

ADIOS, AMIGO! HOLA, GIRLFRIENDS!

In our last issue, we introduced you to our staff. Shortly thereafter, our favorite cappuccino maker, **Carl Huntley**, defected to the F&DA! The nerve! His 12 years of PMB experience will be missed, but we wish him the very best.

Meanwhile, **Ravie Kem**, PharmD has joined our staff and is handling a portfolio of agents. Please join us in welcoming Ravie! (That means "Do not give her a hard time on the phone, OK?")

Meeta Krishnamurthy has also joined us and will be handling inventory management issues. (We hear she's a good cook, too!)

SHAKE IT UP, BABY! TWIST AND SHOUT!

For the last three issues, the **carboxypeptidase** (CPDG₂; NSC 641273) box has been in the other column. We are putting it over here to make sure you don't ignore it.

PMB remains the only source of carboxypeptidase in the United States. Every once in a while, we receive a call from a site where a patient has received an intrathecal (IT) overdose of methotrexate (MTX). Severe neurotoxicity and death may occur following accidental IT methotrexate overdoses. Standard IT doses are usually in the range of 6 to 12 mg. IT MTX doses less than 10-fold the standard dose are likely to be relatively well tolerated. Management can be limited to cerebral spinal fluid (CSF) exchange. Severe toxicity, including neurologic toxicity, brain damage, and death may occur when an IT MTX overdose of more than 600 mg occurs. Recommendations for patients who receive IT MTX doses greater than 100 mg include:

- immediate lumbar puncture to drain the CSF;
- emergency ventriculostomy placement followed by ventriculo-lumbar perfusion;
- administration of systemic corticosteroids (dexamethasone 4 mg administered intravenously every 6 hours for 4 doses, and then as needed) to potentially decrease the severity of the chemical meningitis secondary to MTX and CPDG₂;
- administration of systemic leucovorin 100 mg every 6 hours for 4 doses to prevent systemic MTX toxicity; and
- carboxypeptidase-G2 (CPDG₂) 2000 units IT over 5 minutes.

CPDG₂, an investigational agent, is an enzyme that rapidly hydrolyzes and inactivates MTX. For information on how to obtain CPDG₂ for IT MTX overdoses, call the Pharmaceutical Management Branch at 301-496-5725.

And BTW.....

Carboxypeptidase has a new manufacturer (Protherics), new storage conditions (in the refrigerator), and a new NSC number (732443). The old lot (004 of NSC 641273) passed retest in March and is still OK to use for a limited time. Both lots will probably be in clinical use through the summer 2004. Stay tuned for further updates!

All CTEP forms are available on CTEP's web page (<http://ctep.cancer.gov>).

Look for INSIDE PMB quarterly! Next issue: dog days of August, 2004

ALL THE SCOOP, ALL THE TIME: Designees and Transfers

Remember? November 2003's Inside PMB "scooped" some impending changes to the Drug Ordering process: the need to have all orders signed by the investigator, the shipping designee, or an ordering designee. Your proactive response lead to a smooth transition.

We might extend this policy to Transfer Investigational Agent requests since transfers are variants of ordering. This would require the following:

- L Use of only the most current transfer form version (available on <http://ctep.cancer.gov>)
- L Inclusion of all of the requested contact information
- L An approved shipping designee, ordering designee, or investigator signature

Many sites already do this, so we don't anticipate this will be difficult. Please share concerns or implementation ideas about this proposed change using E-mail to pmbafterhours@mail.nih.gov.

Confused Yet?

BMS-247550 (NSC 710428) has new stability and concentration information:

U Store its Vehicle for Constitution as directed on the product label - either at 2/ to 8/C, or 2/C to 25/C.

AJ Store the initial reconstitution (when the diluent is initially added to the drug vial) at room temperature for ≤ 1 hour. This is a lot shorter than the 24 hours previously recommended.

AJ Keep final dilutions in Lactated Ringers for Injection at concentrations between 0.2 and 0.6 mg/mL, at room temperature and light for a maximum of 6 hours. Better than before!

U BMS-247550 concentrations below 0.2 mg/mL are no longer recommended.

All BMS-247550 protocols will be amended with this new info soon!

QUALITY SERVICE?

If you have had a "noteworthy" (you define noteworthy) experience while on the phone with one of our staff, we'd like to hear about it. Contact PMBAfterHours, Skip Hall or Pat Schettino.

PMB AFTER HOURS

We close at 4:30. The folks at City of Hope in Los Angeles are wondering if or when Oscar and Sharon will be taking a lunch break!

So.....Need to reach us? Try our after hours E-mail address:

pmbafterhours@mail.nih.gov

Expect a response on the next business day!

Question of the Month

"Why are certain agents designated 'dangerous goods'?"

