BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

Checklist

BEFORE the meeting

☐ Print your copy of PL Journal Club LEADER NOTES, which will be emailed to you from Pharmacist’s Letter

☐ Provide the LEADER NOTES to the PL Journal Club discussion leader

☐ Instruct your PL Journal Club participants to go to PharmacistsLetter.com to print their PARTICIPANT NOTES. Instruct them to search for the keyword “Journal Club” and tell them which month PL Journal Club you intend to use

☐ Provide instructions to your PARTICIPANTS and LEADERS about how to obtain PDFs of original articles from your local medical library (Adhere to institution’s copyright policy)

DURING the meeting

☐ Pass out any needed PL Journal Club PARTICIPANT NOTES

☐ Discuss any recommendations that you have made, or new information that you have learned or observed based on the discussion at the last PL Journal Club meeting

☐ Proceed to use your PL Journal Club LEADER NOTES to facilitate the PL Journal Club discussion

AFTER the meeting

☐ Note the next PL Journal Club meeting date and time

☐ Determine who will serve as the next PL Journal Club discussion leader

☐ Go to PharmacistsLetter.com to learn about other topics in this month’s issue, including charts, algorithms, toolboxes, etc, and listen to panelists and experts discuss our recommendations in PL VOICES

LEADER NOTES
INTERACTIONS

New concerns will crop up about an interaction with simvastatin or lovastatin and the direct oral anticoagulant (DOAC), Pradaxa (dabigatran). These combos seem to increase bleeding risk.

Simvastatin or lovastatin might increase Pradaxa absorption and drug levels by inhibiting P-glycoprotein...a transporter protein that pumps drugs out of cells and into the gut, urine, or bile for excretion.

Atorvastatin also seems to inhibit P-glycoprotein...but evidence suggests it doesn’t increase Pradaxa absorption. And other statins (rosuvastatin, etc) don’t seem to inhibit P-glycoprotein.

If you get a simvastatin or lovastatin Rx for a Pradaxa patient, lean toward a different statin or DOAC...especially in renal impairment.

If a patient on warfarin starts an interacting statin...such as simvastatin, lovastatin, or rosuvastatin...advise closer INR monitoring.

Go to our toolbox, Drug Interactions: A Practical Approach, for resources to help with anticoagulant and statin interactions and more.

(For more on this topic, see Clinical Resource #330208 at PharmacistsLetter.com.)


Discussion Questions

Overview of current therapy

1. What is known about statin and direct oral anticoagulant (DOAC) and metabolism and interactions?

- The metabolism of each statin is different. All statins except pravastatin are metabolized by cytochrome P450 enzymes, primarily 3A4 and 2C9. Simvastatin (Zocor) and lovastatin (Mevacor, etc) undergo significant metabolism via CYP3A4, and atorvastatin (Lipitor) to a lesser extent. Fluvastatin (Lescol), pitavastatin (Livalo), and rosuvastatin (Crestor) are metabolized via CYP2C9. Since CYP3A4 is the most common enzyme involved in drug metabolism, simvastatin and lovastatin have the highest number of clinically significant interactions. In addition, fluvastatin and lovastatin inhibit CYP2C9.
- Atorvastatin, lovastatin, pitavastatin, pravastatin, and simvastatin are substrates of the transport protein, P-glycoprotein, that pumps drugs out of cells into the gut, bile, or urine for excretion. Atorvastatin, lovastatin, and simvastatin are also thought to inhibit P-glycoprotein.
- The metabolism of each of the DOACs is also different. Rivaroxaban (Xarelto) and apixaban (Eliquis) are metabolized via CYP3A4 to a moderate extent, but edoxaban (Savaysa) is minimally metabolized by CYP3A4, and dabigatran (Pradaxa) is not metabolized via CYP450 enzymes. None of the DOACs are known to inhibit or induce any of the CYP450 enzymes.
- The absorption of each of the DOACs is also impacted by P-glycoprotein. Drugs that inhibit or induce P-glycoprotein may increase or decrease DOAC plasma concentrations, respectively. However, none of the DOACs is known to inhibit or induce P-glycoprotein. Of note, the bioavailability of dabigatran is only 3 to 7%, compared to at least 50% for each of the other DOACs. Therefore, it is thought that slight changes in absorption may have a greater impact on the plasma levels of dabigatran than the other DOACs.
• Dabigatran is the only DOAC that is a prodrug, requiring metabolism to its pharmacologically active form by carboxylesterase enzymes. Therefore, drugs that inhibit carboxylesterase enzymes could decrease its transformation to the active anticoagulant. Some evidence suggests that simvastatin and lovastatin are inhibitors of carboxylesterase enzyme activity, but that other statins are not.

