instructions outlined in this letter that are intended to prevent the administration of particulate matter that may be found in some of the product. These newly released vials may contain particulate matter on the underside of the stopper, which could 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 as set forth below.

During routine visual inspections of ERWINAZE Batch 185aK, particulate matter was observed bound to the underside of the stopper in some vials.

To respond to the ongoing product shortage, the vials of ERWINAZE from Batch 185K that were previously segregated due to the presence of visible particulate matter on the stopper will now be made available for use as Batch 185aK. Regarding particulate matter on the underside of the stopper, transference studies demonstrated that the particulate matter bound to the stopper in the vials from this batch are unlikely to transfer to the product during reconstitution.

If you observe particulate matter in the vial either before or after reconstitution other than bound to the underside of the stopper, you should quarantine the vial and not administer it to the patient. If no particulates are observed, and in order to minimize the potential risk of adverse events, 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 IM administration or transfer to an IV infusion bag.

If the health care provider decides to administer ERWINAZE IV, health care providers should use an additional 0.2-micron, low protein binding, in-line filter when administering the final IV

admixture to patient. Testing performed with a Baxter IV tubing extension set with 0.2 micron filter (Baxter Catalog ID: 2C8671) demonstrated no impact to Erwinaze product quality.

Because of the critical necessity of this drug, Jazz Pharmaceuticals is asking health care providers to take these necessary steps for patient safety. Please follow the instructions below prior to withdrawing the reconstituted ERWINAZE product from the vials and administering it to patients.

- **Prior to reconstitution, carefully inspect each vial. If you observe particulate matter anywhere other than the underside of the stopper, 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 or transfer to an IV infusion bag.**
- **NOTE: ERWINAZE may be administered by either IM injection or IV infusion. IV administration requires the additional use of a 0.2-micron, low protein binding, in-line filter attached to the primary IV tubing.**
- **If you see particulate matter anywhere in the vial, other than the underside of the stopper, 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 185aK:

REQUIRES 5-MICRON FILTER NEEDLE

IV ADMINISTRATION REQUIRES THE ADDITIONAL USE OF A 0.2-MICRON, LOW PROTEIN BINDING, IN-LINE FILTER

SEE INCLUDED IMPORTANT INFORMATION LETTER

Vials from ERWINAZE Batch 185aK can also be identified by numbering on the individual vial labels. Vials from the affected batch will have one of the following lot numbers: 185aK118, 185aK218, 185aK318, 185aK418, or 185aK518.

Please ensure that 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 steps #1- #7 that include observation of particulate matter and the use of a 5-micron filter needle to withdraw the reconstituted ERWINAZE, and additional requirements for IV use.

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 to 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,

Noam Frey, MD MBA

Vice President, Medical Affairs

Jazz Pharmaceuticals, Inc.

Updated Instructions for Preparation: ERWINAZE Batch 185aK 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 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 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 185aK

ERWINAZE solution may be administered by either intramuscular injection or 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, **use an additional 0.2-micron, low protein binding, in-line filter when administering the final IV admixture to patient.** 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.