May 2012

INSIDE PMB

Pharmaceutical Management Branch

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I'm Dawn Rubicin, news anchor, wishing you a good morning and welcoming you to Inside PMB, where you'll find the latest news and entertainment to help you get through your busy day.
Rex has our top story about OAOP, Mel has the latest weather, Phil with sports, your morning commute,and Flo's mailbag. Now here's Rex with the latest headline…

OAOP BARRIERS. WHAT'S NEXT?

World-renowed self-help guru, Ineeda Order, lists procrastination as one of biggest barriers to getting what you want. In speaking with PMB correspondent Rex Platin about her new book, she said, "Don't put off for tomorrow what you can do today!" referring of course to the last day paper orders will be accepted at PMB. Rex notes that June 1, 2012 is quickly approaching and as of the end of March, approximately 75% of Clinical Drug Requests were submitted through OAOP. We are getting closer, but aren't there yet. Are you in the 25% still using paper orders?

To get you on the right track, there are two requirements before you start using OAOP:

- **Create a CTEP IAM account and maintain an "active" account status and a "current" password on the PMB website at** https://eapps-ctep.nci.nih.gov/iam/

  AND

- **Confirm that you are listed as either the shipping designee (box 11) or an ordering designee (box 12) on the most current Supplemental Investigator Data Form (IDF) on file with PMB for each investigator for whom you want to order investigational agent**

More specific instructions for accessing OAOP are provided in an FAQ available on the PMB website at
http://ctep.cancer.gov/branches/pmb/faq/docs/how_to_access_oaop.pdf

Ineeda Order says you can avoid the proscrastination pitfall by trying OAOP now and not by waiting until June 1st to find out you are having difficulties. If you begin using it for order submissions and are having problems, Ineeda says you can help us help you get what you want by following the instructions below:

STEP 1: logon to OAOP https://eapps-ctep.nci.nih.gov/OAOP/pages/login.jspx ... using your IAM username and password … for problems, contact the CTEP Registration Help Desk CTEPREGHelp@ctep.nci.nih.gov

STEP 2 : click the OAOP List of Values (LOV) for "NCI Investigator Number" … check that all investigators you expect to be there are there … for problems, contact the PMB Registration Help Desk PMBRegPend@ctep.nci.nih.gov

If you still don't understand Ineeda Order, our PMB correspondent and OAOP expert, Rex Platin, will be happy to assist you at PMBafterhours@mail.nih.gov.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Cancer Institute

TRAFFIC REPORT: HOV LANE SERVICE IMPROVED

On April 2, 2012, PMB started using FedEx Ground Service for all non-expedited, room temperature shipments in place of U.S. Priority Mail for continental U.S. sites. FedEx Ground may take up to 5 business days to arrive once the order is shipped. Please plan accordingly. But if you're in a traffic jam or running late, expedite your shipment by providing an express courier number.

Your shipment notification e-mails now contain a link for tracking information for these shipment types. Otherwise, the only significant impact to sites is a change in the way three Dangerous Good (DG) agents are shipped. Bortezomib For Injection (NSC 681239), Romidepsin For Injection (NSC 630176) and Dasatinib Tablets (NSC 732517), were all previously shipped via Priority Overnight service because the DG status dictated they could not be transported through the U.S. Postal Service. Now, these agents will be shipped FedEx Ground.

Overall, the changes should be transparent and our hope is that we're providing a higher level of service for our sites. Let us know how we're doing at PMBafterhours@mail.nih.gov.

TIMEOUT NEEDED DRUG SHORTAGES
PHIL GRASTIM, SPORTS ANNOUNCER

Drug shortages have affected many medical specialties, oncology among them. Recent plays by the FDA have brought relief for some of the most problematic agents used in the treatment of cancer. However, there are still shortages that must be dealt with on a daily basis as struggling pharmacists on the front lines wish they could call a timeout.

