Pharmacy & Therapeutics Committee Meeting
Private Dining Room
February 12, 2015 7:00 a.m.

Next Meeting will be April 9, 2015 at 7:00am in the Private Dining Room

CATHOLIC HEALTH INITIATIVES
Memorial Health Care System

PHARMACY AND THERAPEUTICS COMMITTEE

DATE: August 14, 2014 CALLED TO ORDER: 7:00 A.M.
LOCATION: Private Dining Room ADJOURNED: 8:00 A.M.

Members Present:			**Members Absent**:	**Guests**:
Richard Pesce, M.D.	Karen Babb, PharmD	Melissa Roden, RN	Allen Atchley, M.D.	Eleni Martinez, PharmD
Mark Anderson, M.D.	Michelle Denham, RN	Sandy Vredeveld, DPh	Diona Brown, RN	Matthew Russell, PharmD
Samuel Currin, M.D.	Rodney Elliott, PhT	Hannah Walker, RN	Vickie Burger, Lab	Megan Whittier, PharmD
David Dodson, M.D.	Patrick Ellis, PharmD	Danine Watson, CNO	Nathan Chamberlain, M.D.	
Michael Harper, M.D.	Scott Harbaugh, Finance	Vicki Burger, Lab	Brian Jones, RD, LDN	
Kevin Lewis, M.D.	Lila Heet, PharmD		William Oellerich, M.D.	
Nathan Schatzman, M.D.	Nan Payne, RN		Elvie Smith, RN	
Michael Stipanov, M.D.	Karen Regal, Supply Chain			

This meeting will be convened under the protection of the Tennessee Statute 63-6-219 and the Health Care Quality Improvement Act of 1986, Public Law 99-660. All information, case reviews, meeting minutes, statistics and correspondence are confidential and protected. Included in that protection are those that are involved in the review of the information. Any discussion of this information outside the realm of Peer Review constitutes a breach and violates the protection of the persons involved in the breach.

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
Minutes	The August 14, 2014 minutes were approved as submitted.		Complete
Old Business	**Exparel –** Patrick explained that the ongoing Exparel trial (total joint replacement) was expanded to include additional physicians and the data evaluation will now include a therapeutic comparison to local anesthetic delivery via the OnQ pain pump. Pharmacy will be working with anesthesia and the surgeons on this analysis.	Information	Pending
	Ofirmev (IV APAP) – Patrick and Melissa conveyed to the committee a request from Dr. Ponce for IV APAP in patients undergoing bariatric surgery. The committee recommended that this request be denied based on the past P&T decision and the current corporate "pause" on any expansion of use for this medication.	Not Approved	Complete
Therapeutic Interchanges and Formulary Decisions	The following medications were reviewed:		
	1. **Jardiance® (empagliflozin)** – New oral medication for the treatment of type 2 diabetes. Other medications in this class have previously been denied for formulary addition due to concern of adverse events in elderly and in patients with impaired renal function. It was recommended to follow the previous recommendations for other medications in this class and not add this medication to formulary.	1. Formulary addition denied	Complete
	2. **Uceris® (extended release budesonide)** – Extended release glucocorticosteroid for the treatment of ulcerative colitis. It was recommended by Dr. Shikoh for this medication to be added to formulary due to its advantage over other similar therapies (Entocort) in its ability to treat colitis of the ascending and descending colon. The recommendation was made to add this agent to formulary.	2. Approved	Complete
	3. **Custodial HTK® (crystalloid cardioplegia)** – Crystalloid cardioplegia requested by Dr. Zellner for minimally invasive mitral valve repairs. This solution can be utilized as a single dose cardioplegia and may be beneficial during minimally invasive repairs as opposed to the traditional 2 dose cardioplegia that is used for traditional cases.	3. Approved for trial use	Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	4. **Fluid Resuscitation – 0.9% NS vs. Balanced Crystalloids** – A review of the clinical use of normal saline and balanced crystalloids (LR, Plasma-lyte, etc.) for fluid resuscitation was discussed. Current literature suggests that balanced crystalloids cause less detrimental side effects (hyperchloremic acidosis, increased interstitial edema, renal impairment, etc.) and possibly better clinical outcomes. Dr. Schatzman discussed perioperative fluid management and based on the current literature he suggested a strategy utilizing primarily LR in the operative setting instead of NS 0.9%. All physician members of the committee agreed that the use of NS 0.9% should be phased out in favor of the balanced crystalloids based on current evidence. The use of Plasma-lyte was also discussed, however supply issues and cost issues need to be addressed prior to proceeding with adding this product to the central supply formulary. However, the committee did recommend that this solution be made available if possible for situations in which LR would not be an appropriate solution (patients receiving transfusions, etc.). Dr. Lewis agreed that changing the standard of practice for fluid resuscitation is needed and that widespread physician education will need to be done to disseminate this information. Additionally, Dr. Lewis recommended that a financial analysis be performed to assess the financial impact of making this change and to evaluate the impact of adding Plasma-lyte and for this to be reviewed via the hospital's value analysis process. Karen Garner agreed to follow-up on the financial review and supply availability of these alternative solutions.	4. Recommendation approved	Pending
	5. **Azithromycin vs. Erythromycin for Gastroparesis –** Ongoing drug shortages of IV erythromycin continue to present problems in supplying this therapy for patients with gastroparesis. Patrick reviewed some newer literature that has demonstrated that azithromycin is a possible alternative that can offer similar results as compared to erythromycin. Patrick also reviewed this information with Dr. Patel (gastroenterology) and he felt that this appeared to be a viable alternative based on the available literature. It was recommended to remove IV erythromycin from formulary and interchange a therapeutically equivalent dose of IV azithromycin when ordered for the treatment of gastroparesis or stimulation of gastric motility.	5. Formulary Interchange Approved	Complete
	6. **Levemir – Lantus Formulary Interchange** – A letter from Dr. Heinsohn was reviewed requesting that patients who enter the hospital on Lantus be allowed to continue on this product while hospitalized. The committee discussed this request and recommended that the existing formulary interchange not be modified at this time due to no known patient safety issues resulting from this interchange.	6. Amending existing therapeutic interchange denied.	Complete
	7. **Testosterone Replacement Products –** The use of testosterone replacement products in the inpatient setting was discussed. Pharmacy carries a limited supply of these products (injectable products, patches, etc.) and it was recommended to remove all testosterone replacement products from formulary and any home medication orders for these products may be continued following hospital discharge.	7. Removal from formulary approved.	Complete
Medication Safety/Quality	• **Metformin – IV Contrast Administration –** As requested by Dr. Schatzman, a review was performed of the current hospital practices related to peri-procedural holding of metformin therapy. Currently no clear standard exists and multiple variations exist on	Recommendation approved	Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	current standing orders. Patrick reviewed the current recommendations for withholding metformin for patients receiving IV contrast and the current recommendations recommend discontinuation of metformin containing drugs at the time of procedure and resume 48 hours following procedure. Dr. Schatzman made the recommendation that this process be followed for all contrast related procedures and prior to any surgical procedures per the "Pre-operative anesthesia orders for adults" protocol. The committee agreed that a standardized process needs to exist for peri-procedural holding of metformin and a recommendation was made to approve this recommendation and forward this on to the Medical Executive committee for final approval. Once approved all standing orders with verbiage related to holding metformin will be modified to reflect the above recommendation.		
	• **ADR Review –** Patrick reviewed the most recent ADR data and he pointed out that the majority of our serious errors continue to be related to the use of narcotics. The review of these events revealed continued concerns related to standing order doses of injectable narcotics and opioid dosing in opioid naïve patients. Melissa recommended that a more in depth review of rapid response calls, naloxone use, and standing order PCA dosing be conducted to look for trends related to opioid safety and any recommendations routed through the Medical Executive Committee for discussion. Further discussion tabled until the above additional data is available for review.	Information	Pending
	• **VTE Core Measure – data review/discussion –** Tabled until next meeting.	Tabled until next meeting.	
Policy, Procedure & Protocols	• **Antibiotic Surgical Prophylaxis –** Patrick updated the committee on the progress of this policy and process change. Dr. Anderson and Patrick are finishing discussions with the various surgical specialties to discuss the final antibiotic recommendations and the final protocol will be reviewed for final approval at the next P&T meeting. The policy outlining this new process was approved at the September Medical Executive Committee.	Information	Complete
	• **Unapproved/Unacceptable Abbreviations –** Policy reviewed for annual approval by the medical staff. Melissa asked for Patrick to review if Q.I.D. is still on the JCAHO list of unapproved abbreviations and if not she made the recommendation to remove this abbreviation from the policy.	Approved	Complete
	• **IVP Administration – cefazolin, ceftriazone, cefoxitin –** Patrick reviewed plans for moving to IV push administration of cefazolin, ceftriaxone, and cefoxitin.	Approved	Complete

There being no further business, the meeting was adjourned at 8:00 A.M. The next P&T meeting is December 11, 2014.

Respectfully submitted,

Sandy Vredeveld, D.Ph. Director of Pharmacy
Patrick Ellis, Pharm.D Pharmacy Clinical Coordinator

Approved by,

Richard Pesce, M.D. Chairman

CHI Inhaled Respiratory Market Change to Merck Products

Category	Product Line	Common Canister	Participation Requirement
ICS/LABA*	Dulera®	CC	Formulary
ICS*	Asmanex® Asmanex HFA®	Non-CC CC	Market Share
SABA*	Proventil HFA®	CC	Market Share

***ICS/LABA – Inhaled corticosteroid and long acting beta agonist**
***ICS – Inhaled corticosteroid**
***SABA – Short acting beta agonist**

The Merck market basket initiative requires CHI facilities to add Dulera® Inhalation Aerosol to formulary and gain a minimum market share of seventy percent (70%) for Asmanex® and Proventil® HFA. Our goal is to achieve 100% market share. This initiative is set to begin on January 15, 2015. It is the expectation this be in place by March 31, 2015. Full compliance is mandatory for every facility in CHI and will be closely monitored.

Dulera® is a long acting beta agonist, containing formoterol fumarate dehydrate and an inhaled corticosteroid, mometasone furoate. Dulera® offers a significant cost savings opportunity across the enterprise. We believe the products to be therapeutically equivalent when appropriately titrated to patient needs. In order for us to garner savings from this interchange, we need all combination ICS/LABA (e.g., Advair® Diskus, Advair® HFA, or Symbicort®) use to be converted to either nebulized therapy or Dulera® inhaler. A mixture of purchases of 2 or more ICS/LABA combination inhalers will not only limit our savings, but may increase our costs across the enterprise. In order to participate, Dulera® must be listed as "Available" on your facility's formulary. We are asking each facility to review these agents and present the Merck strategy to your respective Pharmacy and Therapeutics Committees in time to complete your conversion before March 31, 2015.

Asmanex® Twisthaler is mometasone inhalation and the CHI inhaled corticosteroid of choice. Asmanex® HFA which can be used in common canister programs has been approved but not yet released from the FDA. Merck realizes the delay and anticipates release anytime. It is recommended that CHI facilities add Asmanex® to formulary and therapeutically interchange Flovent® Diskus, Flovent® HFA, Pulmicort® Flexhaler and QVAR® to Asmanex®.

The short acting beta agonist Proventil® HFA (albuterol sulfate) Inhalation Aerosol is albuterol sulfate and the CHI short acting beta agonist (SABA) of choice. Ventolin® HFA, Xopenex® HFA, and ProAir® should be therapeutically interchanged to Proventil® HFA.

Additional resources will be provided to the pharmacy group.

