Pharmacy & Therapeutics Committee Meeting
Private Dining Room
June 13, 2013 7:00 a.m.

Agenda Items	Individual Responsible
1. Call to Order	Richard Pesce, MD
2. Approval of February, 2013 Minutes	Richard Pesce, MD
3. Therapeutic Interchanges and Formulary Decisions	Page
A. Invokana® (canagliflozin)	John Jantz, Pharm.D……..5-7
B. Mesalamine formulary review	Patrick Ellis, Pharm.D……..8-9
C. Topical Anti-virals Formulary Review	10-11
D. Neupro® (rotigotine)….	John Jantz, Pharm.D……..12
E. Viibryd® (vilazodone)	..13-14
F. Anti-fibrinolytics – Orthopedic surgery	Patrick Ellis, Pharm.D.....…..…
4. Medication Safety	
A. Promethazine IV – infusion site reactions	Beena Anchanattu, RN…15-16
B. ADR reveiw	Patrick Ellis, Pharm.D.....17-18
C. Antithrombotic Reversal/Surgical Mgt Recommendations	Patrick Ellis, Pharm.D.....…..19
5. MUE	
A. Procalcitonin – antimicrobial use reduction	John Jantz, Pharm.D.....20-23
6. Policy, Procedure & Protocols	
A. Prothrombin Complex Concentrate – warfarin reversal… ..	Patrick Ellis, Pharm.D…....24
B. Renal Dosing Adjustments Policy	……25
C. Pharmacist Ordering of Lab Values..	…...26
7. Adjournment	

Next Meeting will be August 8, 2013 at 7:00am in the Private Dining Room

CATHOLIC HEALTH INITIATIVES

Memorial Health Care System

PHARMACY AND THERAPEUTICS COMMITTEE

DATE: February 14, 2013 CALLED TO ORDER: 7:00 A.M.
LOCATION: Private Dining Room ADJOURNED: 7:56 A.M.

Members Present:		**Members Absent**:		**Guests**:
Richard Pesce, M.D.	Karen Babb, Pharm.D.	Nathan Chamberlain, M.D.	Keith Lockwitz, RN	John Jantz, Pharm.D.
Mark Anderson, M.D.	Brian Jones, RD, LDN	John L. Gwin, Jr., M.D.	Scott Madaris, RN	Ali Roberts, Pharm.D.
Allen Atchley, M.D.	Patrick Ellis, Pharm.D.	Tareck Kadrie, M.D	Deb Moore, RN, SVP	Teresa Bledsoe, Risk Mgmt.
Samuel Currin, M.D.	Patrick Hagan, Finance	Robert Mynatt, M.D.	Nan Payne, RN	Amanda Tolbert, CPT
David Dodson, M.D.	Lila Heet, Pharm.D.	Diona Brown, RN,C.N.O.	Melissa Roden, RN	Blake Carver, Student
William Oellerich, M.D.	Jane Raulston, RN	Vickie Burger, Lab	Beverly Slate, Supply Chain	
Nathan Schatzman, M.D.	Sandy Vredeveld, DPh	Gwen Davis, RN	Elvie Smith, RN	
Michael Stipanov, M.D		Don Jones, RPh	Hannah Walker, RN	

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 December 13, 2012 minutes were approved as submitted.		Complete
Old Business	**Samsca® (Tolvaptan)** - The previous MUE was again discussed and Dr. Atchley made a recommendation to further restrict Samsca to patients with serum sodium of < 130 mmol/L to prevent inappropriate usage.	Approved	Complete
Therapeutic Interchanges and Formulary Decisions	The following medications were reviewed: 1. **Exparel® (bupivacaine iposomal)** – Liposomal formulation of bupivacaine. Recommended to approve for trial use as intercostal nerve block s/p thoracic surgery for Dr. Headrick and Dr. Zellner. Committee again recommended to not add to formulary for incisional use at this time. 2. **Eliquis® (apixaban) –** Oral Xa inhibitor used for stroke prevention in patients with non-valvular atrial fibrillation. Recommended to add to formulary. 3. **Linzess® (linaclotide)** – New treatment for irritable bowel syndrome with constipation and for the treatment of chronic idiopathic constipation. Requested by gastroenterology due to unique mechanism of action and ability to be given via tube. Recommended to add to formulary. 4. **Kyprolis® (carfilzomib)** – Used in the treatment of refractory multiple myeloma. Recommended to add to formulary. 5. **Proton Pump Inhibitor (PPI) formulary** – Gastroenterology requested an additional PPI be added to formulary for patients intolerant of the current formulary PPI (pantoprazole). Lansoprazole recommended to be added to formulary for this purpose. 6. **Azithromycin® 5 Day Automatic Stop Proposal** – Due to the long half-life of azithromycin, the antimicrobial stewardship committee recommended that an automatic 5 day stop date policy for azithromycin when used for treatment of acute respiratory infection. 7. **Prothrombin Complex Concentrate (PCC) –** The committee discussed the possible	1. Approved for trial 2. Approved 3. Approved 4. Approved 5. Approved 6. Approved 7. Information	Pending Complete Complete Complete Complete Pending