Many agents that PMB distributes are **hazardous substances**, but from a shipping standpoint only some of these agents are considered **dangerous goods (DG)**. The International Air Transport Association DG Regulations define dangerous goods as articles or substances which are capable of posing a risk to health, safety, property, or the environment. They list or classify these according to the Dangerous Goods Regulations (a BIG, FAT, BORING book). It is the shipper's responsibility to fully comply with these Regulations, which encompass proper identification, classification, packaging, marking, labeling, and documentation regarding the items being shipped. In addition, all shippers must have received training in these Regulations in order to carry out the responsibilities of shipping dangerous goods.

In general, any agent received from the NCI must be returned to the NCI for appropriate accountability and disposition. Most PMB-distributed agents are not DG. However, you may have received a stock recovery letter in the recent past, attached to a request for local destruction of NCI-supplied agent form. Why? PMB internally maintains a dynamic list of agents classified as dangerous goods. If your facility is not capable of shipping a dangerous good, PMB will allow you to destroy the agent locally. Do not destroy agents locally until PMB provides proper written authorization. **PRIOR APPROVAL IS REQUIRED!!!**

ZARNESTRA FIESTA!

New packaging: For open labeled trials, R115777 (Zarnestra) 100 mg tablets are now available in 126 tablet boxes (3 blister cards of 42 tabs each). This packaging conforms to the 300 mg bid x 21 day dosing that is used in many adult solid tumor studies.

Oral, oral, +co coral, banana fanna fo floral, * fe fi mo moral

OR-RAL! * +

Å Should I log by number of containers or number of tablets? Use either one, but be consistent throughout the entire DARF.

Å Can R115777 tablets be removed from the blister cards? No, stability data is unavailable for R115777 storage outside of the blister cards.

Å Can the R115777 blister cards be removed from the box? Yes, just don't remove the tablets from the blister card and record the number of tablets dispensed (not number of boxes) on the DARF.

Å Can perfosine be removed from its bottle? Nope. Absolutely not. If you need to dispense with a child-proof cap, put the original bottle in a HUGE vial.

Å Does a bottle of perfosine always have 30 tablets in it? Nope again. Perfosine bottles are filled using a weighing system, and some bottles have 31. The manufacturer hopes that this problem will be resolved in the next lot.

ADOPTION NOTICE

PMB is getting ready to say good-bye to the special exception program for 5-azacitadine in patients with myelodysplastic syndrome. "5-AZA" went to a new home - Pharmion - effective April 1, 2004! (And that's no joke!) Our workload will change dramatically.

Number of 5-AZA special exception vials distributed
in the last year:

34,600

Number of patients treated on special exceptions:

>2500

Average length of treatment in months:

3-4

WHAT THIS MEANS: If you need to obtain 5-azacytadine for new patients, call Becky Hubbell, Pharm D, MBA, Director of Clinical Development, Pharmion Corporation, 913-266-0326

WHO ARE WE?

Pharmaceutical Management Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and
Diagnosis
National Cancer Institute
6130 Executive Boulevard
Suite 7149
Rockville, Maryland 20852
(301) 496-5725
Order fax: (301) 480-4612
Other fax: (301) 402-0429
E-mail: pmbafterhours@mail.nih.gov

"DATE NEEDED": THE CLINICAL CHALLENGE

Our Clinical Drug Request form asks you to provide a "date needed." What if you really needed it YESTERDAY? How do you stress URGENCY?

The DATE NEEDED you provide prioritizes drug shipments. Since our Clinical Repository sends more than 200 orders on any given day, this is important!

● If possible, enter a date that is AT LEAST one day before you will treat the patient. Heaven forbid things go awry, this usually gives us the chance to replace the shipment.

● Please do not write 'ASAP.' We ignore it because it has no meaning here.

● Write "STAT" or "URGENT" in the comments field to note urgency, and provide a courier account number; send the order before 2:00 eastern time.

● Worried that it won't arrive in time? CALL PMB FIRST! We can determine if we can get your drug to you in time.

● Of course, the more lead time you give us, the better we prioritize, and the more able we are to handle emergency orders!

● Except (of course!) we can never ship blinded orders for next day delivery. Ever. Never-ever. Takes 2 days. No discussion.

Investigator Brochures...

PMB handles all requests for Investigator Brochures (IBs) where CTEP holds the IND. Our company collaborators consider the information contained in these documents confidential. We can only release IBs to investigators with an approved LOI, concept, or protocol. While CTEP has received approval from some collaborators to distribute the information electronically, the agreement does not allow the posting of these documents on any web site nor does it allow secondary distribution. (That is, when we give it to you, you can't pass it along.) All requests for IBs should be e-mailed to ibcoordinator@mail.nih.gov or the IB Coordinator may be called at 301-496-5725.