



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: February 4, 2011

To: Principal Investigators
Primary Clinical Research Associates

From: Sara Braun / Jack Beranek
Research Protocol Specialists

Re: N0572, A Phase I/II Trial of Sorafenib and CCI-779 in Patients with Recurrent Glioblastoma

N078D, Phase I/II Trial of Rituximab, Cladribine, and Temsirolimus (RCT) Therapy in Newly Diagnosed Mantle Cell Lymphoma (MCL)

Please see the attached letter regarding administration of the drug Torisel which is used in protocols N0572 and N078D. The protocols have been reviewed by the NCCTG Research Base Pharmacy personnel and are in compliance with the information in this letter.

Please review the administration procedures of Torisel at your institution(s) to ensure compliance.

If you have any questions, please feel free to contact me.

Enclosure

Pfizer Inc
235 East 42 Street
New York, NY 10017

Clinical Development & Medical Affairs



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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.

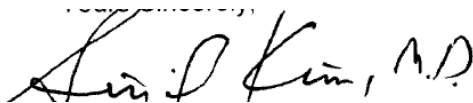
Investigator Actions:

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,



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