Pharmacist Meeting
July 2017

Valve Surgery – Anticoagulation Standardization

- **Surgeon initiated effort to standardize therapy post cardiac valve surgery**
- **Collaboration with cardiologists in development of guidelines**
- **Recommendations per valve surgery type incorporated onto cardiac surgery orders**
  - An additional page has been added to the post cardiac surgery orders (PSO # 722)
  - Provides INPATIENT orders only; outpatient therapy and duration of therapy will be per physician discharge orders
- **Summary of clinical information utilized to compile these recommendations on following slides**

"Target" INR vs INR range

- INR "Target"
  - Guidelines all specify a single INR target for each patient
  - Acceptable range includes 0.5 INR units on each side of this target
- Rationale for a single "Target" value
  - Reduces likelihood of patients having INR values consistently near the upper or lower boundary of the range
  - Fluctuations in INR associated with increased incidence of complications in patients with prosthetic valves.

Aortic Valve Replacement (AVR)

Mechanical AVR

- Patients <u>without</u> additional risk factors (see below)
  - Warfarin: Target INR = 2.5 (range 2-3)
  - Aspirin 75-100 mg Daily recommended in addition to warfarin for ALL patients with a mechanical valve prosthesis
  - Duration: indefinite
- Patients <u>with</u> additional risk factors for thromboembolic events
  - AF, previous thromboembolism, LV dysfunction, or hypercoaguable condistion
  - Warfarin: Target INR = **3** (range **2.5-3.5**)
  - Aspirin 75-100 mg Daily recommended in addition to warfarin for ALL patients with a mechanical valve prosthesis
  - Duration: indefinite

Aortic Valve Replacement (AVR) - continued

- **Bioprosthetic AVR**
  - Warfarin: Target INR = 2.5 (range 2-3)
  - Aspirin 75-100 mg Daily recommended in addition to warfarin for ALL patients with a mechanical valve prosthesis
  - Warfarin duration: for at least 3 months and as long as 6 months after surgical bioprosthetc MVR in patients at low risk of bleeding
    - *Stroke risk and mortality rate are lower in patients who receive anticoagulation for up to 6 months after bioprosthetic AVR. Warfarin decreases risk of thromboembolism until the prosthetic valve is fully endothelialized.*

Aortic Valve Replacement - Mechanical On-X Valve

- **On-X Valve**
  - Newer generation valve that can utilize a lower INR target of 1.5-2 (in conjunction with ASA 81 mg) for long-term treatment
    - Based on single RCT of lower vs standard intensity anticoagulation in patients undergoing On-X AVR, showing equivalent outcomes.
    - Warfarin INR target should be **2.5 for the first 3 months of therapy** (same as any other mechanical AVR)
    - Lower INR target should only be used for patients that are beyond the initial 3 months of therapy

Mitral Valve Replacement/Repair

- **Mechanical Mitral Valve Replacement**
  - Warfarin: Target INR = 3 (range 2.5-3.5)
  - Aspirin 75-100 mg Daily recommended in addition to warfarin for ALL patients with a mechanical valve prosthesis
  - Duration: indefinite
- **Bioprosthetic Mitral Valve Replacement**
  - Warfarin: Target INR = 2.5 (range 2-3)
  - Aspirin 75-100 mg Daily recommended in addition to warfarin for ALL patients with a mechanical valve prosthesis
  - Warfarin duration: for at least 3 months and as long as 6 months after surgical bioprosthetic MVR in patients at low risk of bleeding
    - *Stroke risk and mortality rate are lower in patients who receive anticoagulation for up to 6 months after bioprosthetic AVR or MVR. Warfarin decreases risk of thromboembolism until the prosthetic valve is fully endothelialized.*

Mitral Valve Replacement/Repair (MVR) - *continued*

- **Mitral Valve Repair**
  - Warfarin: Target INR = 2.5 (range 2-3)
  - Aspirin 75-100 mg Daily recommended in addition to warfarin for ALL patients with a mechanical valve prosthesis
  - Duration: 3 months

Tricuspid Valve Replacement/Repair

- **Tricuspid Valve Replacement (bioprosthetic) OR repair**
  - Warfarin: Target INR = 2.5 (range 2-3)
  - Aspirin 75-100 mg Daily recommended in addition to warfarin for ALL patients with a mechanical valve prosthesis
  - Warfarin duration: 3 months
- **Triscuspid Mechanical Valves – <u>extremely</u> rare per Dr. Zellner**
  - Not included on guidelines/order set

Common themes to remember…

- **Aspirin**
  - Indicated for ALL valve replacements (mechanical & bioprosthetic) and valve repairs
  - This is included as a standard on the orders regardless of the type of valve surgery
- **Bioprosthetic valve replacements**
  - Warfarin for 3-6 months for both mitral and atrial mechanical valve bioprosthetics in patients at low risk of bleeding
    - 3 months for mitral valve repair*
- **High intensity warfarin (target INR = 3)**
  - Indicated for ALL mechanical MVR and mechanical AVR <u>with</u> additional risk factors