**Analysis of new study**

2. **What type of study was this? How were the patients identified and data obtained?**

• Authors conducted two separate population-based, nested case-control studies.
• The first study aimed to determine whether there is an association between using the combination of simvastatin or lovastatin and dabigatran, and an increased risk of ischemic stroke or transient ischemic attack (TIA) relative to using dabigatran with other statins.
• The second study aimed to determine whether there is an association between using the combination of simvastatin or lovastatin and dabigatran, and an increased risk of major hemorrhage relative to using dabigatran with other statins.
• Residents of Ontario 66 years of age and older who began dabigatran between May 1, 2012 and Mar 31, 2014 were included in the studies. These patients were assumed have nonvalvular atrial fibrillation since the Ontario Drug Benefit formulary restricted the use of dabigatran to prevention of stroke in patients with nonvalvular atrial fibrillation.
• Patients for both studies were identified using the Ontario Drug Benefit database, which includes complete records of prescriptions dispensed to Ontario residents 65 years of age and older.
• Patients were included if they were receiving ongoing treatment with dabigatran, defined as a prescription refill within 1.5 times the number of days covered by the previous prescription, and if they received a prescription for a statin within 60 days of the date of the index ischemic or hemorrhagic event.
• Patients were excluded if they received prescriptions for multiple statins within the 60 days preceding the occurrence of an ischemic stroke or major hemorrhage, or if they could not be matched to at least one control.

3. **How were the case and control patients identified?**

• International Statistical Classification of Diseases and Related Health Problems codes, 10th revision (ICD-10), were used to identify cases.
• In the first study, cases were patients with a hospital admission or emergency department visit for ischemic stroke or TIA.
• In the second study, cases were patients with major hemorrhage, defined as any hemorrhage resulting in hospital admission or emergency department visit.
• Controls (patients without an ischemic or hemorrhagic event) were randomly assigned an index date for an ischemic or hemorrhagic event. Each case was matched to up to 4 controls by age (within 3 years at the index date) and sex.
• All case and control patients were receiving ongoing treatment with dabigatran and had also received a prescription for a statin within 60 days of the index date of ischemic or hemorrhagic event.

4. **What were the case-control analysis methods?**

• The primary aim of the studies was to determine whether an association exists between ischemic or hemorrhagic events in patients receiving treatment with dabigatran and lovastatin or simvastatin, relative to other statins.
• Each study’s data were analyzed via multivariable logistic regression to provide odds ratios (OR) and 95% confidence intervals (CI).
• Results were adjusted for all baseline variables with a standardized difference greater than 0.1 between cases and controls. The “standardized difference” was calculated by dividing the difference between cases and controls by the standard deviation.
In the study of stroke or TIA, only the first occurrence of stroke was included in the data analysis. And, data from the ischemic study were analyzed in two ways. First, data were analyzed that included all cases of stroke and TIA. Second, data were analyzed for only cases with ischemic stroke. This was done because TIA is known to be less accurately coded.

In the study of major hemorrhage, sensitivity analyses that included patients with chronic kidney disease or recent use of warfarin were performed, since these factors are known to increase the risk of hemorrhage. In addition, analyses were performed for patients who received simvastatin separately from patients who received lovastatin.

5. What were the study results?

From May 1, 2012 to Mar 31, 2014, 45,991 patients were treated with dabigatran.

From this cohort, 836 patients were diagnosed with an ischemic stroke or TIA, with 397 of these patients having also received a statin in the 60 days prior to their ischemic event. These 397 patients were the cases of the ischemic stroke study. All cases were matched to 4 controls, resulting in 1,588 controls.