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	use of PCC for patients with severe life threatening bleeding associated with warfarin. It was recommended that pharmacy develop use guidelines to prevent the inappropriate use of PCC when needed for warfarin reversal. Patrick will work with Dr. Dodson and provide education to the hospitalists once the protocol is developed.		
Medication Safety	• **APAP content-combination prescription products –** Recent reviews of inpatient APAP use have shown that patients are at times receiving an excess of 4 grams of APAP per day which is often due to receiving multiple doses of various APAP containing products. It was recommended to now only dispense hydrocodone and other APAP combination products containing 325 mg of APAP per dosage unit to minimize the risk of exceeding recommended daily maximum doses of APAP. All order sets would be adjusted to reflect this change and orders for 500 mg containing products will be converted to the comparable 325 mg APAP product (example: hydrocodone 5/500 → hydrocodone 5/325). • **Promethzaine IV –** The IV team has reported an increased incidence of phlebitis associated with IV promethazine administration and an increased placement of PICC lines to accommodate IV promethazine use. It was recommended to have the IV team collect data on promethazine associated phlebitis and to re-educate nursing on proper dilution and administration of promethazine prior to IV administration. This will be re-discussed again once more data is available to better quantify the scope of the problem.	Information Information	Complete
Medication Use Evaluation	• **Levemir® (insulin detemir) –** An MUE was conducted to determine how the formulary change from Lantus (insulin glargine) to Levemir (insulin detemir) impacted blood glucose control at MHCS. The evaluation demonstrated that blood glucose control was similar between the agents and that Levemir is an appropriate formulary substitution for Lantus. • **Vancomycin –** An MUE was conducted to evaluate elevated Vancomycin trough results to assess our current Vancomycin dosing strategy and identify any potential patient population that could benefit from changing our dosing strategy. The evaluation demonstrated that the current guideline recommendation to utilize total body weight appears to over-estimate a patient's Vancomycin clearance as evidenced by a higher proportion of obese patients developing troughs in excess of 20 mg/dl. Based on this information, pharmacy will modify their dosing strategy to utilize an adjusted body weight for all patients when dosing Vancomycin.	Information Information	Complete
Policy and Procedure	• **Alcohol Withdrawal Management Protocol –** A draft version of the Alcohol Withdrawal Management Protocol was presented for review and possible additions/edits. Dr. Atchley recommended changing the PRN beta-blocker to labetalol based on better data for this patient population. • **Med Administration – Timeliness of Scheduled Medications –** This policy was created to differentiate between time critical versus non-time critical medications as required by CMS. • **Blood Glucose Control with TPN –** It was recommended to modify the current *TPN Initiation Orders* to allow pharmacists the ability to increase or decrease the	Approved Approved Approved	Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	subcutaneous correction insulin dose to the next appropriate level based on the patient's blood glucose values to achieve better glycemic control while on TPN.		
Pharmacy Clinical Dashboard	Patrick reviewed.	Information	Complete
Nutrition Support Team	**ProSource No-Carb –** A modification to the protein supplement formulary was presented to allow the use of an alternative protein supplement product in place of the current supplement (Pro-Stat 64).	Approved	Complete

There being no further business, the meeting was adjourned at 7:59 A.M. The next P&T meeting is April 4, 2013.

