



IMPORTANT DRUG INFORMATION

12th August 2019

Subject: ERWINAZE® Batch 194K
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 194K.
Notice of Over-label covering Vial Contents section of Erwinaze® carton

Dear Health Care Provider:

The purpose of this letter is to alert you that ERWINAZE (asparaginase *Erwinia chrysanthemi*) from Batch 194K 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. In addition we would like to inform you that the “flag” label (Erwinaze label 5321-1) may have been placed incorrectly over the vial content text, which is printed on the end panel of the carton.

During routine visual inspections of ERWINAZE Batch 194K, particulate matter was observed in some vials. These affected vials were set aside and not released. However, some of the released vials may still contain particulate matter, which, if present in reconstituted ERWINAZE, may pose a safety risk to patients.

If you observe particulate matter in the vial either before or after reconstitution, you should quarantine the vial and not administer it to the patient. If no particulates are observed, you should use a 5-micron filter needle to withdraw the reconstituted ERWINAZE product from the vials. Additionally, for IV administration, use a 0.2-micron, low protein binding, in-line filter attached to the primary IV tubing when administering the final IV mixture to patient. Because of the critical necessity of this drug, Jazz Pharmaceuticals is asking health care providers to take these necessary steps for patient safety.

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 intravenously, 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.

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 in the vial, quarantine the vial. If you do not observe particulate matter in the vials, 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, 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 “flag” label (5321-1), attached to the carton, can identify vials from ERWINAZE Batch 194K:

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 194K can also be identified by numbering on the individual vial labels. Vials from the affected batch will have one of the following lot numbers: 194K 119, 194K 219, 194K 319, 194K 419, 194K 519 or 194K 619.

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.

Approved US carton printed text on end panel

The text below may be obscured: Dosage and strength information including the content of the vial:

Each vial contains:
10,000 International Units of L-asparaginase
Erwinia chrysanthemi, glucose monohydrate
(5 mg), sodium chloride (0.50 mg)

No preservative. No US Standard of Potency


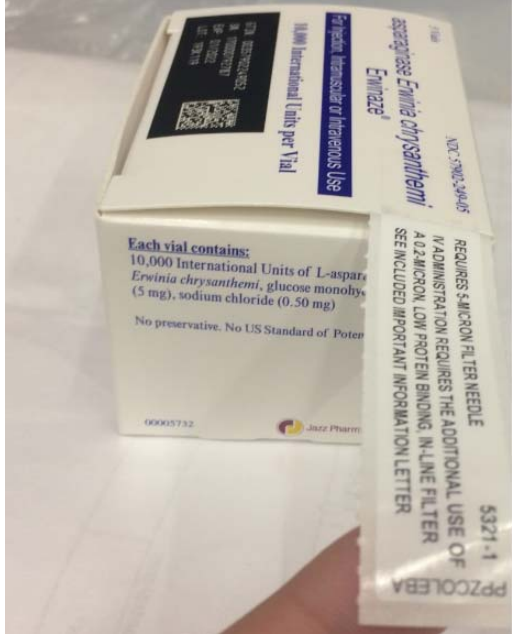
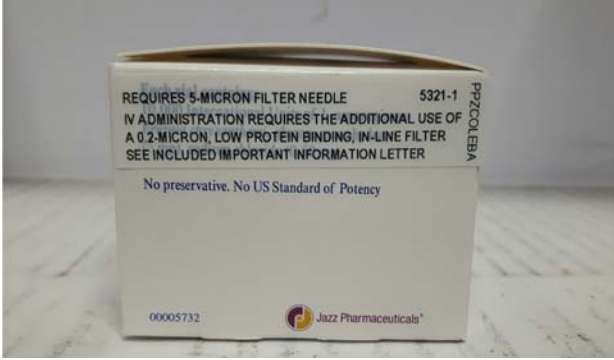
00005732  Jazz Pharmaceuticals®

Figure 1- Excerpt from US artwork 00005732

Correct “flag” placement	Incorrect “flag” placement
<p>The correct placement of the “flag” label (Erwinaze label 5321-1) on the carton is as follows:</p>  <p>Figure 2- Picture of correctly labeled Erwinaze carton</p>	<p>For batch 194K the “flag” label (Erwinaze label 5321-1) may have been placed on the carton incorrectly. This label has been placed over the Vial Contents listing as shown below.</p>  <p>Figure 3- Picture of incorrectly labeled Erwinaze carton</p>

There is no impact to product quality if this over label is incorrectly placed. The wording from the pre-printed carton has been included in this letter for reference, as it may not be clearly visible.

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:

00011057

- 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,

A handwritten signature in black ink, consisting of a series of overlapping, fluid strokes that form a stylized, somewhat abstract representation of the name 'Noam Frey'.

Noam Frey, MD MBA

Vice President, Pharmacovigilance and Medical Affairs

Jazz Pharmaceuticals, Inc.

Updated Instructions for Preparation: ERWINAZE Batch 194K Vial

Preparation and Handling Instructions

1. Carefully inspect each vial. If you observe particulate matter, quarantine the vial. If you do not observe particulate matter, 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 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 194K

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.