Inhaled Corticosteroid (HFA) Daily Dose Conversion Chart:

LOW DOSE (HFA)	
Beclomethasone HFA (QVAR®)[1] 40mcg/inhalation – 2-5 inhalations/day	Mometasone **HFA** (Asmanex®)[2] 200 mcg /inhalation- 1 inhalation once daily
Beclomethasone HFA (QVAR®) 80mcg/inhalation – 1-2 inhalations/day	
Fluticasone HFA (Flovent®)[3] 44mcg/inhalation- 1-5 inhalations/day	
Fluticasone HFA (Flovent®) 110 mcg/inhalation- 1-2 inhalations/day	
Fluticasone HFA (Flovent®) 220 mcg/inhalation- 1 inhalations/day	
Ciclesonide MDI (Alvesco®)[4] 80mcg/inhalation- 2-3 inhalations/day	
Ciclesonide MDI (Alvesco®) 160mcg/inhalation- 1 inhalations/day	
MEDIUM DOSE (HFA)	
Beclomethasone HFA (QVAR®) 40mcg/inhalation – 6-12 inhalations/day	Mometasone **HFA** (Asmanex®) 200mcg /inhalation- 2 inhalations once daily
Beclomethasone HFA (QVAR®) 80mcg/inhalation – 3-6 inhalations/day	
Fluticasone HFA (Flovent®) 44mcg/inhalation- 6-10 inhalations/day	
Fluticasone HFA (Flovent®) 110 mcg/inhalation- 3-4 inhalations/day	
Fluticasone HFA (Flovent®) 220 mcg/inhalation- 2 inhalations/day	
Fluticasone furoate (Arnuity	
Ciclesonide MDI (Alvesco®) 80mcg/inhalation- 4-8 inhalations/day	
Ciclesonide MDI (Alvesco®) 160mcg/inhalation- 2-4 inhalations/day	
HIGH DOSE (HFA)	
Beclomethasone HFA (QVAR®) 40mcg/inhalation – >12 inhalations/day	Mometasone **HFA** (Asmanex®) 200mcg /inhalation- 2 inhalations BID
Beclomethasone HFA (QVAR®) 80mcg/inhalation – >6 inhalations/day	
Fluticasone HFA (Flovent®) 44mcg/inhalation- 11-15 inhalations/day	
Fluticasone HFA (Flovent®) 110 mcg/inhalation- 5-6 inhalations/day	
Fluticasone HFA (Flovent®) 220 mcg/inhalation- 3 or more inhalations/day	
Fluticasone furoate (Arnuity Ellipta) 200 mcg/day	
Ciclesonide MDI (Alvesco®) 80mcg/inhalation- >8 inhalations/day	
Ciclesonide MDI (Alvesco®) 160mcg/inhalation- >4 inhalations/day	

Inhaled Corticosteroid (DRY Powder) Dose Conversion Chart:

Ordered Product and Dose	Substitution Product and Dose
LOW DOSE (Dry Powder Inhaler)	
Budesonide DPI (Pulmicort®)[6] 90mcg/inhalation – 1-3 inhalations BID	Mometasone **HFA** (Asmanex) 200mcg /inhalation -1 inhalation once daily
Fluticasone DPI (Flovent Diskus®)[8] 50mcg/inhalation 1-2 inhalations BID	
MEDIUM DOSE (Dry Powder Inhaler)	
Budesonide DPI (Pulmicort®) 180mcg/inhalation – 2 inhalations BID	Mometasone **HFA** (Asmanex) 200mcg /inhalation -2 inhalations once daily
Fluticasone DPI (Flovent Diskus®) 50mcg/inhalation 3-5 inhalations BID	
Fluticasone furoate (Arnuity Ellipta) 100 mcg/day	
HIGH DOSE (Dry Powder Inhaler)	
Budesonide DPI (Pulmicort®) 180mcg/inhalation– >2 inhalations BID	Mometasone **HFA** (Asmanex) 200mcg /inhalation -2 inhalations BID
Fluticasone furoate (Arnuity Ellipta) 200 mcg/day	
Fluticasone DPI (Flovent Diskus®) 50mcg/inhalation >5 inhalations BID	

FORMULARY REVIEW

GENERIC NAME: LIDOCAINE HYDROCHLORIDE 3.5% OPHTHALMIC GEL

PROPRIETARY NAME: *Akten* (Akorn)

Requested by Dr. Lindquist to be used as a topical alternative to traditional injectable blocks utilizing lidocaine or bupivacaine for cataract surgery.

INDICATIONS: Lidocaine hydrochloride 3.5% ophthalmic gel is indicated for ocular-surface anesthesia during ophthalmologic procedures.

CLINICAL PHARMACOLOGY: Lidocaine is a local anesthetic that stabilizes the neuronal membrane by inhibiting ionic fluxes required for the initiation and conduction of impulses. With topical ophthalmic application of lidocaine gel, anesthesia generally occurs between 20 seconds to 1 minute and persists for 5 to 30 minutes. With proparacaine 0.5% solution, onset of anesthesia is usually within 30 seconds and the duration is approximately 10 to 20 minutes. With tetracaine 0.5% solution, onset of anesthesia is usually within 25 to 30 seconds and the duration is 15 minutes or longer. Gel formulations and other more viscous eye drop formulations (Tetravisc, etc.) have been developed to improve corneal contact time over traditional anesthetic eye drops and increase anesthetic effect.

PHARMACOKINETICS: Lidocaine may be absorbed following topical administration to mucous membranes; however absorption is dependent on multiple factors, including concentration, site of application, viscosity of the agent, and the duration of exposure.

COMPARATIVE EFFICACY: A small single center (randomized, double blind) study (160 total patients) was performed in which a traditional intracameral injection of lidocaine along with conventional proparacaine eye drops was compared to three different gel or viscous eye formulations (Tetravisc, Tetravisc Forte, Akten). Average pain scores were as follows: Tetravisc (tetracaine topical) 1.08, Tetravisc Forte (tetracaine topical) 0.55, Akten (lidocaine topical gel) 0.60, and 1% intracameral lidocaine 0.10. This small study demonstrated that pain control was optimal with the intracameral injection and similar results were seen with the topical viscous/gel formulations that were studied (Tetravisc Forte and Akten).

ADVERSE REACTIONS: The most common adverse reactions are conjunctival hyperemia, corneal epithelial changes, headache, and burning upon instillation. No incidence rates were provided in the product labeling for these adverse reactions.

DRUG INTERACTIONS: Drug interactions have not been described with the ophthalmic local anesthetic products.

DOSING: The recommended dose of lidocaine 3.5% ophthalmic gel is 2 drops applied to the ocular surface in the area of the planned procedure. Additional lidocaine ophthalmic gel may be reapplied as needed to maintain anesthetic effect.

PRODUCT AVAILABILITY and COST: Lidocaine hydrochloride 3.5% ophthalmic gel received FDA approval in October 2008. It is available as a sterile, preservative-free, clear gel packaged for single patient use in 10 mL dropper bottles containing 5 mL of lidocaine gel.

Cost: Akten – $18.08 per single use container
Similar products: Tetravisc Forte – currently not available; Tetravisc - $23.96 (non-contracted product)

CONCLUSION: Lidocaine 3.5% ophthalmic gel provides an alternative to proparacaine ophthalmic solution for local anesthesia for ocular procedures. Currently no viscous/gel formulation of topical ophthalmic anesthetics are available on hospital formulary. The standard of practice at Memorial is predominantly the use of an injectable block +/- the use of standard ophthalmic local anesthetics. The gel forming solutions offer the theoretical advantage of providing longer corneal contact time over traditional local anesthetic eye drops resulting in improved anesthetic effect. If injectable local anesthetics are not used for these procedures the limited data that is available appears to indicate that a viscous or gel formulation may offer an alternative with similar pain control.

FORMULARY REVIEW

GENERIC NAME: PERAMIVIR

PROPRIETARY NAME: Rapivab® (Biocryst)

INDICATIONS: FDA approved for the treatment of uncomplicated acute influenza (seasonal influenza virus A or B infection).

CLINICAL PHARMACOLOGY: Peramivir is an influenza neuraminidase inhibitor with the same mechanism of action as the oral neuraminidase inhibitors (oseltamivir, zanamivir).

PHARMACOKINETICS: Following oral administration, peak peramivir plasma concentrations are reached in 2 to 4 hours.[8] Absorbed drug is eliminated via renal excretion of unchanged drug. In subjects with renal impairment, overall exposure to peramivir is increased in association with decreasing renal function. Mean systemic exposure in patients with moderate renal impairment (creatinine clearance [CrCl] 30 to 49 mL/min) is expected to be approximately 3.4-fold higher than in subjects with healthy renal function. Exposure is expected to be 6-fold higher in patients with severe renal impairment (CrCl 10 to 30 mL/min) and 40-fold higher in patients on hemodialysis. Dosage adjustments are recommended in patients with renal impairment.

ADVERSE REACTIONS: In clinical trials, the most common adverse events related to peramivir administration were diarrhea, nausea, vomiting, and reduced neutrophil count.

DRUG INTERACTIONS: No significant drug-drug interactions have been observed in clinical trials.

DOSING:
FDA labeled dosing (uncomplicated influenza): 600 mg IV x 1 dose (infused over 15-30 minutes)
Unlabeled dosing (influenza requiring hospitalization): 600 mg IV ONCE DAILY (duration typically 5 days)

Renal Adjustment:

- FDA labeled dosing (CrCl): $\geq$ 50 ml/min – 600 mg x 1 dose; 30-49 ml/min – 200 mg x 1 dose; < 30 ml/min – 100 mg x 1 dose
- Unlabeled dosing: $\geq$ 50 ml/min – 600 mg DAILY; 30-49 ml/min – 200 mg DAILY; < 30 ml/min – 100 mg DAILY; CRRT – 600 mg DAILY

PRODUCT AVAILABILITY and COST:
200 mg/20 ml single use vials

Cost - $950 per 600 mg dose

CDC ANTIVIRAL RECOMMENDATIONS: The CDC recommends that for hospitalized patients and patients with severe or complicated influenza illness, treatment with oral or enteral administered oseltamivir (Tamiflu®) should be initiated. Peramivir was approved by the FDA on December 19, 2014 for the treatment of acute uncomplicated influenza in persons 18 years and older. Peramivir efficacy could not be established in patients with serious influenza requiring hospitalization in the study included in the package insert, however CDC does recommend that peramivir or investigational zanamivir should be considered in patients who cannot absorb or tolerate oral or enterally administered oseltamivir. The CDC does recommend antiviral treatment in patients with severe, complicated or progressive illness, and in hospitalized patients. For hospitalized patients and patients with severe or complicated illness, treatment with oral or enterally administered oseltamivir is recommended and the CDC states that there is currently insufficient evidence regarding efficacy of IV peramivir for routine use in hospitalized patients. Data suggests that oseltamivir administered orally or by oro/naso gastric tube is well absorbed in critically ill influenza patients, including those in the intensive care unit, on CRRT, and/or on ECMO.

COMPARATIVE EFFICACY: The FDA approval was based on a placebo controlled trial in non-hospitalized patients with influenza. The only published trial in hospitalized patients (daily x 5 doses) was terminated early due to inability to recruit enough patients based on the study design. However, a significant clinical benefit was not demonstrated for peramivir plus standard of care compared to placebo plus standard of care. Based on current evidence peramivir appears to be effective for treatment of uncomplicated influenza based on placebo controlled trial results although its role in the treatment of hospitalized/severe influenza is unknown and should likely be limited to patients unable to take oseltamivir via oral or enteral route.

CONCLUSION: Due to the lack of data demonstrating efficacy or superiority compared to currently available neuramidase inhibitors (oral oseltamivir, inhaled zanamivir) the use of peramivir should likely be reserved for critically ill patients who are not candidates for oral or enterally administerd oseltamivir. This would also be consistent with the most recent (January 9, 2015) CDC guidance regarding the use antivirals for treatment of influenza infections. The below outlines recommended criteria for use for peramivir as recommended by CHI ID specialists.

Catholic Health Initiatives
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CHI Appropriate Use Guidelines for Peramivir (Rapivab) for Influenza

The CDC recommends that for hospitalized patients and patients with severe or complicated influenza illness, treatment with oral or enterally administered oseltamivir (Tamiflu) should be initiated. Peramivir was approved by the FDA on December 19, 2014 for the treatment of acute uncomplicated influenza in persons 18 years and older. Peramivir efficacy could not be established in patients with serious influenza requiring hospitalization in the study included in the package insert; however CDC does recommend that peramivir or investigational zanamivir should be considered in patients who cannot absorb or tolerate oral or enterally administered oseltamivir. The following guidelines were developed by CHI infections disease pharmacists and reviewed by CHI national pharmacy leadership and Infectious disease physician experts. Local directors of pharmacy should work with local antimicrobial stewardship teams and physicians to implement these guidelines if Peramivir may be appropriate for use at your facility.

1. **Influenza Diagnosis** – patient should be influenza positive or must have symptoms consistent with influenza illness. **A negative Rapid Influenza Diagnostic Test result does NOT exclude a diagnosis of influenza** in a patient with suspected influenza. When there is clinical suspicion of influenza and antiviral treatment is indicated, antiviral treatment should be started as soon as possible without waiting for results of additional influenza testing.
    a. **Development of Symptoms** – patients should have reported first influenza symptoms within previous 5 days (previous 48 hrs preferred); unless symptom history cannot be obtained (use clinical judgment).
2. **Patient Location Guidelines** – Patients must be in a critical care/ICU level of care. Patients with severe influenza with complications that limit the availability of the GI tract would generally be ICU level of care.
    a. **Critical Access Hospitals (CAH)** – due to severity of illness and complications requiring IV antiviral use, patient transfer to a tertiary care facility is most likely warranted. Peramivir may be indicated at a CAH if unable to transfer a patient within a reasonable timeframe (24 hours). It is recommended that CAH obtain Peramivir if this situation arises from a tertiary facility in the region.
3. **Unable to receive PO/PT Oseltamivir (Tamiflu)** – patients cannot absorb oral or per tube oseltamivir. Diagnosis may include gastric stasis/ileus, malabsorption, or GI bleeding. Limited data suggest that oseltamivir administered orally or by oro/naso gastric tube is well absorbed in critically ill influenza patients, including those in the intensive care unit, on continuous renal replacement therapy, and/or on extracorporeal membrane oxygenation.
    a. Majority of published case reports included venous/venous ECMO. Patient receiving venous/arterial ECMO are unlikely candidates for oral oseltamivir.
4. **Facilities should develop a joint approval process** – a joint approval should occur between critical care and/or Infectious Disease and Pharmacy (ID pharmacist specialist, or pharmacy clinical coordinator) where feasible.
5. **Duration of therapy** – If patient meets above restriction guidelines and peramivir is given, peramivir should be evaluated after 5 days of therapy and further discussion between the approving providers and pharmacy should occur before further peramivir therapy is provided.
    a. **IV to PO conversion** – IV to PO conversion should be evaluated daily once peramivir is started and conversion to oseltamivir should be considered once PO/PT route is available.

