Direct Healthcare Professional Communication

Name
Address Line 1
Address Line 2
Town/City
Post Code

[Date]

Arsenic Trioxide (Trisenox®) 1 mg/ml concentrate for solution for infusion - importation and over-labelling of United States (US) Trisenox® stock as Teva UK interim supply

Dear Healthcare professional,

Teva UK Limited would like to inform you of the following:

Summary

- *There are currently manufacturing issues affecting UK supplies of Arsenic Trioxide (Trisenox®) from June 2017. Subsequent resolution will take approximately two months.*
- *As an interim measure, importation of US Trisenox® ampoules will be introduced for supply in Teva UK packaging in order to maintain continuity of supply in the UK.*
- *US Trisenox® has the same composition and method of manufacture as the Teva EU product registered under EMEA/H/C/388, so products are identical*
- *US Trisenox® ampoules will be overlabelled with the EU approved labelling statements*
- *This is considered a licensed product*
- *Over-labelling will be be performed by an authorised facility*

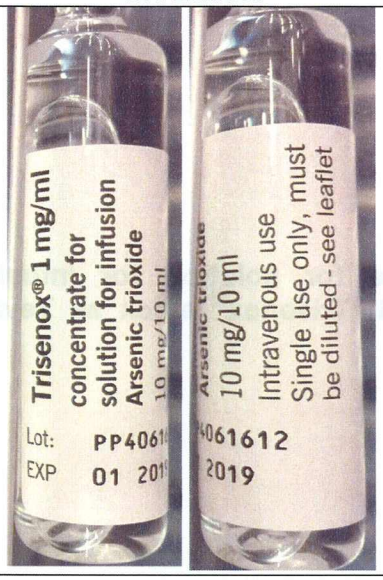
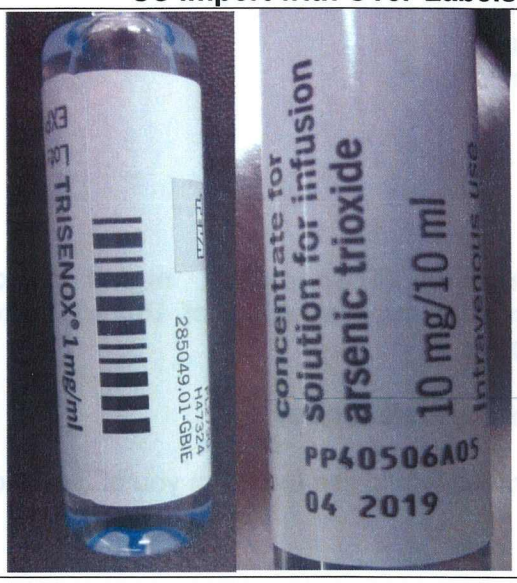
This information is being sent in agreement with the Medicines and Healthcare products Regulatory Agency

Further information on the safety concern and recommendations

Teva UK Limited is the sole market provider of Arsenic Trioxide (Trisenox®) 1 mg/ml concentrate for solution for infusion in the UK. We have potential supply issues due to the registered finished product manufacturing site being unable to produce the product. A variation to add an alternative finished product manufacturing site has been submitted and awaiting approval. There is only a limited amount of Trisenox® currently available and an expected delivery from a new supplier would potentially exceed the stock run out date. We anticipate that normal UK supplies of Trisenox® will resume in *approximately* two months.

In order to mitigate the risk of Teva UK being unable to supply patients with Trisenox® 1 mg/ml concentrate for solution for infusion, we will import Teva US ampoules with the same composition and manufacturing method to supply the UK marketplace. The US ampoules will be packed in UK cartons along with a UK Patient Information Leaflet (PIL).

Teva UK will cover the US inner label on the Trisenox® ampoule with a larger label in line with the labelling approved for the UK. The over-label will present the current authorised UK particulars and the label dimensions will ensure that the US label is completely obscured. The over-labelling will be performed by a registered labelling company

UK Labels	US Import with Over-Labels
	

Further information

Trisenox® is indicated for induction of remission, and consolidation in adult patients with:

- Newly diagnosed low-to-intermediate risk acute promyelocytic leukaemia (APL) (white blood cell count, ≤ 10 x 103/µl) in combination with all-trans-retinoic acid (ATRA)
- Relapsed/refractory acute promyelocytic leukaemia (APL) (Previous treatment should have included a retinoid and chemotherapy) characterised by the presence of the t (15; 17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha (PML/RAR-alpha) gene.

The response rate of other acute myelogenous leukaemia subtypes to arsenic trioxide has not been examined.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.

It is easiest and quickest to report ADRs online via the Yellow Cards website - https://yellowcard.mhra.gov.uk/

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Adverse events should also be reported to Teva UK Limited at: www.tevauk.com

Company contact point

If you have any questions or require additional information regarding the use of Trisenox®, please feel free to contact Teva UK Medical Information on: 0207 540 7117 or *via* email at: medinfo@tevauk.com.

Further information is also located on the Teva UK website at www.tevauk.com under the Healthcare Professional Arsenic Trioxide product page.

Yours Sincerely

Dr Ewan Walters
Senior Director Medical Affairs UK & Ireland