



Pharmacotherapy Update

SPECIAL POINTS OF INTEREST:

Drug Class Review:
Boceprevir

Patient Safety Notice:
Bladder Cancer Risks
Associated with
Pioglitazone

Literature Review:
Dronedarone in High
Risk A. fib.

THIS ISSUE:

Drug Class Review:
Boceprevir 2

Bladder Cancer Risks Associated with Pioglitazone 3

Literature Review:
Dronedarone in High Risk A. fib. 4

Drug Info Corner:
Interesting DI Questions 5

Residency Project Update 6,7

Update on Drug Shortages and Backorders 7

Pharmacy Corner:
Featuring Carol Campbell 8

Pharmacy Phun Phacts 8

WINTER 2012

LEBANON VAMC

Editor's Notes

By Heather Spoonhower, PharmD, PGY2 Ambulatory Care Pharmacy Resident
Sarah Witkowski, PharmD, PGY1 Pharmacy Resident

Alas, Punxsutawney Phil did see his shadow this February, leaving us with 6 more weeks of winter chill. Not to fret, this season's hot pharmacy topics will be sure to melt away your winter blues. In this season's newsletter we explore the pharmacy residents' progress towards

their QI/QA projects, discuss the new direct acting antiviral (boceprevir) in the treatment of hepatitis C, reveal bladder cancer risks with pioglitazone, and among other pharmacy phun topics, educate you on the best way to pick up a pharmacist during this Valentine's Day

season. So, sit back, relax, and enjoy some hot cocoa as you cozy up to the latest edition of the Pharmacotherapy Newsletter.



President's Day: Monday 2/20/2012

President's Day is intended to honor all the American presidents, but most significantly recognizes two great presidents: **George Washington** and **Abraham Lincoln**. Back in the 1790's, Americans were split as to the exact day to celebrate George Washington's birthday (some celebrated his birthday on February 11th and others on February 22nd due to uncertainties resulting from changes between the Gregorian and Julian calendars during the 18th century.) Congress enacted a uniform law responsible for the development of the official federal holiday on the 3rd Monday of February known as President's Day.





Drug Class Review: Boceprevir

By: Heather Spoonhower, PharmD

Boceprevir (brand name *Victrelis*TM), the new “game changing” medication for the treatment of hepatitis C virus (HCV), was approved by the FDA in May 2011.

Boceprevir is a direct acting anti-viral (DAA) oral medication, also referred to as an HCV protease inhibitor. It is indicated for the treatment of chronic hepatitis C genotype 1 infection, in conjunction with peginterferon alfa and ribavirin (prior standard therapy for HCV), in patients with compensated liver disease (including cirrhosis) who were previously untreated or failed standard therapy with interferon and ribavirin in the past.

Both interferon products and ribavirin non-specifically interfere with viral replication versus the new DAA therapies that directly inhibit HCV replication proteins. Boceprevir works by inhibiting the non-structural-3 serine protease, which is responsible for a large amount of HCV virion production.

Boceprevir’s efficacy was demonstrated in two landmark trials that studied treatment naïve patients and patients who previously failed treatment with peginterferon/ribavirin. Boceprevir, in combination with peginterferon/ribavirin, produced 25-30% higher viral cure rates versus standard therapy alone in treatment naïve patients. Patients who previously failed treatment with standard therapy developed 38-45% higher cure rates when boceprevir was added to standard therapy.

In light of its success, boceprevir does not come without treatment related adverse effects. The most common adverse effects associated with boceprevir include anemia, dysgeusia, nausea, diarrhea, and neutropenia. Drug-drug interactions also need to be taken into consideration; boceprevir is a strong inhibitor of CYP3A4/5 and is partially metabolized by CYP3A4/5. Treatment length is based on success of therapy. Response rates, measured by viral load, determine total treatment duration between 28 to 48 weeks or discontinuation if patient fails treatment altogether.