CHI Formulary Recommendation:

- Tertiary Care Centers: should evaluate local formulary definitions and consider formulary with restrictions, or non-formulary with restrictions for appropriate use.
- Critical Access Hospitals and non-Tertiary Care Centers: it is recommended that peramivir be non-formulary, non-stocked and if necessary be procured from a regional tertiary care center when appropriate use guidelines are met.

* Average Wholesale Price

References: (available upon request) Peramivir Trial in Hospitalized Pts.
Peramivir vs. Tamiflu in Outpt Setting Phase III Trial
Peramivir Package Insert

Pneumonia Vaccine Recommendations (13 valent, 23 valent vaccines)

What is currently recommended?

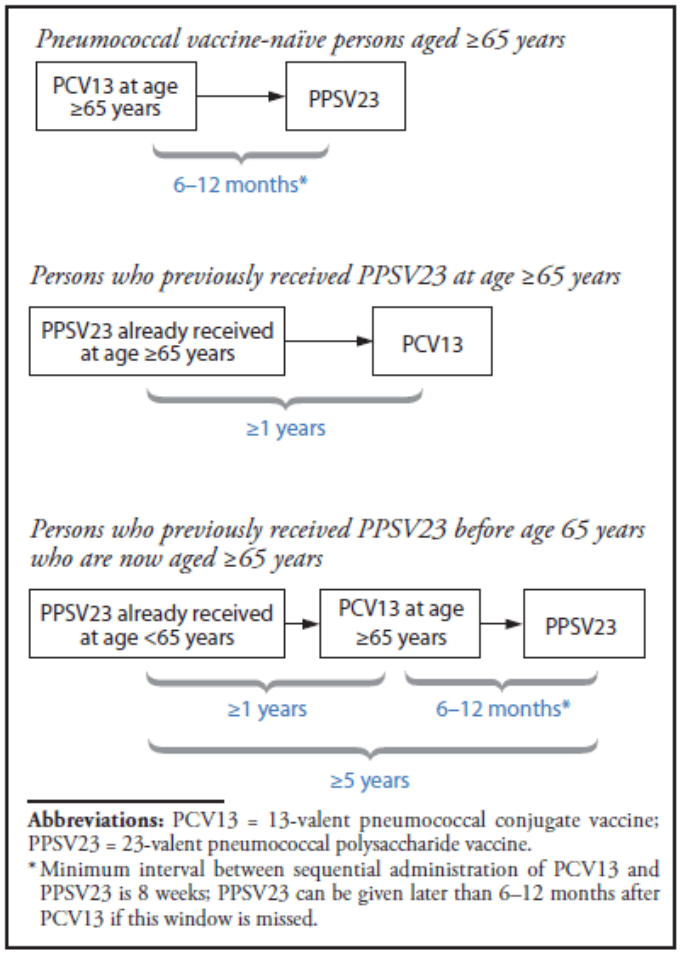
In 2010, the Advisory Committee on Immunization Practices (ACIP) approved revised recommendations that all persons should be vaccinated with 23-valent pneumococcal polysaccharide vaccine (PPSV23) at age 65 years. In 2012, ACIP made recommendations for use of 13-valent pneumococcal conjugate vaccine (PCV13) and PPSV23 for adults aged ≥19 years with immunocompromising conditions.

Why are the recommendations being modified now?

PCV13 was approved by the Food and Drug Administration in late 2011 for use among adults aged ≥50 years. In June 2014, the results of a randomized placebo-controlled trial showing efficacy of PCV13 against community-acquired pneumonia among approximately 85,000 adults aged ≥65 years became available and were presented to ACIP. The evidence supporting PCV13 vaccination of adults was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework and determined to be type 2 (moderate level of evidence); the recommendation was designated as a Category A recommendation.

What are the new recommendations?

Both PCV13 and PPSV23 should be routinely administered in series to all adults aged ≥65 years. The recommendations for routine PCV13 use among adults aged ≥65 years will be reevaluated in 2018 and revised as needed. ACIP recommendations for routine use of PCV13 in adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants remain unchanged.



Abbreviations: PCV13 = 13-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

* Minimum interval between sequential administration of PCV13 and PPSV23 is 8 weeks; PPSV23 can be given later than 6–12 months after PCV13 if this window is missed.

Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

September 19, 2014 / 63(37);822-825

On August 13, 2014, the Advisory Committee on Immunization Practices (ACIP) recommended routine use of 13-valent pneumococcal conjugate vaccine (PCV13 [Prevnar 13, Wyeth Pharmaceuticals, Inc., a subsidiary of Pfizer Inc.]) among adults aged ≥65 years. PCV13 should be administered in series with the 23-valent pneumococcal polysaccharide vaccine (PPSV23 [Pneumovax23, Merck & Co., Inc.]), the vaccine currently recommended for adults aged ≥65 years. PCV13 was approved by the Food and Drug Administration (FDA) in late 2011 for use among adults aged ≥50 years. In June 2014, the results of a randomized placebo-controlled trial evaluating efficacy of PCV13 for preventing community-acquired pneumonia among approximately 85,000 adults aged ≥65 years with no prior pneumococcal vaccination history (CAPiTA trial) became available and were presented to ACIP (*1*). The evidence supporting PCV13 vaccination of adults was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework and determined to be type 2 (moderate level of evidence); the recommendation was categorized as a Category A recommendation (*2*). This report outlines the new recommendations for PCV13 use, provides guidance for use of PCV13 and PPSV23 among adults aged ≥65 years, and summarizes the evidence considered by ACIP to make this recommendation.

Epidemiology of Pneumococcal Disease Among Adults Aged ≥65 Years

Streptococcus pneumoniae (pneumococcus) remains a leading infectious cause of serious illness, including bacteremia, meningitis, and pneumonia, among older adults in the United States. Use of a 7-valent pneumococcal conjugate vaccine (PCV7) since 2000 and PCV13 since 2010 among children in the United States has reduced pneumococcal infections directly and indirectly among children, and indirectly among adults. By 2013, the incidence of invasive pneumococcal disease (IPD) caused by serotypes unique to PCV13 among adults aged ≥65 years had declined by approximately 50% compared with 2010, when PCV13 replaced PCV7 in the pediatric immunization schedule (*3*). However, in 2013 an estimated 13,500 cases of IPD occurred among adults aged ≥65 years (*3*). Approximately, 20%–25% of IPD cases and 10% of community-acquired pneumonia cases in adults aged ≥65 years are caused by PCV13 serotypes and are potentially preventable with the use of PCV13 in this population (*3,4*).

PCV13 Vaccine in Adults

On December 30, 2011, PCV13 was approved for use among adults aged ≥50 years to prevent pneumonia and invasive disease caused by *S. pneumoniae* serotypes contained in the vaccine. The new use for Prevnar 13 was approved under FDA's accelerated approval pathway, which allows for earlier approval of products that provide meaningful therapeutic benefit over existing treatments for serious and life-threatening illnesses (*5*). FDA defined "meaningful therapeutic benefit over existing treatments" as protection of adults aged ≥50 years from nonbacteremic pneumococcal pneumonia or nonbacteremic pneumococcal pneumonia combined with protection from IPD (*7*). On June 20, 2012, ACIP recommended routine use of PCV13 for adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants (*6*). The ACIP decision to recommend PCV13 use among adults aged ≥65 years was deferred until data became available on 1) the impact of PCV13 use in children on disease in adults (i.e., indirect effects) and 2) the efficacy of PCV13 against noninvasive pneumococcal pneumonia among adults. In accordance with accelerated approval requirements, a randomized placebo-controlled trial (CAPiTA trial) was conducted in the Netherlands among approximately 85,000 adults aged ≥65 years during 2008–2013 to verify and describe further the clinical benefit of PCV13 in the prevention of pneumococcal pneumonia (*1*). The results of the CAPiTA trial demonstrated 45.6% (95% confidence interval [CI] = 21.8%–62.5%) efficacy of PCV13 against vaccine-type pneumococcal pneumonia, 45.0% (CI = 14.2%–65.3%) efficacy against vaccine-type nonbacteremic pneumococcal pneumonia, and 75.0% (CI = 41.4%–90.8%) efficacy against vaccine-type IPD among adults aged ≥65 years (*1*).

Two randomized, multicenter, immunogenicity studies conducted in the United States and Europe among older adults showed that PCV13 induced an immune response as good as or better than that induced by PPSV23 (*7,8*). Functional antibody responses were measured 1 month after vaccination using an opsonophagocytic activity (OPA) assay. In adults aged 60–64 years with no prior pneumococcal vaccination, PCV13 elicited OPA geometric mean antibody titers (GMTs) to the 12 serotypes common to both vaccines that were comparable with, or higher than, responses elicited by PPSV23 (*7*). In adults aged ≥70 years who previously had been immunized with a single dose of PPSV23 ≥5 years before enrollment, PCV13 elicited OPA responses that were comparable with those elicited by PPSV23 for two serotypes and higher for 10 serotypes (*8*).

Immunogenicity studies evaluating responses to PCV7 and PPSV23 administered in series showed a better immune response when PCV7 was administered first (*9*–*12*). An evaluation of immune response after a second pneumococcal vaccination administered 1 year after the initial study doses showed that subjects who received PPSV23 as the initial study dose had lower OPA antibody responses after subsequent administration of PCV13 than those who had received PCV13 as the initial dose followed by a dose of PPSV23, regardless of the level of the initial OPA response to PPSV23 (*9*). Studies evaluating the immune response after a sequence of PCV7 or PCV13 followed by PPSV23 with intervals of 2, 6, and 12 months or 3–4 years demonstrated that after the PPSV23 dose, antibody levels were higher than the pre-PCV baseline, and a noninferior response was observed when compared with post-PCV antibody levels (*9*–*12*). None of the studies were designed to evaluate the optimal interval between vaccine doses.

Indirect effects from PCV13 use among children, if similar to those observed after PCV7 introduction, might further reduce the remaining burden of adult pneumococcal disease caused by PCV13-types. A preliminary analysis using a probabilistic model following a single cohort of persons aged 65 years demonstrated that adding a dose of PCV13 to the current PPSV23 recommendations for adults aged ≥65 years, compared with current PPSV23 recommendations, would lead to additional health benefits (*14*). This strategy would prevent an estimated 230 cases of IPD and approximately 12,000 cases of community-acquired pneumonia over the lifetime of a single cohort of persons aged 65 years, assuming current indirect effects from the child immunization program and current PPSV23 vaccination coverage among adults aged ≥65 years (approximately 60%). In a setting of fully realized indirect effects assuming the same vaccination coverage, the expected benefits of PCV13 use among this cohort will likely decline to an estimated 160 cases of IPD and 4,500 cases of community-acquired pneumonia averted among persons aged ≥65 years (*14*).

CDC will assess the implementation and impact of the recommendation for PCV13 use among adults aged ≥65 years, including coverage with PCV13 and PPSV23, and impact of PCV13 on vaccine-type IPD burden and community-acquired pneumonia. Monitoring disease trends among adults who do not receive PCV13 might help quantify indirect effects and the long-term utility of routine PCV13 use among adults. ACIP will be updated routinely on changes in the burden of IPD and community-acquired pneumonia among adults during the next 3 years to determine the need for revisions to the adult PCV13 recommendations.

PPSV23 in Adults

A single dose of PPSV23 is recommended for routine use in the United States among adults aged ≥65 years (*15*). Effectiveness of PPSV23 in preventing IPD in adults has been demonstrated, but the data on the effectiveness of this vaccine in preventing noninvasive pneumococcal pneumonia among adults aged ≥65 years have been inconsistent. PPSV23 contains 12 serotypes in common with PCV13 and 11 additional serotypes. In 2013, 38% of IPD among adults aged ≥65 years was caused by serotypes unique to PPSV23 (*3*). Given the high proportion of IPD caused by serotypes unique to PPSV23, broader protection is expected to be provided through use of both PCV13 and PPSV23 in series. ACIP considered multiple factors when determining the optimal interval between a dose of PCV13 and PPSV23, including immune response, safety, the risk window for protection against disease caused by serotypes unique to PPSV23, as well as timing for the next visit to the vaccination provider.