Respectfully submitted,

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

Approved by,

Richard Pesce, M.D. Chairman

SUMMARY REVIEW

GENERIC NAME: CANAGLIFLOZIN

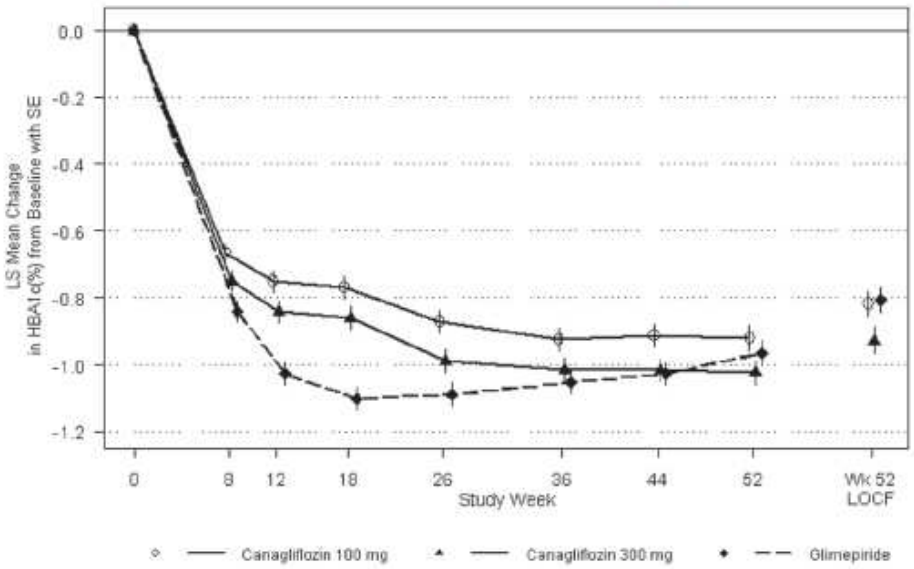
PROPRIETARY NAME: Invokana™ (Janssen)

INDICATIONS:
Canagliflozin was approved by the FDA in March 2013 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus as monotherapy or as part of a combination regimen.

CLINICAL PHARMACOLOGY:
Canagliflozin is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. SGLT2, expressed in the proximal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. By inhibiting SGLT2, canagliflozin reduces reabsorption of filtered glucose and thereby increases urinary glucose excretion.

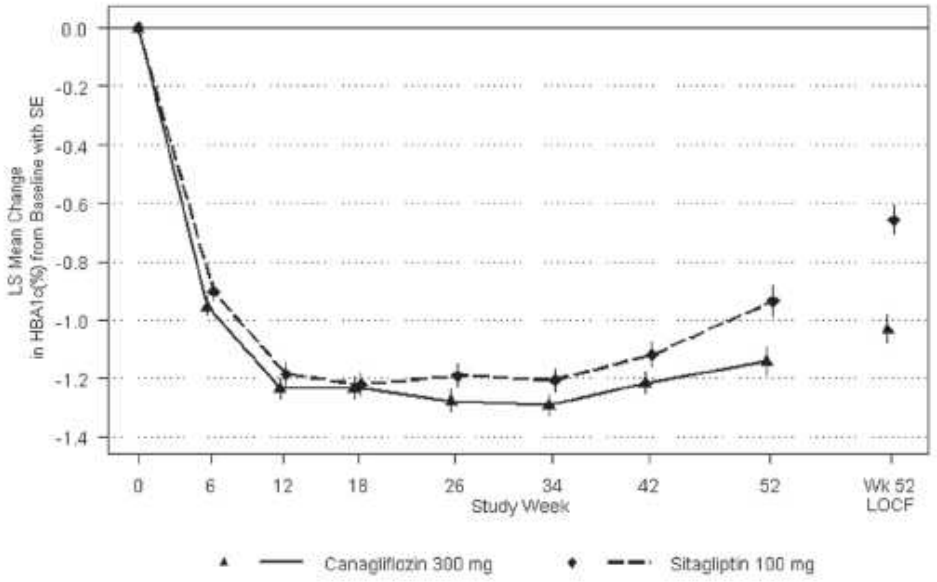
COMPARATIVE EFFICACY:
The efficacy of canagliflozin has been compared to glimepiride and sitagliptin in clinical trials. In a 52 week, double-blind, active controlled study canagliflozin plus metformin was compared to glimepiride plus metformin in patients inadequately controlled on metformin monotherapy. The primary efficacy endpoint was reduction in HbA1C and the trial concluded canagliflozin 100mg and 300mg plus metformin was non-inferior to glimepiride plus metformin.

Figure 1: Mean HbA1C Change at Each Time Point (Completers) and at Week 52 Using Last Observation Carried Forward (mITT Population)



In another 52 week, double-blind, active controlled study compared the efficacy and safety of canagliflozin 300mg vs. sitagliptin 100mg in combination with metformin and sulfonylurea. The primary efficacy endpoint was reduction in HbA1C and the trial concluded canagliflozin 300mg plus metformin and sulfonylurea was non-inferior to sitagliptin plus metformin and sulfonylurea.

