2009
Vol. 21, No. 3

DUR DIGEST

The Bulletin of Medicaid Drug Utilization Review in Iowa

PPI Interactions with Clopidogrel and a Review of Current PPI PA Criteria

Recent reports suggest that omeprazole and other proton pump inhibitors (PPIs) could interfere with the antiplatelet effect of clopidogrel (*Plavix*). Clopidogrel is a prodrug that is activated by CYP450 enzymes in the liver primarily by CYP2C19. All PPI's may inhibit CYP2C19 to some extent, with omeprazole being a strong inhibitor of CYP2C19; pantoprazole (*Protonix*) appears to be the weakest inhibitor.

More data is needed to clarify the clinical significance of the interaction between clopidogrel and PPIs. Studies are being conducted to obtain additional information that will give a better understanding of the effects of other drugs, especially PPIs, on the effectiveness of clopidogrel. In the mean time, the FDA recommends the following:

- Healthcare providers should continue to prescribe and patients should continue to take clopidogrel as directed.
- Healthcare providers should re-evaluate the need for starting or continuing treatment with a PPI in patients taking clopidogrel.

PA Criteria

Currently, prior authorization is not required for the preferred PPIs for a cumulative 60-days of therapy per 12-months. Prior authorization is required for all non-preferred PPIs beginning the first day of therapy. Non-preferred PPIs will be considered only when there is documentation of previous trials and therapy failures with three preferred agents.

PREFERRED PPI (PA REQUIRED AFTER 60 DAYS)	NON-PREFERRED PPI (PA REQUIRED FROM DAY 1)
Prevacid Capsules	*Aciphex*
*Prevacid SoluTabs**	*Nexium*
Prilosec OTC	Omeprazole
Protonix	Pantoprazole
	Prilosec (RX)
	Zegerid

*Prevacid SoluTabs are preferred for children 12 years of age or younger for the first 60 days of therapy. Payment for Prevacid SoluTabs for patients over 12 years of age will be considered for those patients who cannot tolerate a solid oral dosage form.

References

PPI interactions with clpidogrel revisited. Med Lett Drugs Ther 2009; 51:13.

Recommendations for Managing Elevated INRs in Patients on Vitamin K Antagonists

On average, Iowa Medicaid has 45 paid claims for *Mephyton* per month. The following information is based on the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition) on how to manage patients with INRs above therapeutic range, with or without bleeding.[1] In patients with mild-to-moderately elevated INRs without major bleeding, it is recommended that **oral** vitamin K be given. An article in the March 3, 2009 issue of the *Annals of Internal Medicine* reports that low-dose **oral** vitamin K did not reduce bleeding in warfarin receipients with INRs of 4.5 to 10.0 and that withdrawal of warfarin may be all that is necessary to manage elevated INRs.[2]

Condition	Intervention
INR above therapeutic range but < 5.0; no significant bleeding	Lower or omit dose of warfarin, monitor more frequently, resume therapy at appropriate adjusted dose when INR is in therapeutic range. No dose adjustment may be needed if INR only minimally above therapeutic range
INR ≥ 5.0 but < 9.0; no significant bleeding	Omit the next one or two doses of warfarin, monitor more frequently, and resume therapy at appropriate adjusted dose when INR is in therapeutic range. Alternatively, omit a dose and administer 1 to 2.5mg vitamin K **orally** especially if the patient is at risk of bleeding. If rapid reversal is required, administer vitamin K (≤ 5mg) **orally** with the expectation that INR reduction will occur in 24 hours. If the INR is still high, additional vitamin K (1 to 2mg) **orally** can be given.
INR ≥ *9.0;* no significant bleeding	Hold warfarin and administer higher dose of vitamin K (2.5 to 5mg) **orally**, with the expectation that the INR will be reduced substantially in 24 to 48 hours. Monitor INR more frequently and administer additional vitamin K if necessary. Resume warfarin therapy at appropriately adjusted dose when INR reaches therapeutic range.
Serious bleeding at any elevation of INR	Hold warfarin and administer vitamin K (10mg) by slow **IV infusion**. Supplement with fresh frozen plasma, prothrombin complex concentrate, or recombinant factor VIIa depending on urgency of the situations. May repeat vitamin K every 12 hours for persistent INR elevation.
Life threatening bleeding at any elevation of INR	Hold warfarin and administer fresh frozen plasma, prothrombin complex concentrate, or recombinant factor VIIa supplemented with vitamin K, 10mg by slow **IV infusion**, repeat if necessary depending on the INR.

1. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun; 133(6 Suppl):160S-98S.

2. Crowther et al. (2009). Oral vitamin K fails to prevent bleeding due to excess warfarin anticoagulation [abstract]. *Annals of Internal Medicine.* 2009;150:293-300. http://www.mdconsult.com/das/news/body/125596174-3/itwj/0/26135/1.html?nid=20613. Accessed March 12, 2009.

DUR Activities

- The DUR Commission recently looked at data for new starters of clozapine and the frequency of monitoring. Thirty-five members were identified as recently starting clozapine. In order to start clozapine, the WBC must be at least 3500 mm^3, and the ANC must be at least 2000 mm^3. Both values are required before clozapine can be dispensed. For the first 6 months of therapy, patients are required to have blood work drawn weekly and the pharmacist may dispense a 1-week supply of medication. After 6 months of continuous therapy (without interruptions due to a low WBC and/or ANC), blood work can be drawn every 14 days and a 2-week supply of medication can be dispensed. After 12 months of continuous therapy, blood monitoring can be done every 4 weeks and a 4-week supply of medication can be dispensed. The blood work draw date must be within seven days of the clozapine order and the pharmacist must review the results to ensure they are within the normal range before dispensing the medication. A review of the medical claims data showed all members were receiving the appropriate lab work before clozapine was dispensed.

- The DUR Commission recently looked at claims data for members using duplicate long acting narcotics (*Duragesic*, fentanyl, methadone, *Kadian, MS Contin*, morphine sulfate er/sr, and *Opana ER*). Twenty-one unique members were found on duplicate long acting narcotics, of which 16 members were combining methadone with another long acting narcotic. Letters were sent to the providers of those 16 members in March.

- The DUR Commission looked at data for members using a thiazolidinedione (TZD) who also had a diagnosis of congestive heart failure (CHF) in their medical claims data. Letters were sent to providers of 81 members in March.

Medicaid Statistics for Prescription Claims from January 1, 2009 to March 31, 2009

Top Drugs by Number of Prescriptions	Top Drugs by Dollars Spent	Top Therapeutic Class by Dollars Spent
ProAir HFA $43.58/Rx	*Synagis* 100mg/ml $1,948.93/Rx	Antipsychotics – Atypicals $12,146,285.67
Hydrocodone/APAP 5-500 $5.59/Rx	*Adderall* XR 20mg $229.41/Rx	Anticonvulsants $5,619,091.67
Lexapro 20mg $84.85/Rx	*Lexapro* 20mg $84.85/Rx	Antidepressants – Selected SSRI's $4,150,693.23
Cheratussin AC syrup $6.13/Rx	*Abilify* 10mg $392.96/Rx	Stimulants – Amphetamines – Long Acting $3,458,650.99
Loratadine 10mg $10.44/Rx	*Abilify* 5mg $386.52/Rx	RSV Prophylaxis $3,289,406.47

Average amount paid per claim, generic: $65.71

Average amount paid per claim, brand: $192.58

Total dollars paid: $66,620,729.87

Number of claims paid: 1,013,911

Percent controlled substances: 18.47%

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Outgoing Members of the DUR Commission

Dan Murphy, R.Ph., recently completed an eight year term of service with the Iowa Drug Utilization Review Commission. The Commission and the Department of Human Services wish to thank Mr. Murphy for his many years of service to the Commission and the members of Iowa Medicaid.

Dr. Laura Griffith, D.O., recently completed a four year term of service with the Iowa Drug Utilization Review commission. The Commission and the Department of Human Services wish to thank Dr. Griffith for her four years of service to the Commission and the members of Iowa Medicaid.