Bridge Therapy for mechanical valve replacements

- **Bridge Therapy with UFH for <u>new</u> mechanical valve replacements**
  - Discussed with both surgeons and cardiologists
  - Decision made to NOT make this a standard but an option to be used at the surgeon or cardiologists discretion → included as checkbox option on orders
  - Decision to bridge with UFH must be balanced with risk for postoperative bleeding
- **Bridge Therapy for patients requiring invasive or surgical procedures**
  - "…reasonable on an individualized basis, with the risks of bleeding weighed against the benefits of thromboembolism prevention, for patients who are undergoing invasive or surgical procedures with (1) mechanical AVR and any thromboembolic risk factor, (2) older generation mechanical AVR, or (3) mechanical AVR.
  - No RCT's evaluating bridging vs no bridging in adequate numbers of patients needing temporary interruption of VKA
    - Trials of bridging in AF patients w/o mechanical valves have shown higher bleeding risk without increased incidence of thromboembolic events.
    - Strength or Recommendation AND Level of Evidence lowered for this recommendation

Warfarin – dosing clinical pearls

- **Initial Warfarin Dose (valve surgery)**
  - Lower initial starting doses preferred for patients who have undergone heart valve replacement due to higher sensitivity to warfarin (effects of CPB, etc.)
  - Data based on 2001 study comparing 2.5 mg vs 5 mg Daily doses of warfarin
    - Lower dose resulted in reduced excessive variation b/w target and mean INR
  - Protocol lists a "standard" of 4 mg for initial dose but this can be adjusted if/when necessary (patients with elevated INR, multiple interacting meds, etc.) – *consider a dose of 2.5 or 3 mg for these patients*
    - Do not suggest exceeding 4 mg for initial dose
- **When to start warfarin?**
  - Surgeons have requested that warfarin start the evening that pacing wires are removed (usually POD #3)
  - We will need to monitor this daily in order for this to be started appropriately
  - "Couscale" entry with comments to start the evening of pacing wire removal will be included with the pharmacy set (#722)
  - Enter a consult at the time of order entry so this will be tracked on our consult lists

Warfarin – dosing clinical pearls *continued*

- **Please utilize the below stickers for dose recommendations to assist the cardiologist or surgeon with discharge warfarin dosing**

Pharmacy Discharge Warfarin Recommendations

Based on the patient's warfarin dosing as of today _____, the following discharge warfarin dose may be considered for this patient:

Recommended discharge warfarin dose: _____
Recommended f/u INR in _____ days

Pharmacist Signature _____

DOACS: Anticoagulation for Afib in Patients with valvular heart disease (VHD)

- AF and CHADS2-VASc score of 2 or greater with **native** aortic valve disease, tricuspid valve disease, or mitral regurgitation
  - Updated recommendation (2017)
  - DOACs can be used for these patients (excluding mitral stenosis & Afib)
    - NOTE: package labeling for DOACs all still say "nonvalvular Afib"

IIa	C-LD	**It is reasonable to use a DOAC as an alternative to a VKA in patients with AF and native aortic valve disease, tricuspid valve disease, or MR and a CHA_2DS_2-VASc score of 2 or greater (35-38).**	NEW: Several thousand patients with native VHD (exclusive of more than mild rheumatic MS) have been evaluated in RCTs comparing DOACs versus warfarin. Subgroup analyses have demonstrated that DOACs, when compared with warfarin, appear as effective and safe in patients with VHD as in those without VHD.
See Online Data Supplements 3 and 4.			

Titrating Medications Policy

Notice:
Titration Orders for Medications
Source:
The Joint Commission
Relevant to:
Hospital
Date:
April 4, 2017

The Joint Commission (TJC) recently addressed a question about titration orders in a standards FAQ. According to TJC, when titration orders are allowed by the organization, there are specific elements that must be included in the titration order:

- Medication name
- Medication route
- Initial or starting rate of infusion (dose/min)
- Incremental units the rate can be increased or decreased
- Frequency for incremental doses (how often dose/rate) can be increased or decreased
- Maximum rate (dose) of infusion
- Objective clinical endpoint (RASS score, CAM score, etc.)

This ***MUST*** be specified by the provider

The Joint Commission suggests that the following goals for the safe administration of medication be considered when titrating medications:

Titrating Medications Policy – *continued*

- **Key things to know**
  - The circled information on the previous slide MUST be included on the **order**
  - All elements must be included on the order or electronic order for us to be compliant with this standard
  - We **cannot** expect or depend on physicians to include all of these elements along with their order (virtually impossible in paper charting world)
- **How will we comply with this newly modified standard?**
  - Titrating Medications policy currently being modified to include all required elements
  - All necessary order components have been added to the label comments of our pharmacy sets (see next slide) so that this information is part of the order in the absence of this information being specifically provided by the MD/provider.
  - *Note:* some orders (sepsis, etc.) have parameters that differ from the policy. The order set specific parameters have been modified on these specific pharmacy sets so that the correct label comment information is present.