Also from this cohort, 2,406 patients were diagnosed with major hemorrhage, with 1,117 of these patients having also received a statin in the 60 days prior to their hemorrhagic event. These 1,117 patients were the cases for the study of major hemorrhage. Most of these cases were matched to 4 controls, resulting in 4,465 controls.

For each of the studies, atorvastatin and rosuvastatin were ≈50% and ≈37% of statin prescriptions, respectively. The remainder of statin prescriptions were simvastatin (≈8%), pravastatin (≈3%), fluvastatin (<1%), and lovastatin (<1%).

Results of stroke or TIA study
- Case and control patients were ≈82 years old and ≈53% were female.
- Cases used statins for ≈3.6 years versus ≈4 years for controls.
- Comorbidities were generally more common in cases than in controls. Of note, ≈44% of case patients had a Charlson Comorbidity Index score of 2 or higher versus ≈21% of case patients; ≈36% of case patients had a stroke or TIA in the past 5 years versus ≈12% of controls; ≈43% of cases had heart failure versus ≈37% of controls; ≈50% of cases had a history of diabetes versus ≈44% of controls; ≈96% of cases had hypertension versus ≈92% of controls; ≈20% had a previous MI versus 15% of controls; and ≈4% of cases had chronic kidney disease versus ≈2% of controls.
- Use of simvastatin or lovastatin was not associated with an increased risk of stroke or transient ischemic attack relative to other statins in patients receiving dabigatran (OR 1.33, 95% CI 0.88-2.01).
- When only stroke cases were included in the analysis, results were similar (OR 1.44, 95% CI 0.87-2.39).

Results of major hemorrhage study
- Cases and controls were ≈82 years old and ≈42% were female.
- Cases used statins for ≈4.6 years versus ≈4.4 years for controls.
- Comorbidities were generally more common in cases than in controls. Of note, ≈39% of case patients had a Charlson Comorbidity Index score of 2 or higher versus ≈21% of case patients; ≈20% of case patients had a major hemorrhage in the previous 5 years versus ≈10% of controls; ≈52% of cases had heart failure versus ≈37% of controls; ≈47% of cases had a history of diabetes versus ≈43% of controls; ≈95% of cases had hypertension versus ≈93% of controls; ≈24% had a previous MI versus 16% of controls; ≈4% of cases had chronic kidney disease versus ≈2% of controls; and ≈3% of cases had chronic liver disease versus ≈2% of controls.
- The use of medications that could increase the risk of hemorrhage within the 120 days prior to the event were mostly similar between cases and controls with the exception of warfarin, which was used in ≈19% of cases versus ≈7% of controls.
- Use of simvastatin or lovastatin was associated with an increased risk of major hemorrhage relative to other statins in patients receiving dabigatran (OR 1.46, 95% CI 1.17-1.82).
- Results were similar when simvastatin patients were analyzed separately (OR 1.44, 95% CI 1.14-1.81), but not when lovastatin patients were analyzed separately (OR 1.9, 95% CI 0.78-4.61).
6. What were the strengths and weaknesses of this study?