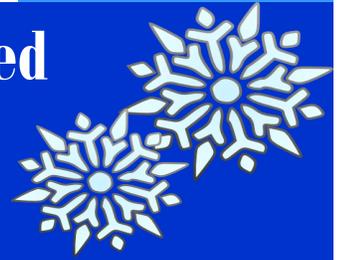
Prior to the development of the direct acting antiviral agents, treatment was limited by low response rates and poor tolerability. Boceprevir has provided new found hope in the world of hepatitis C care, in which standard therapy has essentially remained unchanged for the past two decades.

References:

1. Poordad F, McCane J, Bacon BR, et al. Boceprevir for untreated chronic HCV genotype 1 infection. *N Engl J Med* 2011; 346:1195-206.
2. Bacon BR, Gordon SC, Lawitz E, et al. Boceprevir for previously treated chronic HCV genotype 1 infection. *N Engl J Med* 2011; 364:1207-17.

Drug Safety: Bladder Cancer Risks Associated with Pioglitazone

By: Dina Norris, PharmD, BCPS



In June 2011, the FDA updated the labeling for pioglitazone containing medicines recommending that healthcare professionals not use pioglitazone in patients with active bladder cancer and to use pioglitazone with caution in patients with a prior history of bladder cancer. This outcome was based on a five-year analysis of an ongoing ten-year epidemiologic study.

The five-year interim analysis showed there was not an overall increase in risk of bladder cancer but there was an increased risk of bladder cancer in those patients taking pioglitazone for the longest period of time as well as those patients with the highest cumulative doses. Further, a recent study of epidemiological data, completed in France, suggested an increased risk of bladder cancer associated with pioglitazone use. Due to the findings of this study, France has stopped using pioglitazone and Germany is no longer allowing new starts of pioglitazone.

The FDA has supplied the following teaching points for Patients:

- There may be an increased chance of having bladder cancer when you take pioglitazone.
- You should not take pioglitazone if you are receiving treatment for bladder cancer.
- Tell your doctor if you have any of the following symptoms of bladder cancer: blood or red color in urine; urgent need to urinate or pain while urinating; pain in back or lower abdomen.
- Read the Medication Guide you get along with your pioglitazone medicine. It explains the risks associated with the use of pioglitazone.
- Talk to your healthcare professional if you have questions about pioglitazone medicines.
- Report side effects from the use of pioglitazone medicines to the FDA MedWatch program.

The FDA also supplied the following educational bullets for Healthcare Professionals:

- Do not use pioglitazone in patients with active bladder cancer.
- Use pioglitazone with caution in patients with a prior history of bladder cancer. The benefits of glycemic control versus unknown risks for cancer recurrence with pioglitazone should be considered in patients with a prior history of bladder cancer.
- Counsel patients to report any signs or symptoms of blood in the urine, urinary urgency, pain on urination, or back or abdominal pain, as these may be due to bladder cancer.
- Encourage patients to read the Medication Guide they get with their pioglitazone medicine.
- Report adverse events involving pioglitazone medicines to the FDA MedWatch program.

References:

- 1.Lewis JD, Ferrara A, Peng Hedderson M, Bilker WB, Quesenberry Jr, et al. *Diabetes Care*. 2011;34:916-22.
- 2.SDI, Vector One®: Total Patient Tracker (TPT). January 2010-October 2010. Data extracted 12-15-10

Literature Review & Safety Surveillance

By: Sarah Witkowski, PharmD

PALLAS Trial: permanent atrial fibrillation outcome study using dronedarone on top of standard therapy

Dronedarone in High Risk Permanent Atrial Fibrillation

Connolly SJ, Camm AJ, Halperin JL, et al. N Engl J Med. 2011 Dec 15;365(24):2268-76.

Background: Class III Antiarrhythmic, similar to Amiodarone but with fewer drug interactions and no effects on thyroid function. FDA approved to reduce the risk of hospitalization in patients currently in sinus rhythm with a history of paroxysmal or persistent A. fib.