POLICY:
Medications will be titrated in a safe and accurate manner as established by Pharmacy recommendations from appropriate drug information sources, physician order and clinical assessment. In the absence of specific MD/Practitioner orders for titrating and tapering certain IV medications, the attached guidelines will be followed and titration instructions will be defined on the eMar. Unless otherwise specified by the physician, all the required titration order elements below will be included within the medical record (eMar) as defined by this policy.

- Exception to above: clinical endpoint (SBP, RASS, etc.) must be specified by provider
- If physician orders differed from the standard included on eMar (different max dose, etc.) **then the label comments must be modified**

New Therapeutic Substitution – Relistor (SC) to Movantik (PO)

Substitutions: Peripheral-acting Opioid Antagonists

ORDERED	SUBSTITUTION
Methylnaltrexone (Relistor®) 150 mg PO daily	Naloxegol (Movantik®) 12.5 mg daily
Methylnaltrexone (Relistor®) 450 mg PO daily	Naloxegol (Movantik®) 25 mg daily
Methylnaltrexone (Relistor®) 8 mg SC*	Naloxegol (Movantik®) 12.5 mg PO same frequency**
Methylnaltrexone (Relistor®) 12 mg SC*	Naloxegol (Movantik®) 25 mg PO same frequency**
Methylnaltrexone (Relistor®) weight-based dosing (0.15 mg/kg SC)* Weight-based dose < 12 mg SC Weight-based dose ≥ 12 mg SC	Naloxegol (Movantik®) 12.5 mg PO same frequency** Naloxegol (Movantik®) 25 mg PO same frequency**

* Methylnaltrexone ordered subcutaneously by GI physicians will be given as ordered, not substituted to naloxegol.
** Adjust initial naloxegol dose for CrCl ≤ 60 ml/min to 12.5 mg daily, may increase to 25 mg if ineffective.
For use with concomitant moderate CYP3A4 inhibitors, reduce dose to 12.5 mg daily (use with strong CYP3A4 inhibitors is contraindicated)
*** Contact RN prior to converting methlynaltrexone SC to naloxegol PO to confirm patient is able to take PO.

DO NOT auto-sub orders written by GI physicians without their consent

Movantik vs. Relistor (injection)

	Naloxegol (Movantik)	Methylnaltrexone (Relistor)
Time to peak concentration	<2 hours with secondary plasma peak 0.4-3 hrs after initial peak	30 minutes
Efficacy Onset	**Median time to first SBM:** KODIAC-04: 25mg – 5.9 hrs 12.5 mg – 20.4 hrs KODIAC-05: 25 mg – 12 hrs 12.5 mg – 19.3 hrs	**% of patients with SBM within 4 hrs of first dose:** Study 1: Methylnaltrexone 12 mg daily - 33% (~50% of patients had SBM within 24 hours) Study 3: Methylnaltrexone 0.15 mg/kg – 62% Methylnaltrexone 0.3 mg/kg – 58% Study 4: Methylnaltrexone 0.15 mg/kg – 48%
Adverse Effects	Abdominal Pain: 12-21% Diarrhea: 6-9% Nausea: 7-8% Flatulence 3-6% vomiting 3-5%	Abdominal Pain: 21-29% Nausea: 9-12% Diarrhea: 6% Flatulence: 13% Hyperhidrosis: 6% Dizziness: 7%
Cost (per dose)	$8.27	$95.16

- Note: Oral formulation of Relistor is **non-formulary** and this can also be automatically substituted to therapeutically equivalent dose of Movantik (see form web)

Theradoc Updates

- **Hypoglycemia alert**
  - New EZ alert that will screen for both capillary (whole blood glucose) and plasma glucose (lab draws)
    - Current Theradoc alert only screens for plasma (lab draw) values
  - Rationale: recent audits have revealed that ***~ 30% of all patients receiving insulin*** in our institution experience at least one hypoglycemic event (< 70 mg/dl) per admission!
  - Institution wide audit underway to examine trends regarding hypoglycemia
- **Baclofen renal alert**
  - New EZ alert that will screen for baclofen and patients with renal impairment (CrCl < 50 ml/min)
  - Rationale: recent patient event in patient on chronic baclofen with new onset renal failure resulting in altered mental status likely related to Baclofen.
  - This is not something we can automatically adjust but rather investigate for appropriateness – recommended dosing included in EZ alert display message

Formulary Designations

- **Any questions or confusion on this new process?**
  - Formulary, non-stock
  - Non-formulary, specialty
  - Non-formulary

Miscellaneous

- **TPN/Nutrition**
  - Cyclic TPNs & hyperglycemia
- **Med-rec**
  - ASCOM phones – please have these on you to help with communication at all times when de-centralized to the floors