- These large case-control studies were well done and demonstrated an association between simvastatin or lovastatin use and an increased risk of major hemorrhage in patients with atrial fibrillation who were taking dabigatran relative to other statins, but no association with an increased risk of ischemic stroke or TIA. However, several important limitations should be considered.
- The case-control study is an efficient means to test for an association between an exposure and an outcome, especially when the outcome of interest is rare, such as stroke or major hemorrhage. However, case-control studies can only suggest an association between an exposure and an event, rather than prove causation.
- A nested case-control design was used for these studies. In a nested case-control study, only a subset of controls is compared to cases, usually those that are matched to cases by certain factors. In this study, cases were matched to controls by age and sex, which limits the potential for confounding due to these two factors.
- An appropriate source of data was used for these studies. Residents of Ontario who are 65 years of age and older have universal access to physician services, hospital care, and prescription drug coverage. Comprehensive health data for these patients such as diagnosis codes and prescription refills are maintained in an administrative database.
- Use of diagnosis codes to identify cases and controls is an imperfect means of patient identification, since coders may incorrectly code a patient as having an event or, conversely, miss coding a patient who does have an event. However, authors note that the diagnosis codes that were utilized have been validated by previous studies, which helps limit the risk for misclassification bias and improves internal study validity. In addition, authors included patients 66 and older to limit the risk for incomplete medical data.
- Yet, in the study of major hemorrhage, misclassification bias was likely. Major hemorrhage was defined as any hemorrhage resulting in hospital admission or emergency department visit. It is important to consider that not all emergency department visits for anticoagulation-related bleeding would be considered a major hemorrhage, such as a nosebleed or bruising.
- In addition, patients were assumed to have atrial fibrillation, since the Ontario Drug Benefit formulary restricted the use of dabigatran to prevention of stroke in patients with nonvalvular atrial fibrillation. However, diagnosis codes were not used to confirm this assumption.
- In the study of stroke or TIA, only the first stroke event was counted for each patient. This was appropriate and provides a more conservative estimation of risk than if all stroke events had been counted.
- Atorvastatin and rosvastatin were the statins ≈ 87% of patients were prescribed. Type 2 error (not having the power to detect a significant difference when one may exist) should be considered for nonsignificant findings, especially when the sample size is small. For example, it is possible that an increased risk of stroke or TIA with simvastatin or lovastatin wasn’t found because of the small sample size of these statins in that study (n=189).
- The Ontario Drug Benefit database contains comprehensive prescription medication refill records of all Ontario residents 65 years and older, and ongoing refills should be an indicator of medication adherence. Authors considered patients adherent with dabigatran as long as a prescription was refilled within 1.5 times the days covered by the previous prescription. Therefore, patients could have been up to 50% nonadherent with dabigatran. In addition, authors did not address adherence with statin medications. Included patients simply must have received a statin prescription within 60 days before the ischemic or hemorrhagic event. Based on this study design, the possibility that some patients may not have been taking dabigatran or a statin at the time of the ischemic or hemorrhagic event cannot be ruled out.
- The Ontario Drug Benefit database did not include information about OTCs such as aspirin or other NSAIDs that may have increased patients’ bleeding risk. In addition, the administrative data did not contain substance use or laboratory data that may increase patients’ ischemic or hemorrhagic risk such as smoking status or renal function. For example, renal function is an important data point since dabigatran is mostly renally eliminated, and renal impairment is a risk factor for bleeding with...
dabigatran. However, the sensitivity analysis of patients with chronic kidney disease was not found to impact study results.

- Authors were unable to analyze the potential impact of either the dabigatran or statin dose on the risk of ischemic or hemorrhagic events.
- Based on a review of baseline characteristics and Charlson Comorbidity Index scores, it is likely that case patients were “sicker” than control patients. To address these differences, study results were adjusted for all baseline variables with a standardized difference greater than 0.1 between cases and controls. But it is important to consider that cases and controls were compared by statin group, and it is unknown how baseline characteristics differed by statin group. For example, the use of other P-glycoprotein inhibitors that may have increased dabigatran levels was fairly balanced between cases and controls at baseline. But it is unknown whether the use of other P-glycoprotein inhibitors was balanced among the cases and controls who received simvastatin or lovastatin versus others statins.
- Since the metabolism of DOACs differs among agents, the results of this study should not be generalized to the other DOACs. Also, this study included patients with atrial fibrillation who were at least 66 years old. Therefore, the results of this study may not be generalizable to younger patients or those without atrial fibrillation.

7. Were the results expressed in terms we care about and can use?

- Yes. The outcomes were clinically important and what patients and caregivers are concerned about (stroke or TIA and major hemorrhage).

How should the new findings change current therapy?

8. Do the results change your practice? How?

- Yes. This study raises concern about a clinically significant drug interaction between dabigatran and simvastatin or lovastatin. When dabigatran is the preferred anticoagulant, a statin other than simvastatin or lovastatin should be considered. This is particularly important in patients with renal impairment, since dabigatran is mostly renally eliminated.

Apply the new findings to the following case

J.B. is a 75-year-old white female who presents to your office with her daughter to establish care. Her husband recently passed away, and she has recently moved to the area to be closer to her children. She currently has no complaints and just needs refills of her medications. She has a history of atrial fibrillation, and is taking carvedilol 6.25 mg twice daily for heart rate control and dabigatran 150 mg twice daily for prevention of ischemic stroke. She is taking no other medications chronically, and her past medical history is otherwise unremarkable. She brought a recent copy of her labs with her, and you note a total cholesterol of 230 mg/dL, LDL 147 mg/dL, HDL 45 mg/dL, and triglycerides 190 mg/dL.