Objective: to test if dronedarone would “reduce rates of major vascular events or unplanned hospitalization for cardiovascular causes in patients with permanent A. fib with a high risk of vascular events”

Conduct: prospective, randomized, double-blinded, placebo-controlled, multi-centered

Outcomes:

- composite: stroke, MI, systemic embolism, or death from CV causes
- unplanned hospitalization due to a cardiovascular cause or death

Design: randomization to either dronedarone 400mg BID or matching placebo

- follow up post randomization (days 7, 30, at 4 months, & every 4 months after)
- digoxin level (day 7) and LFTs every month x 6, then every 2 months

Results: (trial stopped early by safety committee less than a year into follow up)

- HR and blood pressure were significantly decreased in dronedarone group
- mean QTc interval increase was significantly higher dronedarone group
- premature discontinuation at significantly higher rates in the dronedarone group

Conclusions and Thoughts:

- dronedarone increased rates of stroke, heart failure, and death from cardiovascular causes in patient with permanent A. fib.
- dronedarone would not replace amiodarone’s place in therapy for CHF patients with A. fib. due to dronedarone’s poor outcomes in CHF patients
- patients were older and sicker than patients in other trials (ATHENA and ANDROMEDA trials) which helped establish dronedarone’s safety and efficacy.

Place in therapy: Patients with paroxysmal or persistent A. fib. Not for use in patients with class III or IV heart failure, permanent A. fib, or those taking other medications that may prolong the QTc interval.

References:

1. Hohnloser SH, Crijns HJ, van Eickels M, et. al. Effect of dronedarone on cardiovascular events in atrial fibrillation. N Engl J Med. 2009 Feb 12;360(7):668-78.
2. Køber L, Torp-Pedersen C, McMurray JJ, et al. Increased mortality after dronedarone therapy for severe heart failure. N Engl J Med. 2008 Jun 19;358(25):2678-87.

Drug Info Corner: They Asked What?!



What options are there to treat hiccups?

There are a few options to treat persistent hiccups. First line pharmacotherapy treatment is chlorpromazine 25-50mg 3-4 times daily PO/IM. Other options, commonly used for chronic persistent hiccups, include metoclopramide 5-10mg IV/IM every 8 hours then 10-20mg PO every 6 hours, baclofen 15mg/day PO divided TID initially, increasing by 15mg/day every 3 days to a maximum of 75mg/day (maximum of 5mg/day for hemodialysis patients). Gabapentin 1200mg/day PO is considered an option if baclofen fails. An assortment of other medications can be tried to treat hiccups as well including benzodiazepines, anticonvulsants (such as valproate and carbamazepine), and anticholinergics. Recommend trialing the option with the least side effects first, based on the severity of the hiccups. -Emily Davies, PharmD, PGY1 Pharmacy Resident

What vaccines should you give after a splenectomy?

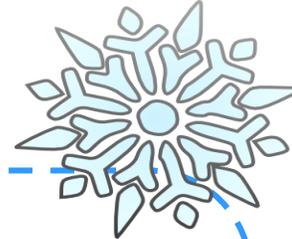
Asplenic patients are at increased risk of infection by encapsulated bacteria and, subsequently, post-splenectomy sepsis related to these organisms. A patient should receive vaccinations against encapsulated bacteria 2 weeks prior to the surgery. These vaccines include: Pneumococcal, Meningococcal, and Haemophilus influenzae type b (Hib). Following an emergent unscheduled splenectomy, vaccinations against encapsulated bacteria are still indicated. Since the spleen is responsible for immune response against these bacterium, a “grace period” should pass before immunizations are given. Studies have shown that those vaccinated within 14 days of splenectomy have a higher rate of insufficient immune response and require revaccination for HIB and Pneumococcal vaccines. There is no data supporting a time interval for the administration of the meningococcal vaccine. -Sarah Witkowski, PharmD, PGY1 Pharmacy Resident

What is the association between statins and myasthenia gravis?