CTEP has been following the field very closely. The options available to the NCI are limited by regulations and resources. For a play-by-play discussion of the NCI actions please go to the CTEP web site. http://ctep.cancer.gov/branches/pmb/drug_shortages.htm

PMB has been asked to provide commercial agents to support the standard treatment arms for NCI sponsored trials as well as for patients not enrolled in NCI sponsored studies. There is the impression that we either have a supply of commercial agents available or that we have an inside track with the pharmaceutical industry to obtain supplies. Some believe that we have sources within the industry to obtain information not available to the public or the FDA. None of these is the case. CTEP has the same batting average as everyone else and can't fix the game.

Questions regarding drug shortages can be addressed to the FDA Center for Drug Evaluation and Research (CDER) Drug Shortage Program at: DRUGSHORTAGES@cder.fda.gov . Current information about the availability of agents can be obtained from the following sites:

FDA http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm

ASHP http://www.ashp.org/shortage

Currently CTEP is collecting data to assess the impact of these shortages on the conduct of NCI sponsored clinical trials. There are anecdotal reports of trials being delayed or patient care being impacted, but specific information has been hard to substantiate. If you experience patient care or if accrual to an NCI sponsored clinical trial is impacted, let us know at PMBAfterHours@mail.nih.gov. (Subject line: Drug Shortage).

PLAYING THE SUBSTITUTION SHELL GAME

Beware when considering substitution because of a drug shortage. For example, not all liposomal products are created equally—in fact most are NOT created equally. With Doxil® specifically, the FDA has approved temporary importation of an equivalent product (Lipodox™) for use in the United States while Doxil® is unavailable. Read more at http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM292634.pdf

When Doxil® is used in an NCI-sponsored protocol, in addition to obtaining the substitute product, the protocol must be amended to use Lipodox™ since Doxil® is usually addressed by its specific brand name in the protocol (as there is such variation between liposomal products). The PI of the study will amend the protocol to include language similar to "Doxil®, Lipodox™, or the equivalent."

Drug shortages create the potential for significant safety issues and protocols can be a complicating factor. We all strive to provide the best possible patient care while maintaining the integrity of the clinical trial, but during these difficult supply times that can be challenging.

CHANGE OF DISTRIBUTION

Agent Name	NSC	Effective Date	Affected Protocol/s	Actions
Ascenta's AT-101 (R)-(-)-Gossypol acetic acid	726190	June 11, 2012	8035 8062 NABTT-0702	Protocols must close to accrual and treatment by June 11, 2012
Lenalidomide (CC-5013)	703813	July 1, 2012	BMTCTN-0702	Amendment 5 describes changes in agent distribution

FLO'S MAILBAG
BY FLO URACIL

If you didn't already know, all sites have until June 1, 2012 to convert to order submission through OAOP for PMB-supplied agents. The paper-based CDR, NIH Form 986, will no longer be accepted after May 31. Two of our listeners wrote in about this very issue and here's what you need to do:

Q: *"The investigator I am trying to place an order for is not available to select. How do I place my order?"*

A: The individual logged on to OAOP will ***only*** have access to investigators who have listed that individual as a Shipping or Ordering Designee. It is extremely important that all Shipping Designees and Ordering Designees logon to OAOP before June 1st and verify their ability to order for all expected investigators. While updating an investigator's Shipping Designee or Ordering Designee is a relatively easy fix, these changes will take time if PMB is bombarded with change requests at the last minute.

Q: *"I tried to logon to OAOP; however, I received a message that I have 'insufficient privileges'."*

A: In this case, the individual attempting to log on is not linked with ***any*** investigators as an Ordering Designee or a Shipping Designee. But the final answer is the same … the Supplemental Investigator Data Form will need to be updated.

BIG NEWS FOR SMALL PATIENTS

Glucarpidase Injection (Formerly available through PMB Special Exception as carboxypeptidase)

On January 17, 2012, the US Food and Drug Administration approved glucarpidase injection (Voraxaze®, BTG International Inc.) for the treatment of toxic methotrexate plasma concentrations (> 1 umol/L) in patients with delayed methotrexate clearance due to impaired renal function.

The commercial launch of Voraxaze® is planned for later in 2012. Continue to contact the Voraxaze Call Center at 877-398-9829 for availability.