Vitals: blood pressure 126/88 mmHg, pulse 62, oxygen saturation 97%, temp 98.2 degrees, BMI 27.

On further discussion, J.B. asks why she needs to continue dabigatran.

9. How do you counsel J.B. regarding her need for anticoagulation?

- Anticoagulation is recommended for many atrial fibrillation patients to lower the risk of ischemic stroke.
- Stroke risk can be estimated by calculating the CHADS2 or CHA2DS2-VASc score.
- The CHADS2 score assigns 1 point each for a history of congestive heart failure, hypertension, age ≥ 75, and diabetes, and 2 points for a history of stroke or TIA. Anticoagulation is recommended for patients with a score of 1 or higher, as these patients are estimated to have a 2.8% or higher annual risk of stroke.
- The CHA2DS2-VASc score assigns 1 point each for age 65 to 74, female sex, history of congestive heart failure, hypertension, or vascular disease, and 2 points each for age ≥ 75 or a history of stroke or TIA. Anticoagulation is recommended for patients with a score of 1 or higher, as these patients are estimated to have a 0.6% or higher annual risk of stroke.
Both scores are well validated to estimate stroke risk. Because the CHADS$_2$ score is simpler to calculate, it is often used first. The CHA$_2$DS$_2$-VASc score can then be employed in patients with a CHADS$_2$ score of 0, to help identify patients who are truly low-risk.

J.B.’s CHADS$_2$ score is 1 due to her age $\geq 75$, with an estimated annual risk of stroke of 2.8% or higher.

You discuss that J.B. is taking dabigatran to lower her annual risk of stroke. She agrees that the annual estimated stroke risk of almost 3% is high enough for her to desire continuing dabigatran.

J.B. brings up that her husband passed away after a myocardial infarction and she and her daughter are particularly concerned about lowering her cardiovascular risk. J.B. says that she has been trying to eat a low-cholesterol diet, is walking for 30 minutes three times a week, and has never smoked. But she wonders if she should be taking aspirin or other medications to lower her cardiovascular risk.

You calculate her 10-year risk of atherosclerotic cardiovascular disease (ASCVD) and find it to be 16%.

**10. What should you consider based on J.B.’s elevated ASCVD risk?**

- Recent guidelines suggest low-dose aspirin for primary CV prevention in patients age 50 to 59 years with $\geq 10\%$ 10-year ASCVD risk who aren’t at an increased bleeding risk and have a life expectancy of at least 10 years. Low-dose aspirin can also be considered for patients 60 to 69 with a 10-year ASCVD risk $\geq 10\%$. However, the benefits of low-dose aspirin in patients under age 50 or 70 and older may not outweigh its risks.
- A moderate-to-high intensity statin is generally recommended for primary prevention of CV disease in patients age 40 to 75 years when the 10-year CV risk is 7.5% or higher.
- High-intensity statins, atorvastatin 40 to 80 mg daily or rosuvastatin 20 to 40 mg daily, decrease the LDL by 50% or more. Moderate-intensity statins such as atorvastatin 10 to 20 mg daily, pravastatin 40 to 80 mg daily, simvastatin 20 to 40 mg daily, or lovastatin 40 mg daily, decrease the LDL by 30% to 50% on average.
- Given the recent data on the increased bleeding risk with either simvastatin or lovastatin in patients taking dabigatran, other statin options seem more appropriate.

You discuss that the risks of aspirin likely outweigh its benefits for J.B., but advise starting a statin. J.B. agrees, and you prescribe atorvastatin 40 mg daily.

J.B. returns for a one-month follow-up and is unhappy because the atorvastatin was expensive. The pharmacy recommended lovastatin as a lower cost option. J.B. asks if you will prescribe lovastatin instead of the atorvastatin.