Although there is limited evidence regarding MG exacerbation with statins, we still need to consider the risk vs. benefit of using statins in patients with this condition. Other cholesterol lowering agents may be considered in patients with low risk of CVD. However, if the benefit of a statin outweighs the risk of MG exacerbation, then statins can be used cautiously in these patients. It is advised to have closer follow-up in patients with this disease when placed on statin therapy. Also, it is very important that we counsel the patient on the potential risk of aggravating myasthenia gravis.

-Lindsay Baun, PharmD, PGY1 Pharmacy Resident





Residency QI/QA Project Updates

Heather Spoonhower, PharmD, PGY2 Ambulatory Care Pharmacy Resident:

Project: Comparing video teleconferencing at a community based outpatient clinic to face-to-face patient visits within the cardio risk reduction clinic at the Lebanon VAMC.

The objective of this quality assurance project is to determine the effectiveness of a pharmacy run video-teleconferencing (VTel) Cardio Risk Reduction (CRR) Clinic established for the Lancaster VA CBOC, as an alternative to patients seen face-to-face at the Lebanon VAMC CRR Clinic.

Preceptor: Dina Norris, PharmD, BCPS

Progress: Progress is underway in terms of securing a location/space, clerk, and nurse for the VTel Clinic at the Lancaster CBOC. Providers will be able to place a consult for patients that are unable/unwilling to travel to Lebanon for a face-to-face visits to the CRR Clinic, by the end of February. Scheduled appointments will begin in March.

Kendra Vong, PharmD, BCPS, PGY2 Health-System Pharmacy Administration Resident:

Project: Designing a non-traditional post graduate year 1 pharmacy residency program: the purpose of designing a Non-Traditional (NT) PGY1 pharmacy residency program is to promote staff development, assist pharmacy recruitment and retention, and comply with ASHP and ACCP recommendations. NT PGY1 residencies typically extend over a course of two years and aim to provide equivalent training as a traditional PGY1 residency for practicing pharmacists. This non-traditional program should allow current staff to maintain work-life balance while advancing their pharmacy practice skills.

Preceptors: Kevin Koons, PharmD, BCPS and Paul Carnes, PharmD, MS

Progress: A brochure and PowerPoint slides, describing program details, were sent to all pharmacists at the Lebanon VAMC. The NT PGY1 survey showed that 8 pharmacists (n=28) may be interested in this program. Following similar PGY1 application and interview standards, three pharmacists submitted their applications prior to the deadline, on January 15, 2012, and underwent interviews. A unique national matching services (NMS) code has been assigned to the NT PGY1 program. ASHP "Match" results will be announced in May 2012. We are anticipating the NT resident to start in the summer of 2012. Lebanon VAMC will be the second facility within the VHA to have a Non-Traditional PGY1 Pharmacy Residency Program.

Emily Davies, PharmD, PGY1 Pharmacy Resident:

Project: Starting a post-discharge telephone follow-up clinic. This clinic is designed to target veterans with a COPD (or) CHF diagnosis or polypharmacy (≥ 7 medications) who are discharged from 1-3A. During post discharge phone follow-up, will conduct medication reconciliation and keep track of any interventions that are made, recording number and type of intervention. Will follow the veteran for 30 days post discharge to assess re-admission or ER visit rates.

Preceptor: Edwin Caudill, RPh, BCPS

Progress: Actively following veterans on 1-3A and calling veterans who meet criteria 3-10 days post discharge.