ACIP Recommendations for PCV13 and PPSV23 Use

Both PCV13 and PPSV23 should be administered routinely in series to all adults aged ≥65 years.

Pneumococcal vaccine-naïve persons. Adults aged ≥65 years who have not previously received pneumococcal vaccine or whose previous vaccination history is unknown should receive a dose of PCV13 first, followed by a dose of PPSV23. The dose of PPSV23 should be given 6–12 months after a dose of PCV13. If PPSV23 cannot be given during this time window, the dose of PPSV23 should be given during the next visit. The two vaccines should not be coadministered, and the minimum acceptable interval between PCV13 and PPSV23 is 8 weeks.

Previous vaccination with PPSV23. Adults aged ≥65 years who have previously received ≥1 doses of PPSV23 also should receive a dose of PCV13 if they have not yet received it. A dose of PCV13 should be given ≥1 year after receipt of the most recent PPSV23 dose. For those for whom an additional dose of PPSV23 is indicated, this subsequent PPSV23 dose should be given 6–12 months after PCV13 and ≥5 years after the most recent dose of PPSV23 (*15*).

Potential Time-Limited Utility of Routine PCV13 Use Among Adults ≥65 Years. The recommendations for routine PCV13 use among adults aged ≥65 years will be reevaluated in 2018 and revised as needed.

ACIP recommendations for routine use of PCV13 in adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants remain unchanged (*6*).

FORMULARY REVIEW

GENERIC NAME: EDOXABAN

PROPRIETARY NAME: SAVAYSA (Daiichi Sankyo Inc.)

INDICATIONS: Edoxaban is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF) and for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) after 5-10 days of initial therapy with a parenteral anticoagulant.

Comparison of the FDA-Approved Indications for similar agents.				
Indication	**Apixaban**	**Dabigatran**	**Rivaroxaban**	**Edoxaban**
Prevention of VTE in patients undergoing hip or knee replacement	X		X	
Treatment of VTE	X	X*	X	X*
Stroke prevention in patients with atrial fibrillation	X	X	X	X

*Require a lead in period of 5-10 days with a parenteral anticoagulant.

CLINICAL PHARMACOLOGY: Edoxaban is an oral inhibitor of factor Xa, which is responsible for the conversion of prothrombin (factor II) to thrombin (factor IIa), ultimately leading to thrombus formation and clotting. Edoxaban is selective for factor Xa; therefore, thrombin and other downstream clotting factors (e.g., IIa, fibrin) are inhibited without affecting factors XIIa, XIa, IXa, or VIIa.

PHARMACOKINETICS: Edoxaban is rapidly absorbed, reaching peak plasma concentrations (C_{max}) within 1-2 hours after administration with an absolute bioavailability of 62%. Edoxaban follows dose-proportional pharmacokinetics. Approximately 50% of an orally administered dose is recovered in the urine as unchanged edoxaban. A 4-hour hemodialysis session only removes ~7% of edoxaban. The terminal half-life is 10-14 hours and steady state concentrations are reached within 3 days of dosing.

ADVERSE REACTIONS: The most common adverse reactions reported in clinical trials were various types of bleeding (most common site: GI).

COMPARATIVE SAFETY & EFFICACY: The ENGAGE AF-TIMI 48 study was a multi-national, double blind, noninferiority study that compared edoxaban 60 mg and 30 mg (dose adjusted for CrCl 15-50 ml/min, weight ≤ 60kg and concomitant use with verapamil, quinidine, or dronedarone) to warfarin (goal INR 2-3). The study included patients with NVAF documented within 12 months before randomization, a $CHADS_2$ score ≥ 2 and anticoagulation therapy planned for the length of the trial. The primary endpoint was the occurrence of first stroke or systemic embolic event that occurred during treatment or within 3 days of the last dose. Results of the study showed that both doses of edoxaban were non-inferior to warfarin for the primary endpoint. However, the 30 mg dose was numerically less effective than warfarin for the primary endpoint and inferior in reducing rates of ischemic stroke. Rate of the primary endpoint with warfarin was 1.5% (median time in therapeutic range = 68.4%) compared to a rate of 1.18% ($p<0.001$ for noninferiority) for high dose edoxaban and 1.61% ($p=0.005$ for noninferiority) for low dose edoxaban. The annualized rate of bleeding 3.43% for warfarin, 2.75% for high dose edoxaban and 1.61% for low dose edoxaban.

A second study, Hokusai VTE, was a multinational, double blind study comparing the efficacy and safety of edoxaban 60 mg once daily (dose adjustment – 30mg once daily) to warfarin (goal INR 2-3) for treatment of acute VTE. The primary efficacy outcome was recurrent, symptomatic VTE and the primary safety outcome was major or clinically relevant nonmajor bleeding. Time in therapeutic range for patients receiving warfarin was 63.5%. Edoxaban was noninferior to warfarin for the primary efficacy outcome, which occurred in 3.2% of edoxaban participants and 3.5% of warfarin participants. The safety outcome occurred in 8.5% of edoxaban participants and 10.3% of warfarin participants. Patients on cyclosporine or antiretroviral therapy (ritonavir, nelfinavir, indinavir, saquinavir) were excluded from the study.

Because of differences in trial design and patient enrollment, efficacy and safety data for rivaroxaban, apixaban, dabigatran and edoxaban cannot be directly compared for the indication of stroke prevention in NVAF. Dabigatran and apixaban demonstrated superiority over warfarin in their respective trials whereas rivaroxaban and edoxaban showed non-inferiority to warfarin for prevention of stroke in NVAF. However, patients enrolled in the rivaroxaban clinical trial (ROCKET-AF) and edoxaban clinical trial (ENGAGE AF-TIMI 48) had a higher mean $CHADS_2$ stroke risk score (3.5 and 2.8 respectively) than those enrolled in either of the pivotal trials examining the use of apixaban or dabigatran (2.1). This reflects higher proportions of patients with a history of heart disease, prior stroke, or other co-morbidities. Patients with multiple risk factors for stroke also have an increased risk of bleeding, which may have contributed to the higher bleeding event rates observed in the rivaroxaban and edoxaban trials as compared to the dabigatran and apixaban trials.

All four drugs showed a reduction in ICH when compared to warfarin although apixaban appears to offer the lowest rate of major bleeding when compared to conventional warfarin therapy (30% reduction). The major bleeding rates of dabigatran and rivaroxaban were similar when compared to warfarin with no statistically significant difference in major bleeding observed. However, apixaban and edoxaban did demonstrate a statistically significant reduction in major bleeding as compared to warfarin (2.1% vs. 3.1% for apixaban and 2.75% vs. 3.43% for edoxaban). Again, the definitions of major bleeding and the differences in the patient population enrolled in each trial make direct comparisons difficult.

Although all four of the novel anticoagulants that are approved for stroke prevention rely on renal elimination, each drug does have differences related to the degree of renal elimination (dabigatran – 80%, rivaroxaban – 33%, apixaban – 40%, edoxaban – 50%). These differences may be significant in patients who present with acute bleeding complications particularly in patients with impaired renal function as this may delay the return of hemostasis in this patient population.

CONTRAINDICATIONS: Edoxaban is contraindicated in patients with active pathological bleeding.

BLACK BOX WARNING: Edoxaban carries three black box warnings. Premature discontinuation of edoxaban without adequate alternative anticoagulation increases the risk of ischemic events. The ENGAGE AF-TIMI 48 study showed that edoxaban has reduced efficacy in NVAF for patients who have a CrCl >95 ml/min. This subgroup of patients had an increased risk of ischemic stroke when compared to patients on warfarin. The last black box warning states there is an increased risk of epidural or spinal hematomas for patients on edoxaban receiving neuraxial anesthesia.

ADVERSE REACTIONS: The most common adverse reactions reported in the clinical trials for treatment of NVAF were bleeding and anemia. The most common adverse reactions reported in clinical trials for the treatment of DVT and PE were bleeding, rash, abnormal liver function tests and anemia.

DRUG INTERACTIONS: Edoxaban is a substrate of P-glycoprotein (P-gp). The serum concentration of edoxaban is decreased when taken concurrently with P-gp inducers (e.g., carbamazepine, phenobarbital, St. John's Wort, etc.). Use with Rifampin is contraindicated. Inversely, edoxaban serum concentrations are increased with the use of P-gp inhibitors (e.g., ketoconazole, verapamil, amiodarone, dronedarone, etc.). However, a dose reduction with these medications is only recommended when the indication is treatment of DVT/PE. Use caution when administering edoxaban with other anticoagulants, antiplatelets or thrombolytics due to an increased bleeding risk.

MONITORING: No specific laboratory tests are recommended for patients on edoxaban therapy.

DOSING:

Nonvalvular Atrial Fibrillation

- CrCl > 50 to ≤95 ml/min: 60 mg once daily
- CrCl 15 – 50 ml/min: 30 mg once daily

DVT/PE

- Recommended dose: 60 mg once daily
- Dose adjustment: 30 mg once daily
    - CrCl 15 – 50 ml/min
    - Body weight ≤ 60 kg
    - Use of certain P-gp inhibitors (verapamil, quinidine, azithromycin, clarithromycin, erythromycin, ketoconazole, itraconazole, dronedarone)

DISCONTINUATION FOR SURGERY & OTHER INTERVENTIONS: Edoxaban should be discontinued at least 24 hours prior to any invasive or surgical procedures. If this is not possible, the risk of bleeding should be weighed against the urgency of the intervention.

CONVERTING TO/FROM OTHER ANTICOAGULANTS:

- Switching from warfarin to edoxaban: warfarin should be discontinued and edoxaban started when the INR ≤ 2.5.
- Switching from edoxaban to warfarin:
    - Oral option: For patients taking 60 mg daily, reduce the dose to 30 mg and start warfarin concomitantly. For patients taking 30 mg daily, reduce the dose to 15 mg and start warfarin concomitantly. INR should be measured just prior to edoxaban dose to minimize effect of edoxaban on the INR. Discontinue edoxaban once a stable INR ≥ 2 is reached.
    - Parenteral option: Discontinue edoxaban and begin a parenteral anticoagulant and warfarin at the time of the next scheduled edoxaban dose. Once a stable INR ≥ 2 is reached, discontinue the parenteral anticoagulant.
- Switching from edoxaban to other anticoagulants (excluding warfarin): Discontinue edoxaban and start the oral or parenteral anticoagulant at the time of the next edoxaban dose.
- Switching from oral anticoagulants (excluding warfarin) and LMWH to edoxaban: Discontinue the current anticoagulant and start

edoxaban at the time of the next schedule dose or administration of LMWH.
- Switching from UFH to edoxaban: Discontinue the infusion and start edoxaban 4 hours later.

COST & COMPARISON TO SIMILAR AGENTS – *atrial fibrillation stroke prevention indication*
Edoxaban – 60 mg once daily: $8.80 per day
Apixaban – 5 mg twice daily: $7.50 per day
Rivaroxaban – 20 mg once daily: $7.49 per day
Dabigatran – 150 mg twice daily: $9.00 per day

CONCLUSION: Edoxaban is an oral agent that appears to offer similar efficacy to the other three novel oral anticoagulants currently available for prevention of stroke in patients with NVAF.

FORMULARY REVIEW

GENERIC NAME: DENOSUMAB

PROPRIETARY NAME: *Prolia* (Amgen)

INDICATIONS: Denosumab is indicated for the treatment of osteoporosis in postmenopausal women who are at high risk of fracture. Patients considered to have a high risk of fracture include patients with a history of bone fracture, patients with multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapies. Denosumab is also undergoing evaluation for use in the treatment of several other conditions associated with bone loss, including rheumatoid arthritis (RA) and the prevention of postmenopausal osteoporosis. It may also delay bone metastases, be effective in the treatment of cancer, and inhibit and treat bone destruction associated with cancer.

CLINICAL PHARMACOLOGY: Denosumab is a fully human monoclonal antibody to the receptor activator of nuclear factor kappa B ligand (RANKL). RANKL is a mediator of osteoclast formation, function, and survival. RANKL binds to its receptor (RANK) on the surface of precursor and mature osteoclasts, and stimulates these cells to mature and resorb bone. Denosumab binds to RANKL with a high specificity and affinity, resulting in the inhibition of osteoclast-mediated bone resorption and inhibits osteoclast maturation and survival.

