

Pfizer Inc
235 East 42 Street
New York, NY 10017

Clinical Development & Medical Affairs



THIS DOCUMENT CONTAINS CONFIDENTIAL AND/OR TRADE SECRET INFORMATION THAT IS DISCLOSED ONLY IN CONNECTION WITH THE LICENSING AND/OR REGISTRATION OF PRODUCTS FOR PFIZER INC OR ITS AFFILIATED COMPANIES. THIS DOCUMENT SHOULD NOT BE DISCLOSED OR USED, IN WHOLE OR IN PART, FOR ANY OTHER PURPOSE WITHOUT THE PRIOR WRITTEN CONSENT OF PFIZER INC.

Date: 29 December 2010

To: Investigators Participating in Torisel (temsirolimus) Clinical Studies

Re: Important Information regarding use of bags and/or IV administration sets containing (di-2-ethylhexyl) phthalate (DEHP) for Torisel administration

Dear Investigator,

This letter is to inform you that Pfizer recently became aware that some investigator sites participating in Torisel clinical studies sponsored by Pfizer have been utilizing bags and/or IV administration sets that are not in compliance with the Torisel clinical study protocols. Specifically, some investigator sites have used bags and/or tubing when infusing IV Torisel that contains the plasticizer DEHP, which is explicitly prohibited by the protocols. Use of any components (such as bags or IV administration sets) containing DEHP constitutes a protocol deviation.

By way of reminder, the Torisel package insert (label) and Investigators' Brochure provides the following instructions:

- In order to minimize the patient exposure to the plasticizer DEHP (di-2-ethylhexyl phthalate), which may be leached from polyvinyl chloride (PVC) infusion bags or sets, the final temsirolimus dilution for infusion should be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets.
- The sodium chloride injection container should be composed of non-DEHP containing materials, such as glass, polyolefin or polyethylene, and the administration set should consist of non-DEHP tubing to avoid extraction of (di-2-ethylhexyl) phthalate (DEHP). Torisel contains polysorbate 80, which is known to increase the rate of DEHP extraction from PVC.

The amounts of DEHP extracted from the use of DEHP-containing bags and/or IV administration sets and the significance of the risks arising from the use of DEHP-containing bags and/or IV administration sets while infusing Torisel in patients with renal cell carcinoma are currently being investigated.

However, in accordance with the Torisel protocol, PVC bags or IV administration sets containing DEHP **must not be used** for the preparation, storage and administration of TORISEL solutions for infusions.

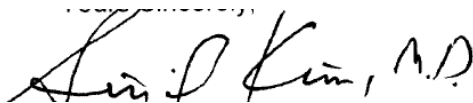
Investigator Actions:

1. As soon as possible, please confirm that the infusion bags and IV administration sets being used at your site are compliant with the Torisel protocol.
2. If the infusion bags and/or IV administration sets being used at your site are not compliant, i.e. you are currently using any bags and/or IV administration sets that contain DEHP, you will need to comply with the protocol immediately by using bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and by administering Torisel only through administration sets which are entirely lined with polyethylene, including any extension tubing through which Torisel may be in contact.
3. If the infusion bags and IV administration sets being used at your site are not compliant with the Torisel protocol, please inform and report the protocol deviation to your local IRB/Ethics Committee.
4. Please discuss the use of appropriate infusion materials/equipment for Torisel with your Pharmacists, IV administration nurses, coordinators and study staff.

If you have any difficulties with the above actions, questions or concerns, please do not hesitate to contact your Country Medical Director, Regional Medical Research Specialist (RMRS), IIR Grant Manager or any of us.

We appreciate your review of this important matter in your IIRs (investigator initiated trials).

Yours Sincerely,



Sinil Kim, MD
Global Clinical Lead, Axitinib & Temsirolimus
Telephone: +1 (858) 622-7997
Email: sinil.kim@pfizer.com



S. Hariharan, MD
Global Medical Lead, Torisel
1-212-733-8889
s.hariharan@pfizer.com