Figure 2: Mean HbA1C Change at Each Time Point (Completers) and at Week 52 Using Last Observation Carried Forward (mITT Population)



PHARMACOKINETICS:

Absorption	T_{max}: 1-2 hours Oral bioavailability: 65% Co-administration with a high-fat meal had no effect on the pharmacokinetics
Distribution	V_d 119 L Extensive tissue distribution 99% protein bound in plasma, primarily to albumin Protein binding is independent of plasma concentration
Metabolism	Mainly metabolized by by O-glucuronidation, primarily by UGT1A9 and UGT2B4 Approximately 7% is metabolized by CYP3A4 Canagliflozin is a substrate and weak inhibitor of P-glycoprotein (P-gp)
Elimination	Excreted unchanged in feces (41.5%); feces metabolites (10.2%) & urine metabolites (31%) Renal clearance: 1.3 – 1.55 mL/min Elimination $t_{1/2}$: 10.6 hr for the 100mg dose and 13.1 hr for the 300mg dose

ADVERSE REACTIONS:

Most common adverse effects (>2%) *of four 26-week placebo controlled trials*

Female genital mycotic infections (10.4-11.4%), urinary tract infections (4.3-5.9%), increased urination (4.6-5.3%), male genital mycotic infections (3.7-4.2%), vulvovaginal pruritis (1.6-3.0%), thirst (2.3-2.8%), constipation (1.8-2.3%), nausea (2.2-2.3%).

Canagliflozin is an osmotic diuretic, which may lead to reductions in intravascular volume. In clinical studies, canagliflozin was associated with a dose-dependent increase in the incidence of volume depletion related adverse events (i.e. hypotension). The three factors other than dose associated with the largest increase in adverse reactions were the use of loop diuretics, moderate renal impairment (eGFR 30-60 ml/min/1.73m², and age greater than 75.

In the pool of eight clinical trials with a longer mean duration of exposure (68 weeks), the incidence rate of bone fracture was 14.2, 18.7, and 17.6 per 1000 patient years of exposure to comparator, Invokana 100mg, and Invokana 300mg, respectively.

CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS:
Contraindications:

- Severe renal impairment, ESRD, or on dialysis

Warnings and Precautions:

- Hypotension
- Impairment in renal function
- Hyperkalemia
- Hypoglycemia with concomitant use with insulin and insulin secretagogues
- Genital mycotic infections
- Hypersensitivity reactions
- Increases in LDL
- Macrovascular outcomes

DRUG INTERACTIONS:

	Severity	**Mechanism**	**Effect**
Digoxin	Major	Unknown (P-gp mediated)	Increase digoxin exposure
Rifampin	Major	Induction of UGT-mediated canagliflozin metabolism	Decreased canagliflozin exposure
Phenytoin	Major	Induction of UGT-mediated canagliflozin metabolism	Decreased canagliflozin exposure
Fosphenytoin	Major	Induction of UGT-mediated canagliflozin metabolism	Decreased canagliflozin exposure
Phenobarbital	Major	Induction of UGT-mediated canagliflozin metabolism	Decreased canagliflozin exposure
Ritonavir	Major	Induction of UGT-mediated canagliflozin metabolism	Decreased canagliflozin exposure

DOSING:
Assess renal function prior to initiating canagliflozin. Do not initiate therapy if eGFR is below 45mL/min/1.73m². In addition, if eGFR falls below 45 treatment should be discontinued.

The recommended starting dose is 100mg once daily, taken before the first meal of the day.

The dose may be increased to 300mg once daily in patients tolerating 100mg once daily who have an eGFR of 60 or greater and require additional glycemic control.

Canagliflozin is limited to 100mg once daily in patients who have an eGFR from 45 – 60.

PRODUCT AVAILABILITY and COST:

	30 day supply	**Cost per dose**
Invokana 100mg & 300mg	**$263.10**	**$8.77**
Januvia 100mg	**$235.50**	**$7.85**

CONCLUSION:
It is recommended to add Invokana (canagliflozin) to formulary based on the unique mechanism of action and comparable effectiveness to currently available agents. This will allow patients admitted to Memorial Hospital that have been started on Invokana as an outpatient to continue therapy during their hospitalization thus improving continuity of care. Canagliflozin use in patients with in-dwelling foley catheters should be monitored closely due to the potential increase in urinary tract infections. Additionally, patients undergoing aggressive diuresis with loop diuretics will need to be monitored closely for potential volume depletion related adverse events (hypotension) due to increased urination caused by canagliflozin.