**11. What options do you discuss with J.B.?**

- Lovastatin and simvastatin may be lower cost options for some patients, but recent data suggests these statins may increase the risk of bleeding in patients who are taking dabigatran.
- Fluvastatin, pitavastatin, pravastatin, and rosuvastatin are other statin options that don’t seem to interact with dabigatran. However, pravastatin is likely the best alternative since it is usually a low-cost option, while fluvastatin, pitavastatin, and rosuvastatin are likely to be expensive.
- Switching to another anticoagulant is also an option. Warfarin is the least expensive medication, but requires frequent lab monitoring which may lead to additional expense. Or switching to a DOAC other than dabigatran, such as apixaban or rivaroxaban, may be an option if they’re on J.B.’s insurance formulary at a reasonable cost.

You discuss these options and J.B. decides to remain on dabigatran and switch to pravastatin.


Welcome to PL Journal Club

PL Journal Club gives you insights and guides you to the discoveries that Pharmacist's Letter researchers and editors uncover. Each month we analyze many new studies and help you discover the answers to the hard questions. “What are the real advantages and disadvantages of new therapies?” “How do they compare with other options?” “What do pharmacists and prescribers need to know?” We look beyond the headlines and promotional materials to interpret the clinical studies and data. Sometimes the marketing spin doesn’t stand up to scrutiny. Sometimes studies do not really prove what they are reported to prove.

PL Journal Club helps guide you to the truth and how to apply new findings to patient care.

PL Journal Club builds on Pharmacist’s Letter to provide you with background for your own journal club discussions. We won’t bring up every possible question, but you can...in your own group meetings. If a question comes up, go to Pharmacist’s Letter to find more background. As a PL Journal Club participant, you get access to all of Pharmacist’s Letter. Feel free to call or email us with suggestions or if we can be of assistance... 209-472-2240 or PLJournalClub@pletter.com.

Instructions

Go to Pharmacist’s Letter to get the PL Journal Club PARTICIPANT NOTES. Use the search function to look for “Journal Club.” You’ll also get great background materials, including Pharmacist’s Letter and clinical resources. PL Journal Club functions like a typical group meeting, except that it is organized for you with the expert analysis of important new studies done by the large Pharmacist’s Letter research and editorial staff. Let the questions serve as a springboard for your discussions. Use our patient cases or your own cases to shape the discussion. Each month, PL Journal Club reviews a topic that is also covered in Pharmacist’s Letter. You’ll also find a library of previous PL Journal Clubs online for your use.

PL Journal Club Contributing Editors:
Lori Dickerson, PharmD, FCCP, Editor; Jennifer Nieman, PharmD, BCPS, Assistant Editor; Lisa D. Mims, MD, Department of Family Medicine, Medical Univ of South Carolina, Charleston, SC; Maribeth Port, MD, Department of Community Health and Family Medicine, Univ of Florida, Gainesville, FL.

Editors and Authors: Jeff Jellin, PharmD, Editor-in-Chief; Sherri Boehringer, PharmD, BCPS, Senior Editor, VP Content; Karen Davidson, PharmD, Senior Editor; Tamnie Armeni, RPh, PharmD, Editor, Director of Continuing Education; Melissa Blair, PharmD, FASHP, FCCP, BCPS; Sandye Chabot, PharmD; Lori Dickerson, PharmD, FCCP; Rachel Maynard, PharmD; Kimberly Palaciz, PharmD, Editors; Stacy Hester, RPh, BCPS; Tanveer Khan, PharmD, Crystal Marie, BSc Pharm, MBA, ACPR, Associate Editors; Bethany Bryant, PharmD, BCPS; Vickie Danaher, PharmD; Flora Harp, PharmD; Tanner Higginbotham, PharmD; Jennifer Nieman, PharmD, BCPS; Brea Rowan, PharmD, BCPS; James Van, BSc Pharm; Don Weinberger, PharmD; Marlea Wellein, PharmD, BCPS, Assistant Editors; Karen Wilson, BA, Manuscript Editor; Minda Paglinawan, BA, Assistant Manuscript Editor; Jenni Mangrum, BS, CPHT, Assistant Education and Accreditation Editor.