This approval and launch are not to be confused with procedures to acquire **glucarpidase under the intrathecal (IT) emergency use IND.**

> Glucarpidase for intrathecal (IT) administration is available in the US free of charge for emergency use to treat IT methotrexate (MTX) overdose. An outline of the procedure can be obtained from the website: http://www.btgplc.com/products/voraxaze-us-treatment-protocol (go midway down the page).

Erwinia Asparaginase

Erwinaze™ (Asparaginase *Erwinia chrysanthemi*) was approved by the FDA on November 18, 2011. It is approved to treat patients with acute lymphoblastic leukemia (ALL), who have developed an allergy (hypersensitivity) to E. coli derived asparaginase and pegaspargase.

Erwinaze™ is supplied as a sterile, white lyophilized powder in a clear 3 ml glass vial. Each carton contains 5 vials. Each vial contains 10,000 International Units of asparaginase *Erwinia chrysanthemi*. Store unused or unopened vials and cartons at 36°F to 46°F (2°C to 8°C). Protect from light.

Erwinaze™ is manufactured by EUSA Pharma in Langhorne, PA, and is commercially available. More information is available at http://Erwinaze.com.

MAY JUNE JULY AUGUST SEPTEMBER OCTOBER

THE CAPITOL WEATHER WITH MEL FALAN'S FORECAST

Mel Falan here with your 6-month tru-weather forecast… As summer approaches and temperatures soar in the coming months, excursion questions rain on PMB like cats and dogs. So there's no time like now to get your pharmacies ready.

Readers called into the weather tip line to provide this helpful list so you can be made in the shade rather than throwing caution to the wind:

- Check to see that refrigerator, freezer and room temperature monitoring systems are functional
- Check that temperature logs are up-to-date
- Instruct staff about how to handle agents that have experienced temperature excursions
- When temperature excursion occurs, contact PMB to ask about whether an agent is still acceptable for clinical use. Provide the following information:
    - Agent name and NSC
    - Agent lot number
    - NCI protocol number
    - Minimum and maximum temperature
    - Length of time outside of storage range

THE SKINNY ON CHEMOTHERAPY DOSING IN OBESE

A recent clinical practice guideline from the American Society of Clinical Oncology (ASCO) titled "Appropriate Chemotherapy Dosing for Obese Adult Patients with Cancer," ahead of print April 2, 2012 www.jco.org, tried to answer questions of possible excessive toxicity in overweight and obese patients. Surveys have shown that up to 40% of obese patients receive limited doses not based on actual body weight and there's considerable variation in dosing of overweight and obese patients. The Centers for Disease Control and Prevention state that most Americans have a BMI greater than 25, which categorizes them as being overweight or obese. As this number continues to rise, addressing these inconsistencies is paramount.

The ASCO panel proposed and answered six clinical questions focusing on excess toxicity, dose modifications, reduced efficacy, the role of pharmacokinetic and pharmacogenetic parameters, calculation of BSA, and the use of fixed-dose regimens. The panel recommended full weight-based chemotherapy dosing in overweight and obese patients, particularly when the treatment goal is cure. Multiple clinical trials have shown no difference in toxicities between obese and non-obese patients, but in fact poorer outcomes in obese patients who receive less than full weight dosing. The panel recommended clinicians manage toxicities in obese patients in the same ways they do in non-obese patients. The panel stated that fixed-dose (weight or BSA –independent) chemotherapy is only justified in select agents that limit doses due to known toxicities. The panel acknowledged lack of evidence for both selecting a preferential BSA formula and the impact of obesity on pharmacokinetic or pharmacogenetic parameters.

While these guidelines made great strides in answering some clinical questions, the recommendations are limited due to the overwhelming lack of clinical evidence in this patient population. The majority of representative trials were in breast, colon, lung and ovarian cancers, and dosing of novel targeted therapies was left out because of insufficient evidence. The ASCO panel of experts acknowledges the need for continued clinical research in this population to fully answer these clinical questions.

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