

PHARMACY AND THERAPEUTICS NEWSLETTER

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<http://www.tarzanacme.com/pharmacy/pharmacy.html>

P&T COMMITTEE ACTIONS

FORMULARY:

Additions:

- **Ticagrelor (Brilinta®)** – Anticoagulant. Third line agent for patients who cannot take clopidogrel (Plavix®) and have contraindications to prasugrel (Effient®)
- **Rivaroxaban (Xarelto®)** – Anticoagulant for prevention of DVT post hip or knee replacement surgery and for prevention of stroke and embolism in patients with non valvular atrial fibrillation.

Deletions:

Tiagabine (Gabitril®), droperidol (Inapsine®), Lortab® (hydrocodone & acetaminophen 500mg) all strengths – therapeutically substitute with Norco® (hydrocodone & acetaminophen 325mg), Fiorinal with codeine®, Fioricet with codeine®, Midrin®

POLICY UPDATE:

Therapeutic Substitution Policy

| When Ordered | Substituted With |
|---|--|
| Tablet & liquid PO route when patient is switched to NG | NG route |
| Lortab® (hydrocodone & acetaminophen 500mg) | Norco® (hydrocodone & acetaminophen 325mg) |
| Azelastine (Astepro®) Nasal Spray | Azelastine (Astelin®) Nasal Spray |

Renal Dose Adjustment Policy

A pharmacist will contact the physician for an alternatives or dose adjustment for the following medications:

- Metformin or metformin combinations
- Enoxaparin (Lovenox®)
- Dabigatran (Pradaxa®)
- Rivaroxaban (Xarelto®)

IV to PO Conversion Policy: When a patient meets the following criteria, the IV route of the medications listed in the policy will be switched to PO route:

| |
|---------------------------|
| Metoclopramide (Reglan®) |
| Famotidine (Pepcid®) |
| Pantoprazole (Protonix®) |
| Ranitidine (Zantac®) |
| Ampicillin |
| Azithromycin (Zithromax®) |
| Fluconazole (Diflucan®) |
| Levofloxacin (Levaquin®) |
| Metronidazole (Flagyl®) |
| Linezolid (Zyvox®) |

Patient Selection Criteria

1. Ability to tolerate oral or tube feedings x 24 hours or tolerating oral medications.
2. IV antibiotic conversion:
 - a. Afebrile or temperature trend down x 24 hours
 - b. WBC normalizing
 - c. Patient is not septic
 - d. Improving or stable radiographic findings.

Exclusion Criteria

1. NPO patients;
2. Failure to tolerate oral/enteral intake, e.g., large residuals - NG output > 150 ml for 2 or more times in a 24 hour period
3. GI bleeding-active;
4. Patient is hemodynamically unstable (HR >100, RR > 24, and SBP < 90 mmHg)
5. Excluded Diagnoses for IV antibiotics
 - a. Neutropenia;
 - b. Meningitis;
 - c. Infective endocarditis;
 - d. Abscess, undrained;
 - e. Osteomyelitis, initial treatment

MEDICATION UPDATE

Ticagrelor (Brilinta®)

Ticagrelor is an antiplatelet agent similar to clopidogrel (Plavix®) and prasugrel (Effient®) [antagonist of the adenosine diphosphate (ADP) receptor **P2Y12** on platelet]. Unlike other two medications, it is **reversible** and does not need to be metabolized to an active drug.

Ticagrelor is indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction [NSTEMI], or ST elevation myocardial infarction [STEMI]).

Ticagrelor has a more rapid onset and offset of platelet inhibition compared with clopidogrel and has a higher percent inhibition (80%) compared to prasugrel (70%) at 1 hour. Its quicker offset of antiplatelet activity will allow platelet function to return to baseline quicker and may result in fewer CABG-related bleeding events in patients needing emergent intervention. However, the twice-daily dosing compared with once-daily administration of clopidogrel and prasugrel may be a problem with compliance in some patients.

The dose of aspirin given with ticagrelor is 325mg loading dose then 81mg daily. The investigator of the PLATO trial attributed the decreased outcome to the high dose of aspirin given in North American patients.

The P&T committee added ticagrelor to the formulary with the following restrictions:

1. Third line agent for patients who are not a candidate for clopidogrel and have contraindications to prasugrel (e.g. patients older than 75 years and history of stroke or TIA, or when CABG is planned or likely).
2. Therapeutically substitute the concomitant maintenance aspirin dose larger than 100mg to 81mg.

REFERENCES

1. Ticagrelor [package insert]. Sodertalje, Sweden: AstraZeneca; 2011
2. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes (PLATO). *N Engl J Med*. 2009; 361: 1045-1057.

PCC Guideline

PCC Guideline for rivaroxaban has been added. The dose is different from the reversal of warfarin induced intracranial bleed dose¹. The guideline is linked to the medication in LexiComp in the PTMC formulary section.

The following guideline is based on animal models, expert opinions, and one human study. The physician should consider the limitations of applying the information in clinical situations prior to ordering.

PCC (Profilnine, Bebulin®)

A. Dabigatran (Pradaxa®) associated Intracranial Hemorrhage (ICH) and life-threatening bleed.

- i. Order STAT aPTT.
Do not administer if aPTT = control
- ii. PCC dose to be administered 5 mL/min, maximum 10 mL/min^{2,4}.
 - a. **≤ 90 Kg: 4000 units (4 vials) of PCC**
(1 vial = 1000 units)
 - b. **> 90 Kg: 5000 units (5 vials) of PCC**
- iii. Recommend adding FFP 2 – 4 units¹ in addition to above PCC dose
- iv. Consider hemodialysis if the last dose of dabigatran was administered within last 12 hours in overdose patients, or in renal failure patients.
- v. Consider activated charcoal if the last dose was administered within last 6 hours.

B. Rivaroxaban (Xarelto®) associated Intracranial Hemorrhage (ICH) and life-threatening bleed.

- i. Order STAT PT.
Do not administer if PT = control
- ii. PCC dose to be administered 5 mL/min, maximum 10 mL/min^{2,3}.
 - a. **≤ 90 Kg: 4000 units (4 vials) of PCC**
(1 vial = 1000 units)
 - b. **> 90 Kg: 5000 units (5 vials) of PCC**

C. Warfarin associated ICH – Refer to PTMC PHARM 14-28 PCC Policy

aPTT = Activated Partial Thromboplastin Time
PT = Prothrombin Time

REFERENCES

1. Morgenstern LB et al. *Stroke* Jul 2010;41:00-00
2. Van Ryn et al. *Haematologica* 2008;92(s1)
3. Eerenberg et al. *Circulation*. 2011;124:1573-1579
4. www.clotconnect.wordpress.com

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