Jazz Pharmaceuticals®

IMPORTANT DRUG INFORMATION

January 9, 2017

Subject: Notice of Temporary Shortage of the 100 mcg/mL 1 mL Vial of PRIALT® (ziconotide) Solution, Intrathecal Infusion and Updated Temporary Preparation Instructions for Priming and Initial Pump Fill of the Medtronic SynchroMed® II Infusion System Using Diluted 100 mcg/mL 5 mL Vials of PRIALT® (ziconotide) Solution, Intrathecal Infusion

Dear Health Care Provider,

Jazz Pharmaceuticals (Jazz) is writing to inform you of a temporary interruption in the supply of the PRIALT 100 mcg/mL 1 mL vial (used for pump refills of the Medtronic SynchroMed® II Infusion System), in addition to the 25 mcg/mL 20 mL vial (used for naïve pump priming, initial pump fill, and subsequent refills of the Medtronic SynchroMed® II Infusion System) as previously communicated in a letter dated October 27, 2016. This shortage is not related to any safety or efficacy concerns, but due to a manufacturing event. The reason for the interruption in supply does not impact the quality, safety, or efficacy of PRIALT currently available on the market. We are working closely with our manufacturer to have additional PRIALT 100 mcg/mL 1 mL and 25 mcg/mL 20 mL vials available as soon as possible to meet patient needs.

The PRIALT 100 mcg/mL concentration in the 5 mL vial (500 mcg of PRIALT total) is not affected by the shortage and is available through normal distribution channels. The 25 mcg/mL, 20 mL vials are used for naïve pump priming and initial pump fill, and subsequent refills of the Medtronic SynchroMed® II Infusion System ("SynchroMed® II Pump").[1] In an effort to minimize any disruption of the initiation of PRIALT treatment for your patients, we are recommending healthcare providers dilute PRIALT 100 mcg/mL (using the available 5 mL vial) to 25 mcg/mL for naïve pump priming and for the initial pump fill according to the instructions below if your facility does not have PRIALT® 25 mcg/mL, 20 mL vials available. For subsequent refills (after the initial pump fill), we are recommending health care providers use the available 5 mL Prialt vial (100 mcg/mL concentration).

Dosage and Administration

In an effort to minimize impact to patients during the shortage, Jazz Pharmaceuticals worked with U.S. Food and Drug Administration ("FDA") to come up with a temporary preparation alternative for PRIALT for naïve pump priming and initial fill in the SynchroMed® II Pump. Below you will find:

(1) information on how to dilute 100 mcg/mL vials (using the available 5 mL vial) to 25 mcg/mL concentration, Prime, and Fill the SynchroMed® II Pump,
(2) pump compatibility data for the 25 mcg/mL concentration, diluted from the 100 mcg/mL vials, for priming and initial pump fill (collectively, "Prime and Fill") for the SynchroMed® II Pump,

[1] The CADD-Micro Ambulatory Infusion Pump is not affected by the shortage of the 25 mcg/mL 20 mL vials of PRIALT and instructions for use remain the same.

(3) previous clinical trial data in which PRIALT 100 mcg/mL was diluted to 25 mcg/mL with 0.9% Sodium Chloride Injection, USP (preservative free) for naïve pump priming and the initial pump fill (Synchromed Infusion System)

Temporary Preparation Instructions for the SynchroMed® II Pump

The pump compatibility data, previous clinical trial data, and proposal for a temporary preparation option for healthcare providers to consider were reviewed by the FDA. The temporary preparation instructions for the SynchroMed® II Pump involve diluting PRIALT 100 mcg/mL vials with 0.9% Sodium Chloride Injection, USP (preservative free) for naïve pump priming and initial pump fill with refill within 8 days for the SynchroMed® II Pump. No objections were raised by FDA regarding the proposed recommendation. **Please note that this information is different than the directions in the Prescribing Information.**

Naïve Pump Priming (i.e. first time use with Prialt) and Initial Pump Fill:

Dilute the 100 mcg/mL concentration (5 mL vial) with 0.9% Sodium Chloride Injection, USP (preservative free) using aseptic procedures (in a physician's office or in a pharmacy) to achieve the 25 mcg/mL concentration (see below). Rinse the internal surfaces of the pump with 2 mL of the PRIALT 25 mcg/mL. Repeat twice for a total of 3 rinses (per PRIALT Section 2.3 "Instructions for Use with the Medtronic SynchroMed II Infusion System" of the PRIALT Prescribing Information). Replace the initial fill solution in the SynchroMed® II Pump ***within eight (8) days****.* (See Pump Compatibility Data section below)

Instructions on How to Dilute the PRIALT 5 mL vial (100 mcg/mL)

1. Withdraw 5 mL of the PRIALT 100 mcg/mL solution
2. Add 15 mL of 0.9% Sodium Chloride Injection, USP (preservative free) solution to achieve a total of 500 mcg in 20 mL of PRIALT solution with a concentration of 25 mcg/mL

For Subsequent Pump Refills (after the Initial Pump Fill) see Section 2.3 "Instructions for Use with the Medtronic SynchroMed II Infusion System" of the PRIALT Prescribing Information (above changes do not affect these instructions):

- Fill the pump at least every 40 days if PRIALT 100 mcg/mL is used diluted
- If undiluted PRIALT 100 mcg/mL is used, refill the pump within 84 days

Based on a complete assessment of the data and proposed instructions, healthcare providers should use their clinical judgment and experience to determine if diluting the PRIALT 100 mcg/mL 5 mL vial for the naïve pump priming and initial pump fill is the most appropriate treatment method for their patients. Please ensure your staff and any provider in your institution who may prescribe or prepare PRIALT receives a copy of this letter and specifically reviews the Temporary Preparation Instructions for the SynchroMed® II Pump.

Jazz recognizes the importance of PRIALT to you and your patients and remains committed to this product. Healthcare providers should use their clinical judgment and expertise to determine treatment options for your patients. We regret any inconvenience the temporary shortage of the PRIALT 1 mL and 20 mL vials may cause.

Pump Compatibility Data

Pump compatibility studies were carried out with PRIALT and the SynchroMed® II Pump under simulated clinical conditions (at 37°C) to determine acceptable refill intervals. Based on those compatibility studies, naïve pumps filled with PRIALT 25 mcg/mL solution prepared by diluting PRIALT 100 mcg/mL with saline should be refilled within 8 days of initial fill.[2]

Previous Clinical Trial Data

In one of the pivotal studies assessing the efficacy and safety of intrathecal PRIALT in the management of severe chronic pain (220 patients: 112 PRIALT, 108 Placebo), PRIALT 100 mcg/mL was diluted to 25 mcg/mL with 0.9% Sodium Chloride Injection, USP (preservative free) for naïve pump priming and the initial pump fill (Synchromed Infusion System).[3]

Further Information

PRIALT solution, intrathecal infusion is indicated for the management of severe chronic pain in adult patients for whom intrathecal therapy is warranted, and who are intolerant of or refractory to other treatment, such as systemic analgesics, adjunctive therapies, or intrathecal morphine.

Please see accompanying Full Prescribing Information for PRIALT.

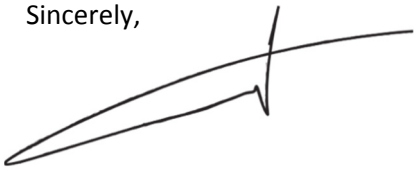
For more information, visit www.prialt.com or call 1-800-520-5568.

Call for reporting

Healthcare providers should report product quality problems and all suspected adverse events associated with the use of PRIALT. If you become aware of a patient experiencing an adverse event while taking PRIALT or product quality problems with PRIALT, 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 from 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.

[2] Technical Report AQS-1924, Summary of Pump Compatibility Studies with Ziconotide and Medtronic SynchroMed Infusion Systems at Simulated Clinical Conditions, Amended Version 2, February 20, 2007.

[3] Clinical Study Protocol for Study ELN92045-301 (Protocol Date March 27, 2002) : A Randomized, Double-Blind, Placebo-Controlled Study of Intrathecal Ziconotide in Adults with Severe Chronic Pain