PHARMACOKINETICS: Denosumab has nonlinear, dose-dependent pharmacokinetics.[30] Following subcutaneous administration, denosumab serum levels are detectable in as early as 1 hour, and maximum serum concentrations are reached within 3 and 21 days. Within 72 hours of administration, the serum levels of denosumab are 70% to 80% of maximum. The mean half-life is 25.4 days. The serum levels decline over a period of 4 to 5 months and markers of bone resorption return to baseline levels within 12 months.

ADVERSE REACTIONS: The most frequently observed adverse reactions (more than 5% and greater than placebo) reported with denosumab therapy include back pain, pain in extremity, hypercholesterolemia, musculoskeletal pain, and cystitis.[1] Other common adverse reactions are various types of infections, anemia, vertigo, peripheral edema, and sciatica. Serious adverse reactions have included hypocalcemia, serious infections, dermatologic reactions, pancreatitis, and osteonecrosis of the jaw.

DRUG INTERACTIONS: No drug interactions have been identified, but the Food and Drug Administration (FDA) is requiring Amgen to conduct an in vivo drug-drug interaction study with a CYP3A4 substrate. The deadline for submission of the results of this study to the FDA is March 2012.

DOSING: The recommended dosage is denosumab 60 mg subcutaneously every 6 months. The product labeling states the injection should be given by a health care provider in the upper arm, upper thigh, or abdomen. All patients should also receive daily doses of calcium 1,000 mg and at least 400 units of vitamin D. Dosage adjustments on the basis of renal function are not necessary. However, patients with creatinine clearance less than 30 mL/min or those receiving dialysis are at a greater risk of developing hypocalcemia. No clinical studies have evaluated the safety and efficacy of denosumab in patients with moderate to severe hepatic impairment.

PRODUCT AVAILABILITY and STORAGE: Denosumab received FDA approval on June 1, 2010. Denosumab is available as a single-use prefilled syringe containing 60 mg in a 1 mL solution and also a single-use vial containing 60 mg in a 1 mL solution. Prior to first use, the denosumab syringe and vial should be stored in a refrigerator, between 2° and 8°C (36° and 46°F) in the original carton. When the syringe or vial is not in use, it should be protected from light and heat. Neither product should be shaken.

COST: $881.01 per dose ($1762.02 per year of therapy)
(cost comparison to Reclast (zoledronic acid): $77.03 per year)

DISCUSSION: Denosumab offers a unique mechanism of action in increasing BMD and reducing bone turnover, suggesting a variety of potential uses, including osteoporosis treatment and prevention and the treatment of various cancers. It effectively increases BMD and reduces fracture rates in postmenopausal women, as well as improves BMD in patients with cancer and rheumatoid arthritis. The unknown long-term safety, twice-yearly administration, and cost may initially limit the use of this product in the treatment of postmenopausal women who are intolerant to, achieving an inadequate response with, or having poor adherence rates with bisphosphonate therapy.

FINANCIAL ANALYSIS
See next page for detail.

PREVIOUS P&T COMMITTEE DECISIONS
At a previous P&T meetings (February & June 2011) it was voted to only utilize Prolia for patients in which Reclast (zoledronic acid) use is contraindicated – CrCl < 35 ml/min.

MEMORIAL HEALTH CARE SYSTEM

PHARMACY FINANCIAL PRO FORMA: PROLIA (FOR OSTEOPOROSIS)

	Total							Per Case				
Payer	Cases	Mix	Days	Charges	Payments	Direct Costs	Dir Contribution Margin	ALOS	Charges	Payments	Direct Costs	Dir Contribution Margin
Commercial / Mgd Care	175	18.8%	0	$505,199	$92,568	$34,928	$57,640	0.0	$2,887	$529	$200	$329
Medicaid	20	2.2%	0	$37,209	$4,385	$2,737	$1,648	0.0	$1,860	$219	$137	$82
Medicare	721	77.5%	0	$2,460,632	$386,143	$169,249	$216,894	0.0	$3,413	$536	$235	$301
Other	8	0.9%	0	$39,543	$11,964	$1,859	$10,105	0.0	$4,943	$1,496	$232	$1,263
Self-Pay	6	0.6%	0	$14,788	$299	$856	($558)	0.0	$2,465	$50	$143	($93)
	930	**100.0%**	**0**	**$3,057,372**	**$495,359**	**$209,630**	**$285,729**	**0.0**	**$3,287**	**$533**	**$225**	**$307**
Based upon the following patient population:							**Baseline**		**$3,287**	**$533**	**$225**	**$307**
- FY14 Outpatients												
- Principal Diagnosis:	*733.0 -*	*Osteoporosis*					**Less:**					
	733.09			***$43.68***	<<<<<<<<<<< ZOLEDRONIC ACID 1MG/1.25ML VL				$1,805		$33	
- Charge Markup Factor	*270%*			***$218.41***	<<<<<<<<<<< ZOLEDRONIC ACID 5MG/100ML				$441		$22	
				Medicare Reimbursement (J3489 Zoledronic Ac			**Adjusted Baseline**		**$1,042**		**$171**	
							Add:					
				$797.64	<<<<<<<<<<< PROLIA (DENOSUMAB) 60MG				$2,379		$881	
				Medicare Reimbursement (J0897 Denosumab Injection)								
				($13.29 per 1MG)			**Final**		**$3,421**	**$554**	**$1,052**	**($498)**

FORMULARY REVIEW

GENERIC NAME: IBUPROFEN INJECTION

PROPRIETARY NAME: *Caldolor* (Cumberland)

Requested by Dr. Harper for trial use in ICU patients with severe sepsis, ARDS, ECMO, etc. to assess if COX inhibition provides any meaningful clinical benefit in the management of these patients.

INDICATIONS: Ibuprofen injection is indicated for use in adults in the management of mild to moderate pain, management of moderate to severe pain as an adjunct to opioid analgesics, and for reduction of fever.

CLINICAL PHARMACOLOGY: Ibuprofen is a propionic acid nonsteroidal anti-inflammatory drug (NSAID). It is an inhibitor of prostaglandin synthetase with anti-inflammatory, analgesic, and antipyretic activity. Additionally, some studies have also assessed ibuprofen's ability to inhibit COX to ameliorate the physiological and immune responses during severe sepsis related to prostacyclin and thromboxane production.

Off label dosing – patients with sepsis to decrease prostaglandin & thromboxane synthesis
Some data is available (human and animal data) that may suggest a potential role for IV ibuprofen in patients with sepsis due to its ability to inhibit COX and thereby decreasing the production of prostaglandin and thromboxane which has been linked with abnormalities of airway mechanics, pulmonary hypertension, hypoxema, cardiovascular collapse, and multiple organ failure in animals and humans with the sepsis syndrome. The most recent clinical trial in humans (NEJM 1997) demonstrated that treatment with ibuprofen is safe in patients with sepsis and markedly reduced the synthesis of prostacyclin and thromboxane, but that it has no effect on survival or the development of shock or ARDS. However, treatment with ibuprofen did have positive physiologic effects on fever, tachycardia, oxygen consumption, and lactic acidosis in patients with sepsis. It is important to note that there was not a difference observed in regards to the rates of renal failure or GI bleeding in the patients receiving ibuprofen.

PHARMACOKINETICS: The pharmacokinetics of intravenous (IV) ibuprofen following a 30-minute infusion are summarized in Table 1. Ibuprofen is a racemic mixture. The S(+) isomer is clinically active; the R(−) isomer is inactive, but approximately 60% is interconverted to the active S(+) isomer in adults.

ADVERSE REACTIONS: The most common adverse reactions observed in patients treated with IV ibuprofen included nausea, flatulence, vomiting, headache, hemorrhage, and dizziness.

DRUG INTERACTIONS: The drug interactions associated with injectable ibuprofen are the same as those associated with oral ibuprofen. NSAIDs may reduce the antihypertensive effects of angiotensin-converting enzyme (ACE) inhibitors, and the natriuretic effects of furosemide and thiazides. Concomitant use with aspirin is not recommended because of the potential for increased adverse effects. Concomitant use with warfarin may increase the risk of serious GI bleeding. Lithium levels may be increased and renal clearance reduced. When lithium and ibuprofen are administered concurrently, patients should be monitored for signs of lithium toxicity. NSAIDs may enhance the toxicity of methotrexate.

DOSING: In the management of pain, the recommended dosage of injectable ibuprofen is 400 to 800 mg IV over 30 minutes every 6 hours as needed. For reduction of fever, the dosage is 400 mg IV over 30 minutes, followed by 400 mg every 4 to 6 hours or 100 to 200 mg every 4 hours as needed. Dose and frequency should be adjusted based on response; however, the total daily dose should not exceed 3,200 mg. Patients should be well hydrated before administration to reduce the risk of renal adverse effects. Ibuprofen injection must be diluted prior to administration to a final concentration of 4 mg/mL or less. Appropriate diluents include sodium chloride 0.9% injection, dextrose 5% injection, or Ringer's lactate solution. Infusion time should not be less than 30 minutes.

Off label dosing (severe sepsis): 10 mg/kg (max dose 800 mg) Q 6 hrs X 8 doses – based on clinical trial regimen

PRODUCT AVAILABILITY and COST: Ibuprofen injection received Food and Drug Administration approval on June 11, 2009. It is available as a 100 mg/mL solution supplied in a 800 mg per 8 mL single-dose vials in cartons of 25 vials. Cost = $9 per 800 mg vial

CONCLUSION: Ibuprofen does offer an IV alternative to oral ibuprofen for the treatment of mild to moderate pain although the benefit over ketorolac in this setting has not been established. However, the limited data available in the treatment of patients with sepsis may provide some clinical benefit although positive benefits related to outcomes such as mortality and shock are not available at this time.

Requested by Dr. Harper for trial use in ICU patients with severe sepsis, ARDS, ECMO, etc. to assess if COX inhibition provides any meaningful clinical benefit in the management of these patients.

FORMULARY REVIEW

GENERIC NAME: CISATRACURIUM

PROPRIETARY NAME: Nimbex®

INDICATIONS: For neuromuscular blockade as an adjunct to general anesthesia, to facilitate endotracheal intubation and to provide skeletal muscle relaxation during surgery or mechanical ventilation in the ICU.

CLINICAL PHARMACOLOGY: Non-depolarizing neuromuscular blocking agent that binds competitively to nicotinic receptors on the motor end-plate to antagonize the action of acetylcholine, resulting in blockade of neuromuscular transmission. Cisatracurium is one of several isomers of atracurium and is three times as potent as atracurium.

PHARMACOKINETICS: Cisactracurium undergoes rapid non-enzymatic degradation (organ independent metabolism) in the bloodstream to form two inactive metabolites, neither of which has any neuromuscular blocking activity.

Onset of action: 2-3 minutes
Peak effect: 3-5 minutes
Elimination half-life: 22-29 minutes (average time to 95% recovery is ~ 64 minutes; range 25-93 minutes)

ADVERSE REACTIONS: Adverse reactions are similar in nature and scope to the other commercially available neuromuscular blockers. Compared to atracurium, cisatracurium has a lower propensity for causing histamine release.

