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September 2, 2015

IMPORTANT PRESCRIBING AND SAFETY INFORMATION

Subject: **UPDATE: IMPORTANT SAFETY AND COMPATIBILTY INFORMATION FOR TREANDA® (bendamustine HCl) INJECTION (45 mg/0.5 mL or 180 mg/2 mL solution)**

Dear Health Care Provider:

On March 10, 2015, Teva Pharmaceuticals sent a communication to healthcare professionals highlighting important safety and incompatibility information for TREANDA® (bendamustine HCl) Injection, the TREANDA solution formulation. TREANDA Injection contains N,N-dimethylacetamide (DMA), which is incompatible with devices that contain polycarbonate or acrylonitrile butadiene styrene (ABS). This letter provides you with a list of specific devices Teva has tested and found to be compatible with TREANDA Injection.

Table 1 lists devices that do NOT contain polycarbonate or ABS and are compatible with TREANDA Injection (solution in the vial). Table 2 includes compatible IV administration sets for use with TREANDA Injection following dilution in 500 mL 0.9% Sodium Chloride or 500 mL 2.5% Dextrose/0.45% Sodium Chloride Injection IV bags. Compatibility studies did not include testing with 2.5% Dextrose/0.45% Sodium Chloride Injection; however, the results of these studies are not expected to change, so either diluent, 0.9% Sodium Chloride or 2.5% Dextrose/0.45% Sodium Chloride Injection, can be used with TREANDA Injection.

This letter informs you that the TREANDA labeling has been revised to include important safety information regarding the safe preparation and administration of TREANDA Injection **before** and **after** dilution of TREANDA Injection. (*See Sections 2 and 16 of the US PI*).

Table 1 lists the compatibility of TREANDA Injection with specific closed system transfer devices (CSTDs), syringes, vial adapters, and gloves.

Table 1: Compatible Devices for Use with TREANDA Injection (based on testing conducted by Teva from February 2015 through June 2015)

Component Tested	Component Brand Name (Part Number)
Closed System Transfer Devices (CSTDs)	BD Phaseal™ System consisting of: BD Phaseal Protector P14 (REF 515100), BD Phaseal Injector Luer Lock N35 (REF 515003), BD Phaseal Infusion Adapter C100 (REF 515306), BD syringe 5 mL (REF 309646 and 309657)
Vial Adapters	Baxter CHEMO-AIDE Dispensing Pin (REF 2N9106) Medimop Swabable Vial Adapter (REF 8070101) Alaris® Smartsite® (REF 2202E and 2203E)
Polypropylene Syringes	BD™ (Becton Dickinson), 5 mL (REF 309646); 3 mL (REF 309657) Covidien Monoject™, 5 mL (REF 1180600777); 3 mL (REF 1180300777) B. Braun, 5 mL (REF 4617053V-02); 3 mL (REF 4610303-02) Air-Tite Norm Jet®, 5 mL (REF 4050.X00V0) and 3 mL (REF 4020.X00V0) Medline 5 mL (REF SYR105010) and 3 mL (REF SYR103010) Terumo®, 5 mL (REF SS-05L)
Disposable Gloves*	ChemoPlus™ (REF CT0194-1) EP-Blue™ (REF 181350) Jackson Safety G29™ (REF 49824) NeoPro® (REF NPG-888) NitriDerm® (REF 182350) Purple™ (REF 50604) Purple KC 500™ (REF 55084) UltraSense EC® (REF USE-880)

*Part numbers reflect a specific size glove used in the compatibility tests. Brand names are trademark of the respective manufacturer.

Table 2 lists the IV administration sets tested and found to be compatible with TREANDA Injection **after** dilution in a 500 mL 0.9% Sodium Chloride IV infusion bag.