(Continued on PAGE 7)



Update on Backorders and Shortages: as of 2/14/12

By: Sarah Witkowski, PharmD, PGY1 Pharmacy Resident and
Ralph Bryant, Pharmacy Procurement Technician



Current Drug Shortages:

- Amino Acid Products
- Bleomycin Inj
- Daunorubicin HCl Inj
- Desmopressin Inj
- Doxorubicin Inj
- Etoposide Inj
- Fluorouracil Inj
- Haloperidol Decanoate Inj
- Leucovorin Ca Inj
- Methotrexate Inj
- Paclitaxel Inj
- Sulfamethoxazole 80mg/
trimethoprim 16mg/ml Inj

Backordered:

- Diclofenac gel
- Fluoxet Os 20mg/5ml
- Flutamide 125mg
- Naltrexone 50mg
- Methazolamide 25mg
- Valsartan, all strengths
- Valsartan/HCTZ 320/25mg

Resolved Drug Shortages:

- Isoniazid Tablets 20mg



Residency QI/QA Project Update (Continued from PAGE 6)

Lindsay Baun, PharmD, PGY1 Pharmacy Resident:

Project: The primary objective is to educate providers on the appropriate use of dabigatran. Education is also being provided to patients who are started on this medication. Currently, dabigatran must be ordered via the non-formulary process. Restricting the use of this medication, for patients who meet the criteria for use, will limit unnecessary and unsafe medication use.

Preceptors: Susan Sincavage, PharmD, BCPS, CDE and Kevin Koons, PharmD, BCPS

Progress: In the process of developing a restricted use/non-formulary template for ordering dabigatran in CPRS to ensure the medication is safely used in the appropriate patient population. Currently, contacting all patients on dabigatran and mailing each patient a brochure on dabigatran.

Sarah Whitkowski, PharmD, PGY1 Pharmacy Resident:

Project: Starting a Pharmacy Medication Management Clinic: as we all know, medications only work if taken and work better when taken properly. This clinic is designed to target veterans with suspected or documented compliance issues and offer them education on how to get more out of their medications.

Preceptor: Michele Margut, PharmD

Progress: Scheduling and screening for patients referred to the clinic from previous consults and consults coming from our clinical staff is underway. As appropriate patients are identified they are being contacted to be offered entrance into the clinic. Soon we'll move toward seeing our first patients. There is an electronic consult being developed in CPRS for referrals and we have been reaching out to primary care to familiarize our providers with this opportunity. So, spread the word!!!

Pharmacy Corner Featuring: Carol Cambpell, RPh



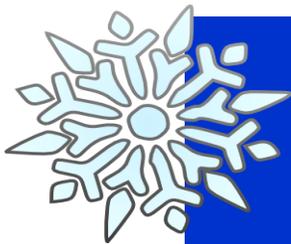
Our new inpatient supervisor has now been here for a few months and is settling into life at the VA. So let's get to know a little more about her!

Carol, who wanted to be a pharmacist to help people, attended pharmacy school at PCP in Philadelphia. Her shift into administration was not planned, as she transitioned into a managerial role at a previous facility unexpectedly. She soon found that she enjoyed administration because the job fits her nature as a problem-solver. Carol's family (her husband of 20 years, 15 year old son, and 2 German Sheppards) share interests in outdoor activities like four wheeling, gardening, and hunting (Carol doesn't hunt but has taken a hunter's safety course with her son).

Her favorite city is Las Vegas; visiting there every year with her husband, where they usually attend the NASCAR race at Las Vegas International Speedway. She's looking forward to their traditional yearly family vacation to Ocean City, NJ.

She's famous for her homemade salsa which we all got to sample at our Mexican Potluck during Pharmacy week.

Carol has a hobby in collecting Campbell's Soup products and memorabilia ever since she and her husband got engaged. Welcome Carol!



Pharmacy Phun Phacts: Pharmacy Pickup Lines

By Emily Davies, PharmD, PGY1 Pharmacy Resident



- Just call me Lasix... cuz I'll keep you up alllll night!
- I'm your plan A... we'll worry about Plan B tomorrow!
- I must have a low creatinine clearance because I can't seem to get you out of my system.
- I think I need an ACE-I because I feel my heart getting congested and failing when your around.
- Excuse me do you happen to have a chewable aspirin? Because I just got chest pain when I laid eyes on you.
- You're the trimethoprim to my sulfamethaxazole, let's synergize.