DOSING:
Bolus: 0.15-0.2 mg/kg
Maintenance Dose: 1-3 mcg/kg/min following the initial bolus dose
Normal maintenance dose 0.5-10 mcg/kg/min titrated based on clinical response

COST COMPARISON:
Based on 80 kg patient
Cisatracurium - $575/day
Rocuronium - $53/day

CONCLUSION & RECOMMENDATION:
Due to the unique organ-independent metabolism of cisatracurium it can be safely used in patients with multisystem organ failure since its metabolism is independent of hepatic or renal function. Currently rocuronium is most commonly used when neuromuscular blockade is required in mechanically ventilated ICU patients. **Although rocuronium can safely be used in patients with renal failure it does present problems if patients also have coexisting liver disease due to its primary hepatic metabolism. For this reason it might be advantageous to add cisatracurium to formulary for use in patients with multi-system organ failure requiring a neuromuscular blocking agent. However, due to ongoing drug shortage issues regarding cisatracurium and the greater cost per day of therapy this agent should be reserved for patients with multi-system organ failure.**

Ofirmev™ Literature Summary

Introduction

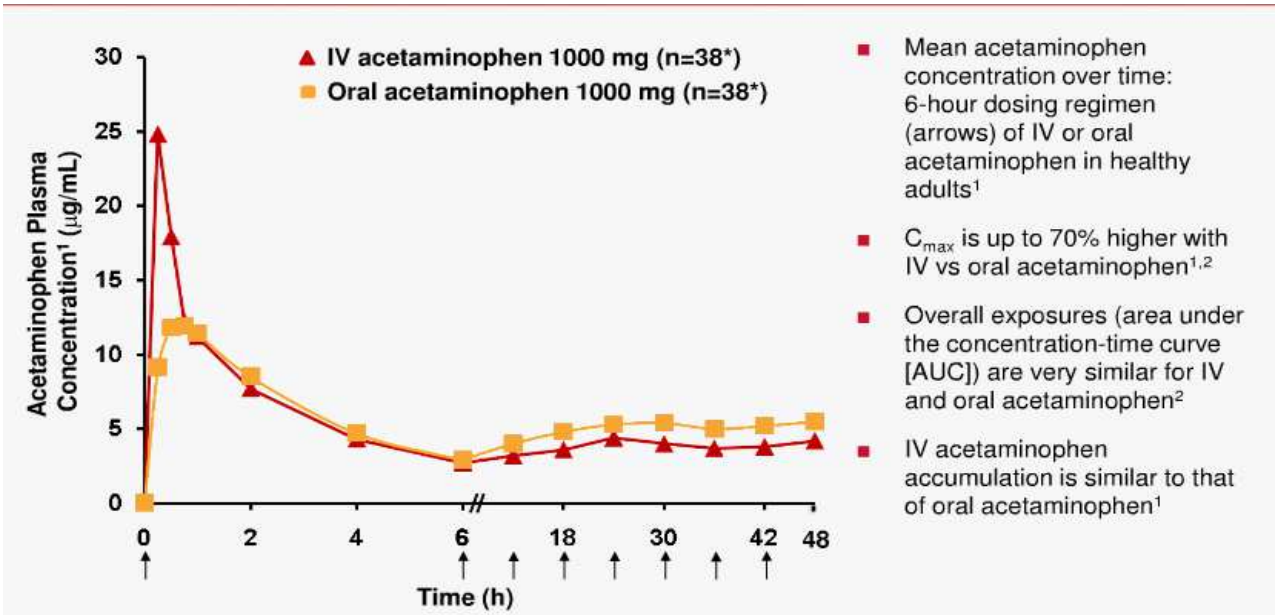
Postoperative pain is reported in more than 80% of surgical patients, and a focus on managing pain utilizing therapy with varying mechanisms of action is considered the current best practice. Multimodal techniques for pain management include the administration of two or more drugs that act by different mechanisms for providing analgesia. These drugs may be administered *via* the same route or by different routes. Approved by the FDA in November 2010, acetaminophen injection (Ofirmev™) is the first non-opioid, non-NSAID analgesic available for IV administration in the United States.

Pharmacology/Pharmacokinetics

Acetaminophen is thought to exert its analgesic and antipyretic effects centrally through inhibition of cyclooxygenase.

The maximum blood concentration (Cmax) of Ofirmev is higher than with oral or rectal administration; however, it is important to note that the Cmax with Ofirmev (29 mcg/mL) remains below the 150 mcg/ mL concentration considered potentially hepatotoxic. Despite the difference in Cmax, overall volume of distribution and area under the curve (AUC) values remain similar for all acetaminophen formulations.

Form	PO	IV
onset of action	<1 hour	5-10 minutes peak effect 1 hour
duration of action	4-6 hours	4-6 hours
time to peak	10-60 minutes	15 minutes
AUC	42.2 h*mcg/ml	47 h*mcg/ml
Cmax	15.1 mcg/ml	28.4 mcg/ml



* Of the 38 randomly assigned patients, 34 patients who received IV acetaminophen 1000 mg and 33 patients who received oral acetaminophen 1000 mg had plasma concentrations measured.

Efficacy Pain Studies

In the US, three pivotal trials evaluating IV acetaminophen efficacy in pain and fever resulted in its approval by the FDA. In both pain trials, IV acetaminophen was superior to placebo as measured by the primary outcome of weighted sum of pain intensity difference over 24 hours.

In a meta-analyses of the efficacy of acetaminophen for the prevention or treatment of postoperative pain, IV acetaminophen was found to be superior to placebo, however there was no difference between IV acetaminophen and either NSAIDs or opioids for the treatment of pain.

In regards to morphine consumption, six placebo controlled trials showed a significant decrease in consumption of rescue medication (morphine, meperidine, oxycodone) compared to placebo. Three placebo controlled trials showed no difference between the groups.

A meta-analysis evaluating 7 studies comparing patient-controlled analgesia (PCA) with morphine plus APAP against PCA morphine alone (6 studies involving IV APAP and 1 involving PO APAP) aimed to determine the effects of acetaminophen on morphine side-effects and consumption after major surgery. The analysis found that, relative to PCA morphine alone, administration of PCA morphine with acetaminophen resulted in no significant reduction in post-operative nausea and vomiting despite a 20% decrease in morphine use in the first 24 hour postoperatively.

In reviewing the literature for pain studies specifically done in the abdominal surgery population, six articles were found. The first study looked at women undergoing laparascopic sterilization who received IV paracetamol versus placebo with alifentanyl as rescue PCA. During the four hour post-operative study period, alifentanyl consumption was reduced in patients who received IV paracetamol. A second RCT looking at postoperative analgesia in laparascopic cholecystectomy studied 30 females under 50 who were given 1 gm of IV acetaminophen or placebo ten minutes after induction of anesthesia. Patients with liver or kidney disease were excluded, as were those with opioid or alcohol dependence. No significant difference was appreciated for IV morphine consumption or first morphine requirements.

A meta-analysis reviewed nine eligible studies (five orthopedic, one liver surgery, one C-section delivery) and found that 24 hour morphine consumption was reduced, with a mean reduction of 9 mg. The clinical significance of this has not been validated.

A randomized, double-blind, placebo-controlled multicenter study of two acetaminophen dosing regimens for the treatment of pain after abdominal surgery was published in 2010. Comparison was made between two doses of IV acetaminophen and placebo, and rescue PCA of either morphine or dilaudid was available. Ofirmev in combination with either morphine or dilaudid PCA was superior to placebo in reducing pain intensity scores but not in time to rescue medication. Significant, important exclusion criteria limit the applicability of this study.

Conclusions

The American Society of Anesthesiology published practice guidelines for management of acute pain in the perioperative setting and strongly recommends the use of acetaminophen, NSAIDs, or COX-2 inhibitors as a part of the multimodal approach to managing pain. However, the guidelines suggest that the medication choice, strength, route, and duration should be individualized.

While many years of non-US clinical experience exist to support the safety and efficacy of IV acetaminophen in the treatment of pain, most of the data is lacking statistical significance, robust sample size, or involves significant exclusion criteria that make applicability difficult. Only a small number of studies were head-to-head or active-controlled trials.

In acute pain, the advantages of IV acetaminophen when used for short periods include a slightly faster onset of action than oral acetaminophen; potential decreased risk of adverse events relative to injectable morphine (although this finding requires better designed trials for confirmation); and lower risk of gastrointestinal adverse events relative to oral NSAIDs. The combination of IV acetaminophen and morphine postoperatively compared with PCA morphine alone may lower opioid requirements to a relatively small degree, but seems to have no effect on the incidence of opioid-related gastrointestinal effects.

The possible advantages of IV acetaminophen are offset by a drug acquisition cost that is significantly higher than alternative non-oral agents currently available on Memorial Hospital Formulary.

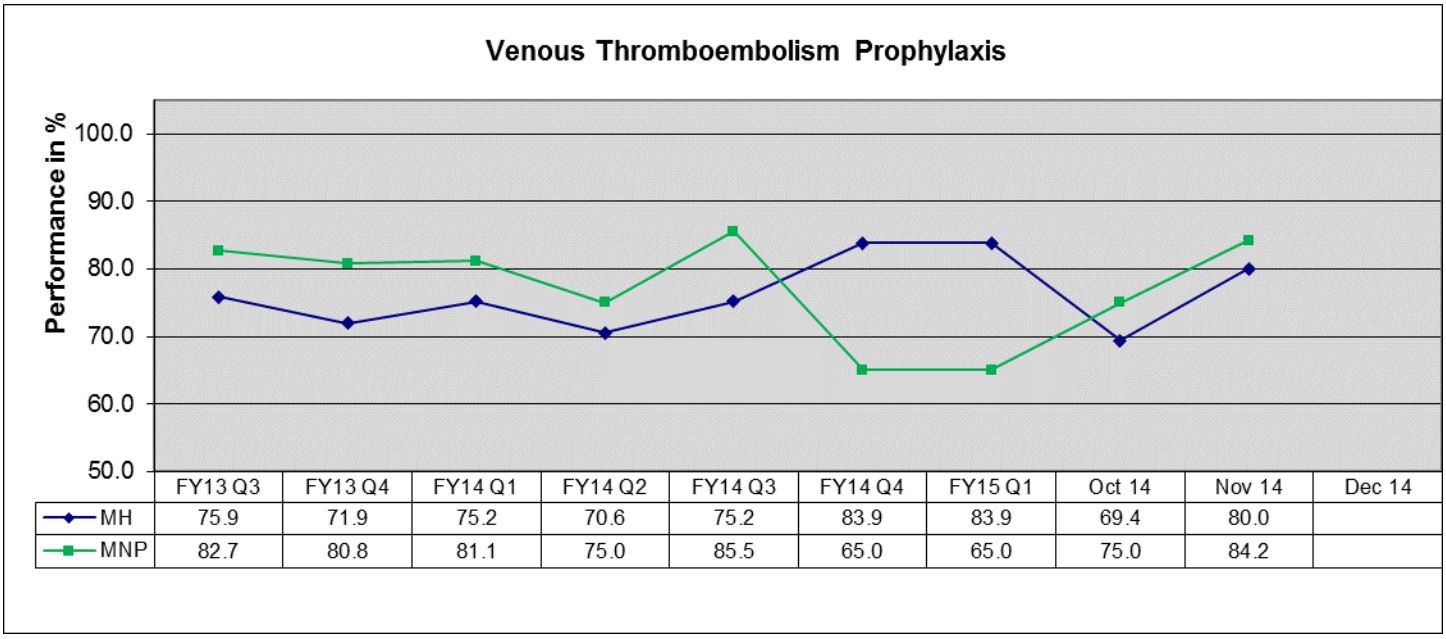
VTE P&T Report

Based on the Premier monthly Core Measure Report

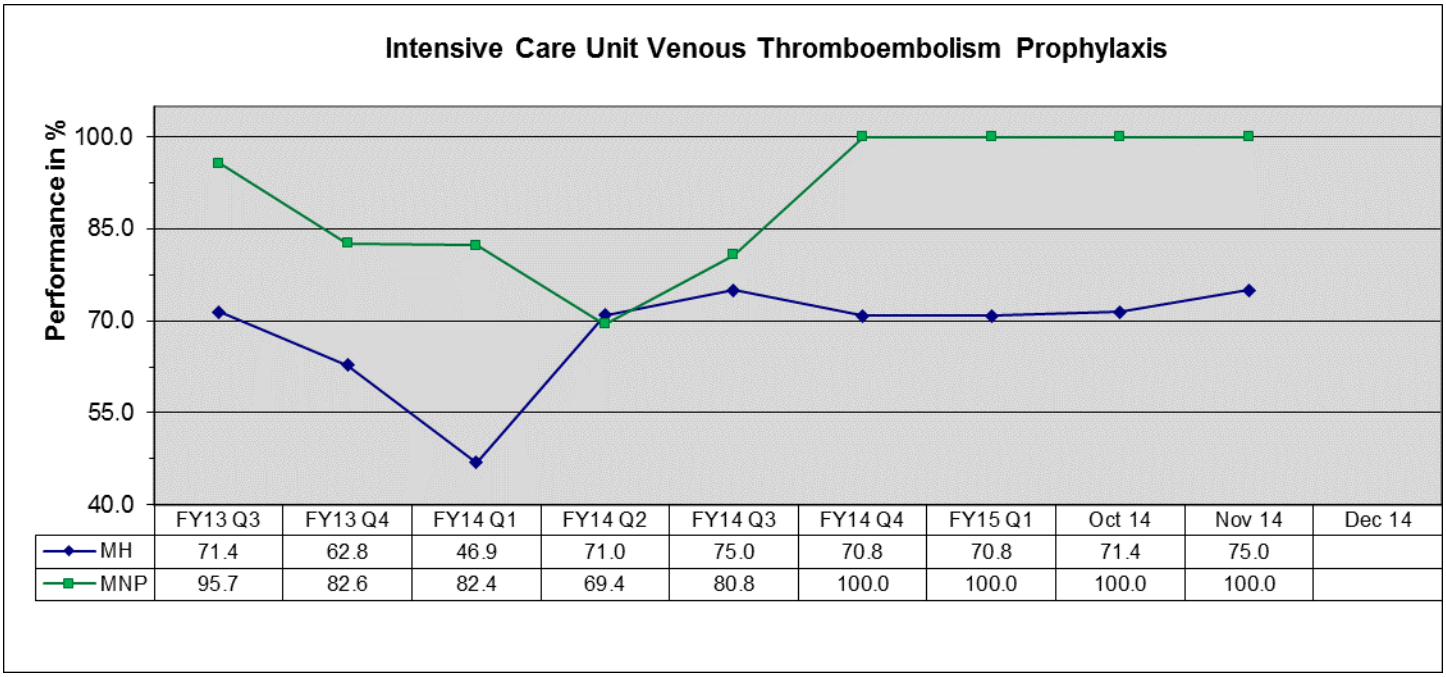
1. Specific Indicator Trends:

Disclaimer: Preliminary data is collected concurrently for reporting in a timely manner and is not absolutely reflective of final patient population submitted externally via vendor (6 months retrospective) and may vary by 1-5% margin based on final coding. The information detailed does not reflect the care of all VTE Patients only those who are required to be submitted via vendor (primary diagnosis).