Senior Editor: Mark Graber, MS, MSHCE, FACEP, Associate Clinical Editor. Consultants: Jill Allen, PharmD, BCPS; Melanie Cupp, PharmD, BCPS; Katie Lacaria, BSc Pharm, ACPR; Heidi Liston, BSc Pharm, PharmD; Lu-An Mooder, BSc Pharm; Annette Murray, BSc Pharm; Neeta O’Mara, PharmD, BCPS; Jennifer Pennington, RN, BSN. Editorial Advisors: Thomas Barringer, MA, FFAFP; Christopher Barry, PA-C, MMS; William Bednar, MD; Larissa Bossard, PharmD, BCPS; Robert Browne, MD, FFAFP; Stephen Brunton, MD; Holley Bush, PharmD; Peter Carek, MD, MS; Gary Cough, PharmD; Matthew Cline, MD; John Connolly, MD, FACP, FCCP; Sandra Counts, PharmD; Hitkam Fikrat, PhD; Rex Force, PharmD, FCCP; Laurence Frank, MD, FACP; Peter Garbeff, MD; Mark Garofoli, PharmD, MBA, CPG; Charles Green, RPh; Susan Halasi, MSc Pharm; John Hambright, PharmD; Roland Hart, MD; Kyle Herold, MD; Patricia Hatton, MD; Sydney Hendry, MD; Raissa Hill, DO; Jerry Jones, MD; Sheela Kapre, MD, BCPS; Adam Kaye, PharmD, FASHP, FCPA; William Kehoe, PharmD, MA, FCPA, BCPS; Joshua Lenchus, DO, RPh, FCPA; SFHM; Stanley Leong, PharmD; Kevin Maeda, PharmD; Rachel Maynard, RPh; Christine McLaughlin, CPHT, EMT; Kay Niegel, RPh; Mike Pastrick, RPh; Ernest Pieper, PharmD; Daren Primack, MD, FACP; Barbara Rankin, MD; Jenna Reel, PharmD, BCPS, CPP, CDE; George Rishwain, MD; Sandy Robertson, PharmD; Edward Rogan, PharmD, BCACP; Gerald Rubley, MSN, PharmD; Ruth Ruffle, PharmD; AnnieMarie Santos, MD; David Schneider, MD; Allen Shaugnessy, PharmD, MMedEd; Jonathan Szkotak, PharmD, BCACP; Joshua Tessier, DO; Bruce Uch, PharmD; John David Williamson, MD, FFAFP; Raymond Wong, MD; William Yee, PharmD, FASHP, FCPH; Kent Yeo, RPh.

Advisory Board: Evan Ballard, MD, Jonesville Family Medical Ctr; Melvin Baron, PharmD, MPA, Univ of Southern Calif; Jan Basile, MA, FACP, Medical Univ of South Carolina; Robert Bickerton, MD, FACP; Reid B. Blackwelder, MD, FAAFP, East Tennessee State Univ; Kevin Brown, MD, FACOG, CDCE, Washington State Univ; Andrea Darby-Stewart, MD, HonorHealth; Anthony A. Donato, Jr., MD, MPH, Reading Health System; Jan Drutz, MD, FACP, Baylor College of Med; Margaret A. Fitzgerald, DNP, FNP-BC, NC, FAANP, CSP, FAAN, DCC, Fitzgerald Health Ed Associates; Barry Gidal, PharmD, RPh, Univ of Wisc; Martin Grajower, MD, FACP, FACE, Albert Einstein College of Med; B. Joseph Guglielmo, PharmD, UC San Francisco; Stuart Haines, PharmD, BCPS, BCACP, BC-ADM, FCCP, FASHP, FAPhA, Univ of Miss; Jeffrey Harman, Jr., MD, Col, USAF, MS, FS; B. Mark Hess, MD, FACP, Medical Univ of South Carolina; Allen Shaugnessy, PharmD, MMedEd; Jonathan Szkotak, PharmD, BCACP; Joshua Tessier, DO; Bruce Uch, PharmD; John David Williamson, MD, FFAFP; Raymond Wong, MD; William Yee, PharmD, FASHP, FCPH, Kent Yeo, RPh.

© 2017 by Therapeutic Research Center. All rights reserved. Therapeutic Research Center does not receive any commercial support and does not accept any advertising. It is completely independent and is supported entirely by subscriptions. Pharmacist's Letter focuses on delivering completely objective, unbiased drug information and advice for the benefit of subscribers.