Table 2: Compatible IV Administration Sets for Use with TREANDA Injection Following Dilution in 500 mL 0.9% Sodium Chloride* IV Bags (based on testing conducted by Teva from February 2015 through June 2015)

Component Tested	Brand Name / Part Number
IV Administration Sets†	B. Braun Safeline® (REF NF3482) and AdditIV® (REF V1921) Baxter DuoVent Spike (REF 2C7575) and Clearlink System (2H8480) BD Phaseal™ Secondary set (REF 515301) ICU Medical Clave®(REF CH3011)

* 2.5% Dextrose/0.45% Sodium Chloride Injection can also be used.
†Representative sampling based on materials of construction in the fluid path. Brand names are trademark of the respective manufacturer.

The above lists of compatible devices can be found on www.TREANDAHCP.com and these lists will be updated on a quarterly basis. Device manufacturers may change the composition or components of the device(s) without Teva's knowledge. Please consider contacting the device manufacturer or Teva U.S. Medical Information (1-800-896-5855) regarding compatibility of the device with TREANDA Injection (45 mg/0.5 mL or 180 mg/2 mL solution).

Action for Drug Preparation

The underlined text below indicates changes made to the TREANDA labeling.

Safe Preparation and Handling for IV Administration of TREANDA Injection (S*ee Sections 2 and 16 of US PI*)

- **When preparing and transferring the concentrated TREANDA Injection solution into the infusion bag, do not use devices that contain polycarbonate or ABS. However, after dilution of TREANDA Injection into the infusion bag, devices that contain polycarbonate or ABS, including infusion sets, may be used.**
  TREANDA Injection contains N,N-dimethylacetamide (DMA), which is incompatible with devices that contain polycarbonate or ABS. Devices, including CSTDs, adapters, and syringes that contain polycarbonate or ABS have been shown to dissolve when they come in contact with DMA which is present in the product. This incompatibility leads to device failure (e.g., leaking, breaking, or operational failure of CSTD components), possible product contamination, and potential serious adverse health consequences to the practitioner, including skin reactions; or to the patient, including but not limited to, the risk of small blood vessel blockage if they receive product contaminated with dissolved ABS or polycarbonate. Devices that are compatible for use in dilution of TREANDA Injection are available.
- **If using a syringe to withdraw and transfer TREANDA Injection from the vial into the infusion bag, only use a polypropylene syringe with a metal needle and polypropylene hub to withdraw and transfer TREANDA Injection into the infusion bag. After dilution of TREANDA Injection into the infusion bag, devices that contain polycarbonate or ABS, including infusion sets, may be used.**
- If a CSTD or adapter that contains polycarbonate or ABS is used as supplemental protection prior to dilution, only use TREANDA for Injection, the lyophilized powder formulation. (*See Section 16.1 of US PI*)

- The use of gloves and safety glasses is recommended to avoid exposure in case of breakage of the vial or other accidental spillage. If gloves come in contact with TREANDA Injection prior to dilution, remove gloves and follow disposal procedures. If a solution of TREANDA contacts the skin, wash the skin immediately and thoroughly with soap and water. If TREANDA contacts the mucous membranes, flush thoroughly with water.

Reporting Adverse Events

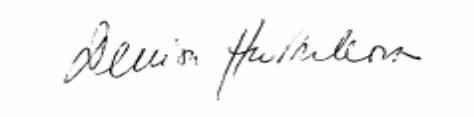
Health care providers and patients are encouraged to report adverse events in patients taking TREANDA Injection (45 mg/0.5 mL or 180 mg/2 mL solution) to Teva Pharmaceuticals at 1-800-896-5855.

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.

You also may contact our medical information department at 1-800-896-5855 if you have any questions about the information contained in this letter or the safe and effective use of TREANDA Injection (45 mg/0.5 mL or 180 mg/2 mL solution).

Sincerely,



Denisa Hurtukova, MD
Vice President, Head of North America Medical Affairs
Teva Pharmaceuticals

Enclosure(s): Full Prescribing Information for TREANDA® (bendamustine HCl) Injection (45 mg/0.5 mL or 180 mg/2 mL solution), TREANDA® (bendamustine HCl) for Injection (25 mg/vial or 100 mg/vial lyophilized powder). Full Prescribing Information.