No VTE Measures are patients who go home without a diagnosis of VTE while in the hospital

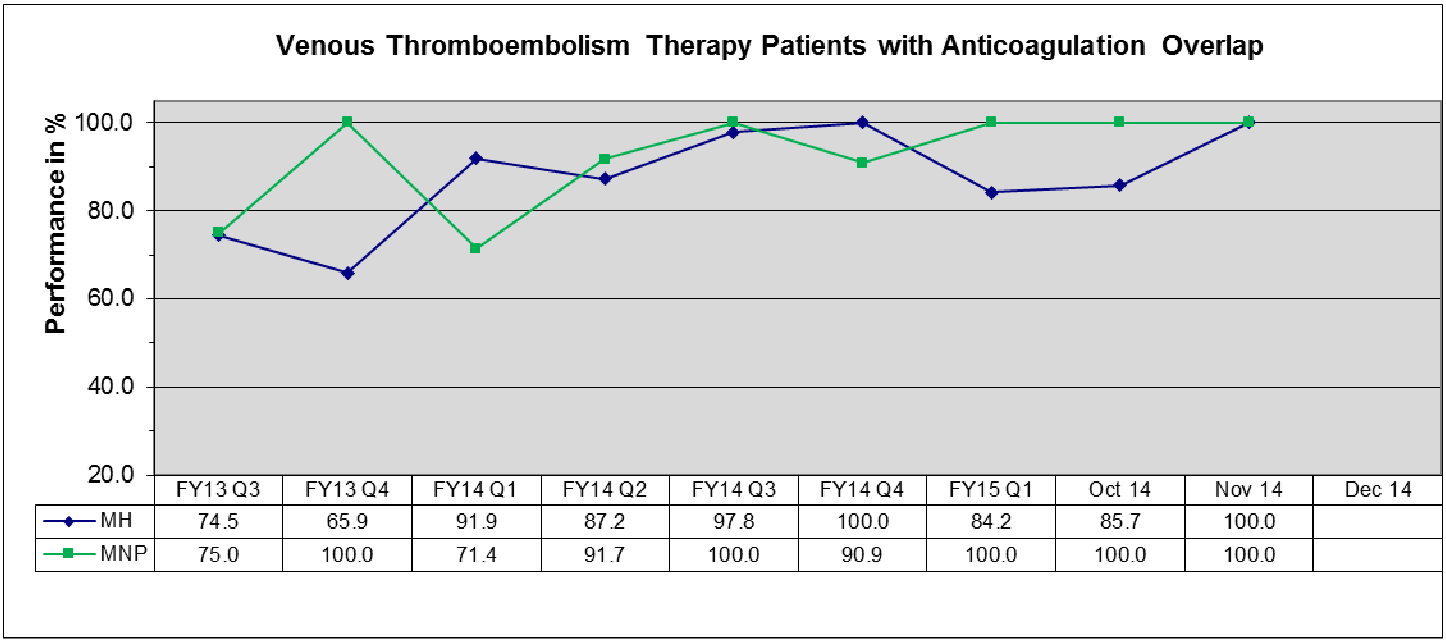


	FY13 Q3	FY13 Q4	FY14 Q1	FY14 Q2	FY14 Q3	FY14 Q4	FY15 Q1	Oct 14	Nov 14	Dec 14
MH	75.9	71.9	75.2	70.6	75.2	83.9	83.9	69.4	80.0	
MNP	82.7	80.8	81.1	75.0	85.5	65.0	65.0	75.0	84.2	



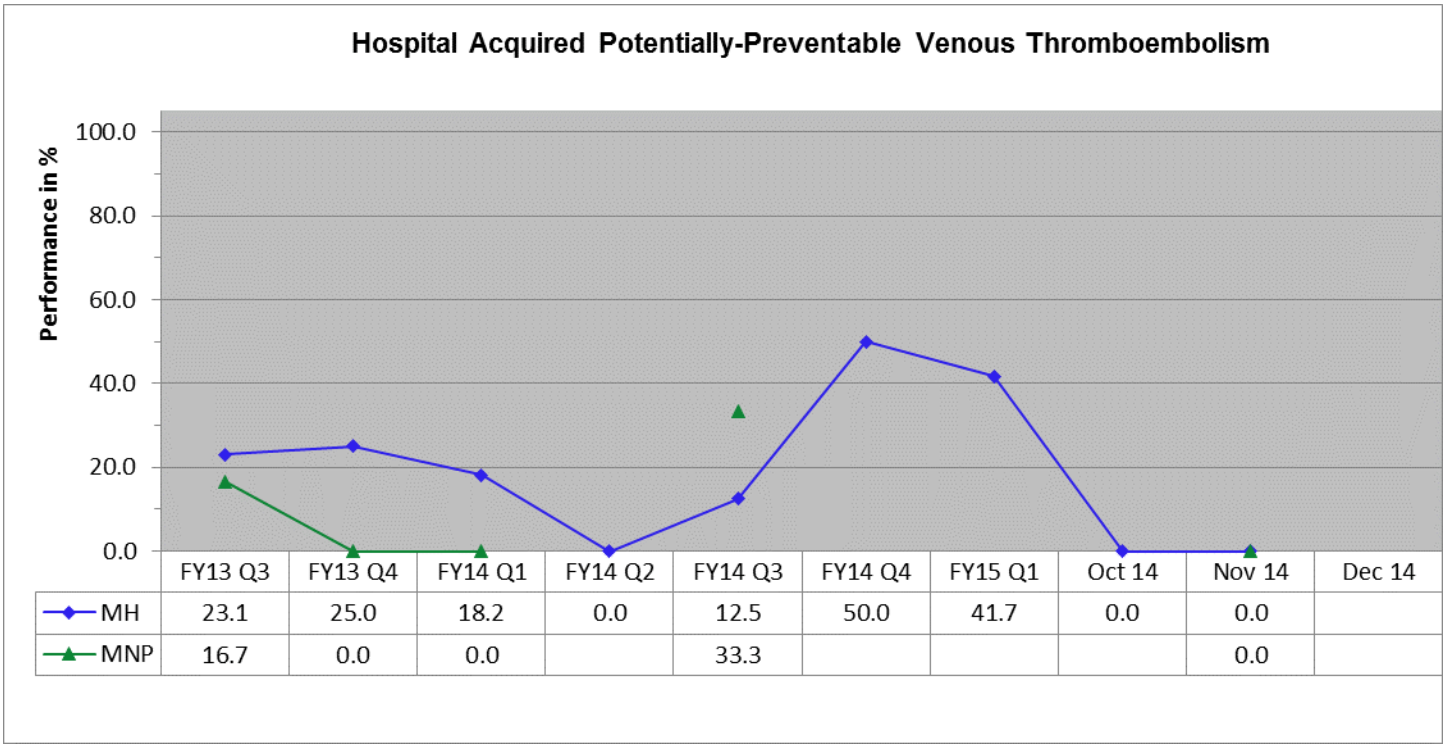
	FY13 Q3	FY13 Q4	FY14 Q1	FY14 Q2	FY14 Q3	FY14 Q4	FY15 Q1	Oct 14	Nov 14	Dec 14
MH	71.4	62.8	46.9	71.0	75.0	70.8	70.8	71.4	75.0	
MNP	95.7	82.6	82.4	69.4	80.8	100.0	100.0	100.0	100.0	

Principal & Other Diagnosis VTE



	FY13 Q3	FY13 Q4	FY14 Q1	FY14 Q2	FY14 Q3	FY14 Q4	FY15 Q1	Oct 14	Nov 14	Dec 14
MH	74.5	65.9	91.9	87.2	97.8	100.0	84.2	85.7	100.0	
MNP	75.0	100.0	71.4	91.7	100.0	90.9	100.0	100.0	100.0	

Other Diagnosis VTE are patients who come into the hospital without a VTE and later develop a VTE prior to discharge.



	FY13 Q3	FY13 Q4	FY14 Q1	FY14 Q2	FY14 Q3	FY14 Q4	FY15 Q1	Oct 14	Nov 14	Dec 14
MH	23.1	25.0	18.2	0.0	12.5	50.0	41.7	0.0	0.0	
MNP	16.7	0.0	0.0		33.3				0.0	

*All blank fields reflect there were no patients who meet the requirements to be included in the measure.

2. Findings:

- VTE prophylaxis both in and out of the ICU is impacted by both physicians and nurses. It is important for physicians to order prophylaxis or document a reason for not giving prophylaxis (both pharmacological AND mechanical) and for nurses to document prophylaxis as given.

- Overlap therapy is impacted mainly by physicians.

- Hospital Acquired VTE should ideally be 0%. Volumes for this element are low so even one case could skew us upwards on a monthly basis. Each hospital acquired VTE case is being reviewed for reason and opportunity.

VTE Core Measures are divided into three separate categories:
No VTE are patients who go home without a diagnosis of VTE while in the hospital **Principle VTE** are patients who come into the hospital with a diagnosis of VTE, and **Other VTE** are patients who come into the hospital without a VTE and later develop a VTE prior to discharge.

No VTE has two measure elements:
- VTE prophylaxis
- ICU VTE prophylaxis admitted/transferred to ICU

Principle VTE has two measure elements:
- VTE therapy with anticoagulation overlap if on Warfarin (5 days of overlap required or reason documented for less than 5 days overlap)
- Written discharge instructions provided to patients who go home on Warfarin

Other VTE has three measure elements:
- VTE therapy with anticoagulation overlap if on Warfarin (5 days of overlap required or reason documented for less than 5 days overlap)
- Written discharge instructions provided to patients who go home on Warfarin
- Hospital Acquired Potentially-Preventable VTE

PHYSICIAN VENOUS THROMBOLISM PROPHYLAXIS ORDERS - *Draft*

Low Risk (1pt)

Early ambulation.
May choose one of the following:

- TED Knee High
- TED Thigh High
- Other
  _____
  _____

Moderate Risk to Very High Risk (≥2pts)
Core Measures Require
Pharmacologic and/or Mechanical Prophylaxis required *OR*
MD documented contraindication for each intervention

Pharmacological

Fondaparinux 2.5 mg SC q 24 hr
(contraindicated CrCl<30ml/min)
Heparin 5000 units SC q 8 hr
Enoxaparin 40 mg SC q 24 hr
Enoxaparin 30 mg SC q 24 hr
(creatine clearance < 30ml/min)
Other _____

Mechanical

TED Knee High
TED Thigh High
SCD's
Other _____

Prophylaxis Contraindications

Pharmacological **AND** Mechanical Prophylaxis contraindicated or not needed at this time.

- Already on therapeutic anticoagulation
- Other Reason or Contraindication_____

Physician's Signature _____Date:_____Time:_____

PHYSICIAN STANDING ORDERS - *Draft*

DVT Prophylaxis
Pharmacologic and/or mechanical prophylaxis required OR MD documented contraindication for both

Pharmacological Prophylaxis
□ Enoxaparin 40 mg SC Q 24 hrs (reduce dose to 30 mg Q24 if CrCl < 30 ml/min)
□ Heparin 5000 units SC Q 8 hrs
□ Heparin 5000 units SC Q 12 hrs
□ Fondaparinux 2.5 mg SC Q 24 hrs

Pharmacological prophylaxis contraindicated due to:
□ Active bleeding
□ Bleeding risk
□ Already on therapeutic anticoagulation
□ other _____

Mechanical Prophylaxis – only required if pharmacologic prophylaxis not chosen or if mechanical PLUS pharmacological prophylaxis desired
□ TED knee high
□ TED thigh high
□ SCDs
□ Contraindicated reason _____

Adverse Drug Reaction (ADR) Summary
1st Quarter (FY15) July-September 2014

Category 1: Commonly recognized ADR's which are expected and do not result in serious medical consequences or extended hospitalization (e.g. antibiotic rash, nausea, mild hypokalemia).

Category 2: Significant ADR's which extend hospitalization and/or require extensive therapeutic measures (e.g. gastrointestinal bleed secondary to NSAIDs, Aminoglycoside nephrotoxicity.

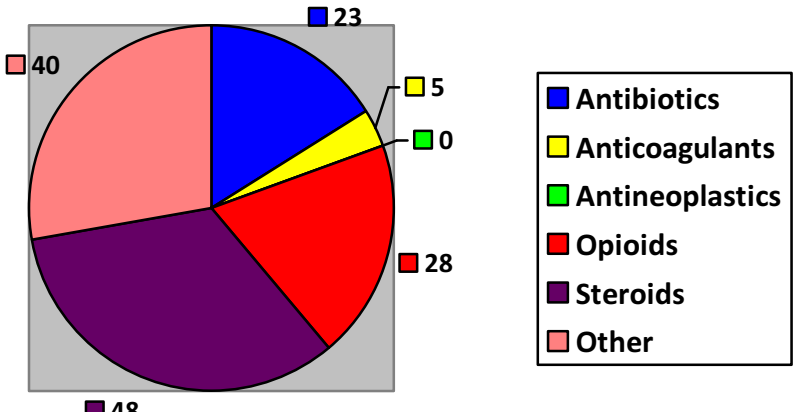
Category 3: A serious or rare ADR which has abnormal characteristics compared with published reports of the reaction (e.g. heparin induced platelet aggregation resulting in limb amputation). ADR's from this category should be reported to the manufacturer and/or the FDA (MedWatch or the Vaccine Adverse Event Reporting System).

Inpatient: 142 (25%)
Prior to hospitalization: 409 (75%)
Total: 551

Category 1: 417
Category 2: 113
Category 3: 1

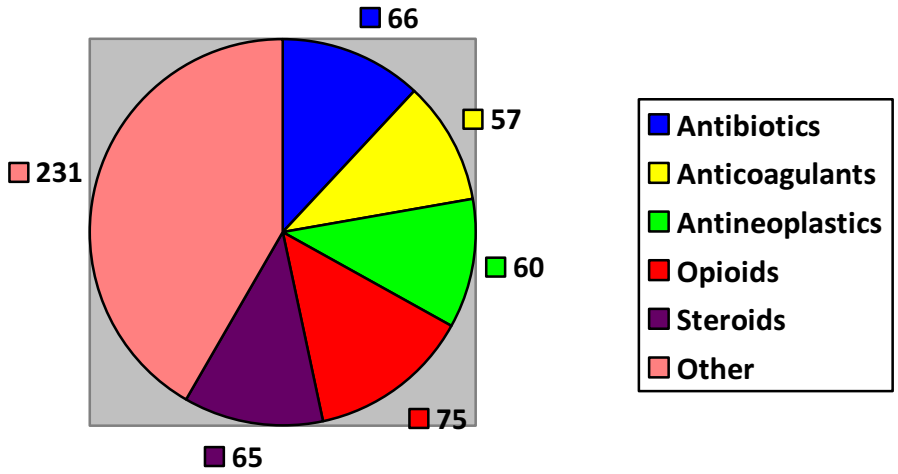
Category 3 to discuss: 86 yo male who developed conjunctivitis symptoms, then developed a desquamating, full body rash. He was followed initially by an ophthalmologist who expressed concern for Stevens-Johnson reaction, who then referred him to primary care for further evaluation. He was immediately admitted and seen by ID. It was felt the etiology for the allergic reaction of this type was possibly due to Bumex, which was a recent addition to his medicine list. He had a prior reaction to hydrochlorothiazide, so perhaps the sulfa moiety in the Bumex led to the SJS reaction. Supportive care was initiated. Two days after being admitted, the patient had an apparent ventricular fibrillation arrest. He received full ACLS protocol intervention, including intubation. Lab data revealed significant acidosis. Despite all efforts, the patient expired. It was felt that his cardiac event was probably triggered by the stress of the SJS reaction.

Inpatient ADRs



Antibiotics: Vancomycin was most common---AKI. Others included rash, nausea, and diarrhea.
Anticoagulants: Heparin and Warfarin were most common---nose bleed and hematuria.
Narcotics: Reactions included confusion, nausea, constipation, and respiratory distress. One patient was transferred to a higher level of care.
Steroids: Hyperglycemia.

Total ADRs



Antibiotics: Multiple medications, but Bactrim most common—AKI, swelling, rash, nausea
Anticoagulants: Warfarin, Plavix, Xarelto, ASA—Various bleeds
Chemo: Neutropenia, nausea, vomiting, dehydration
Narcotics: Constipation, rash, nausea
Steroids: Hyperglycemia

Exparel (liposomal bupivacaine)

Preliminary data - orthopedics

Surgeon	Proced	Group	Data	Total
HARTLEY	TKA	Control	Average Pain 1st 24 hrs	5.5
			Average Pain 2nd 24 hrs	4.0
			Average Pain 3rd 24 hrs	4.2
			Average Pain at 48 hrs	4.7
			Average Pain at 72 hrs	5.0
			Average Total Morphine Eqv (mg)	274.6
			Count of Procedure	22
			Average of Length of stay (midnights)	2.3
			Average of Length of stay (hours)	57.4
			Average Morphine Eqv per Hour (mg/hr)	4.8
		Exparel	Average Pain 1st 24 hrs	4.9
			Average Pain 2nd 24 hrs	3.7
			Average Pain 3rd 24 hrs	3.5
			Average Pain at 48 hrs	4.3
			Average Pain at 72 hrs	4.3
			Average Total Morphine Eqv (mg)	178.0
			Count of Procedure	28
			Average of Length of stay (midnights)	2.4
			Average of Length of stay (hours)	59.4
			Average Morphine Eqv per Hour (mg/hr)	3.0
		Naropin Cocktail	Average Pain 1st 24 hrs	3.8
			Average Pain 2nd 24 hrs	3.6
			Average Pain 3rd 24 hrs	5.7
			Average Pain at 48 hrs	3.7
			Average Pain at 72 hrs	4.5
			Average Total Morphine Eqv (mg)	171.5
			Count of Procedure	11
			Average of Length of stay (midnights)	2.2
			Average of Length of stay (hours)	53.9
			Average Morphine Eqv per Hour (mg/hr)	3.2
BALLARD	TKA	OnQ Pump	Average Pain 1st 24 hrs	4.4
			Average Pain 2nd 24 hrs	5.0
			Average Pain 3rd 24 hrs	5.5
			Average Pain at 48 hrs	4.7
			Average Pain at 72 hrs	5.0
			Average Total Morphine Eqv (mg)	237.4
			Count of Procedure	24
			Average of Length of stay (midnights)	2.3
			Average of Length of stay (hours)	56.5
			Average Morphine Eqv per Hour (mg/hr)	4.1
		Exparel	Average Pain 1st 24 hrs	4.1
			Average Pain 2nd 24 hrs	3.7
			Average Pain 3rd 24 hrs	3.5
			Average Pain at 48 hrs	3.8
			Average Pain at 72 hrs	3.7
			Average Total Morphine Eqv (mg)	157.0
			Count of Procedure	23
			Average of Length of stay (midnights)	2.3
			Average of Length of stay (hours)	56.3
			Average Morphine Eqv per Hour (mg/hr)	3.0

Look Alike/Sound Alike Drug List 2015

Drug Name	Drug Name	Potential Errors	Prevention Strategies
CeleBREX®	CeleXA® and CereBYX®	Similar names	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
cloniDINE	KlonoPIN®	Similar names	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
DOXOrubicin *Liposomal*	DOXOrubicin *Conventional* and DAUNOrubicin	Similar names	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
hydrOXYzine	hydrALAzine	Similar names	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
Keppra®	Ketamine®	Similar names	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR 5. Witness required
metroNIDAZOLE	metFORMIN	Similar names and strengths	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
MuciNEX®	MucoMYST®	Similar names	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
NovoLIN 70/30	NovoLOG MIX 70/30	Similar names and strengths	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR 5. Witness required
oxyCODONE controlled-release	oxyCODONE immediate-release	Similar names	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
Plavix®	Pradaxa®	Similar names and strengths	1. Pyxis pop-up warning. 2. Do NOT store next to each other. 3. Name alert on MAR
PrednisoLONE	predniSONE	Similar names and strengths	1. Tall man lettering in Pyxis &Meditech 2. Pyxis pop-up warning. 3. Do NOT store next to each other. 4. Name alert on MAR
Wellbutrin SR®	Wellbutrin XL®	Similar names	1. Pyxis pop-up warning. 2. Do NOT store next to each other. 3. Name alert on MAR

POLICY

POLICY

Title: **APPROVED DIET MANUAL**		
	Page 1 of 2	
Policy Number: PC- 07021	***Date Last Revised:*** 2/15	***Valid Until:*** 2/18
Department(s) Affected: Nutrition Services, Nursing, Medical Staff, Center for Cancer Support, Diabetes and Nutrition Center	***Review Period:*** every 3 years	

OUTCOME:

The Academy of Nutrition and Dietetics Nutrition Care Manual is the approved diet manual and will serve as the reference tool to provide standardization of nomenclature in ordering diets, and to ensure consistency in communicating and standardizing nutritional care and education. The Sodexo Hospital Diet Manual will be used as a supplement for menu planning purposes.

DEFINITIONS:

AND	Academy of Nutrition and Dietetics
NCM	Nutrition Care Manual
P&T	Pharmacy and Therapeutics Committee

POLICY:

The AND Nutrition Care Manual will be:

1. Reviewed annually and revised accordingly by the AND.

2. Approved by the Pharmacy and Therapeutics (P&T) Committee (at least every three years). Annual revisions/additions must also be approved by the P & T Committee, as evidence by appropriate signatures.

3. Approved by the medical staff and signed by the current Chief of Medical Staff.

4. Accessible via the Intranet to serve as a guide and reference for the health care team.

A printed copy of the approved NCM (meal plans) is located in the Memorial and Memorial Hixson Nutrition Services Diet Office, and Nursing Administration.

A CD-ROM Version of the approved NCM will is located in the Memorial Nutrition Services Diet Office.

Diets provided by the Nutrition Services department will be in accordance with the standards of nutritional care as outlined in the manual. The manual will be used as a guide in menu /meal preparation to assure meeting nutritional requirements.

NOTE: Several reference medical nutrition manuals from professional organizations are kept as references in the Nutrition Services Department for unusual dietary restrictions/conditions.

1. The A.S.P.E.N. Nutrition Support Core Curriculum
   A case-based Approach- the Adult Patient-Second Edition 2007
   Michele M. Gottschlich, PhD, RD. CNSD

2. Nutrition Diagnosis and Intervention 3rd Edition
   Standardized Language for the Nutrition Care Process
   2011 Edition ADA

3. Pocket Guide for International Dietetics and Nutrition Terminology (IDNT)
   Standardized Language for the Nutrition Care Process
   Reference Manual- First Edition ADA- 2008

4. A manual of Laboratory and Diagnostic Tests
   7 edition Lippincott Williams & Wilkins 2004
   Frances Talaska Fischback, RN, BSN, MSN

Key Contact: Brian Kyle Jones MS, RD, LDN - CNM, Dori Neufeld, RD, Lester Poe, Manager
Approved/Reviewed by: Diona Brown, Chief Nurse Executive; Nursing Practice Council
Joint Commission Standard: Provision of Care Chapter (PC)
Attachment(s): AND Nutrition Care Manual Exception Sheet
Date First Effective/Revisions: 1/89, (4/09) (2/13)
Distribution: MHCS Intranet

AND Nutrition Care Manual Exception Sheet

For Memorial Healthcare System-Memorial Hospital

1. Foods allowed on the **low sodium diet** may be calculated into patient's daily allowance of sodium if the total does not exceed the prescribed level of sodium.

2. The amount of fiber in the **low residue diet** will be kept <15 grams of fiber per day. Selected vegetables with > 1.5 grams of fiber may be included in the low residue diet if the daily total of fiber is not exceeded.

3. Information from the Diabetes and Nutrition Center may be used in addition to what AND Nutrition Care Manual provides for **diabetic diets**.

4. Sodexo Health Care Services' "**Feed your Body of Knowledge**" education handouts may be used for patient education.

5. **GI soft diet & education material** is approved by Memorial Hospital's Pharmacy and Therapeutics Committee (Feb/March 2009) for use in patient care/education.

6. **Chyle diet & education material** is approved by Memorial Hospital's Pharmacy and Therapeutics Committee (Feb 2010) for use in patient care/education.

7. Nutritional supplements such as Ensure and Glucerna will be added to Full Liquid and Full Liquid gastric Bypass diets to increase nutrient density.

8. Any oral supplements will be provided to patients as compliant to prescribed diet orders if documented oral intake is less than 50% and or per RD's recommendation to meet estimated needs and goals.

9. For purposes of hospital menu planning, diet order interpretation and Partnership for Healthy America compliance, the Sodexo Hospital Diet Manual will be utilized. A hard copy of this manual is on file in the Glenwood and Hixson diet office.