FORMULARY REVIEW

DELAYED RELEASE MESALAMINE

CURRENT FORMULARY AGENTS: In 2010 this class was reviewed and at that time it was decided to only stock *Asacol* and *Pentasa* on formulary and a therapeutic interchange would be utilized to interchange *Apriso* and *Lialda* to conventional *Asacol*. Since this decision, the conventional formulation of *Asacol* is no longer available and has been replaced by a new brand name product (*Delzicol*) and a new higher dose *Asacol* product (*Asacol HD*) which is also now available.

AMINOSALICYLATES: The active moiety of all the aminosalicylates used to treat inflammatory bowel disease is 5-aminosalicylate (5-ASA), also called mesalamine.

MECHANISMS OF ACTION: The anti-inflammatory effects of 5-ASA are probably due to inhibition of leukotriene production, anti-prostaglandin and antioxidant effects, and inhibition of other inflammatory pathways. Also, 5-ASA activates a colonocyte differentiation factor and has other anti-proliferative effects that may protect against development of colon cancer, which occurs at a higher incidence in patients with ulcerative colitis.

FORMULATIONS: Oral mesalamine is mostly absorbed in the small intestine and does not reach the colon. *Asacol HD* tablets and *Delzicol* are coated with a pH-sensitive film that disintegrates and releases the drug at the higher pH of the terminal ileum and proximal colon. *Pentasa* is an ethylcellulose-coated formulation that releases mesalamine gradually throughout the gastrointestinal tract. *Lialda* and *Apriso* both delay the release of the drug until it reaches the distal ileum and colon. Mesalamine is also available as an enema (*Rowasa*, and others) and as a rectal suppository *(Canasa)*.

In advance of the *Asacol* patent expiration, the drug company has now stopped producing conventional *Asacol* and replaced this product with two newer branded products (*Delzicol* and *Asacol HD*). *Delzicol* is available in the same 400 mg dosage strength as the previous *Asacol* formulation and possesses very similar release mechanisms as conventional *Asacol*. *Asacol HD* is a longer acting mesalamine product that has a longer half life that helps reduce the daily pill burden for patients requiring maintenance mesalamine therapy.

EFFICACY: In the clinical trials that led to their approval by the FDA, aminosalicylates generally achieved remission in about 35-50% of patients with mild or moderate ulcerative colitis and maintained the remission for 6 months or more in about 55-75%. In distal ulcerative colitis, mesalamine suppositories or enemas may be more effective than oral formulations. In Crohn's disease, 5-ASA drugs are only modestly more effective than placebo, and those that are released in the colon are ineffective for ileal Crohn's disease.

ADVERSE EFFECTS: The most common adverse effects of mesalamine have been nausea, vomiting, diarrhea, headache and abdominal pain. Nephrotoxicity can occur. A lupus-like syndrome, pancreatitis and hepatotoxicity have been reported.

DRUG INTERACTIONS: Mesalamine inhibits thiopurine methyltransferase and may decrease the metabolism of azathioprine and mercaptopurine, which theoretically could also increase their myelotoxicity, but seldom does except in patients with an inherited deficiency of thiopurine methyltransferase. Extended- and delayed-release mesalamine formulations with pH-sensitive coatings *(Asacol HD, Lialda, Apriso, Delzicol)* should not be co-administered with antacids, which might cause premature dissolution of the drug coating. Theoretically, a similar interaction could occur with proton-pump inhibitors (PPIs) such as omeprazole (*Prilosec*, and others) or H2-receptor antagonists such as ranitidine (*Zantac*, and others).

PRODUCT COMPARISON

Indication	*AsacolHD*	*Lialda*	*Pentasa*	*Apriso*	*Delzicol*
Induction of remission: active, mild to moderate ulcerative colitis	X	X	X		X
Maintenance of remission of ulcerative colitis		X	X	X	X

Site of Absorption for Various Oral Mesalamine Products				
Generic Name	Brand Name	Formulation	Active or Prodrug	Target Site of Release
Mesalamine	*Asacol HD*	Tablet	Active	Terminal ileum and colon
Mesalamine	*Lialda*	Tablet	Active	Colon
Mesalamine	*Pentasa*	Capsule	Active	Duodenum, jejunum, ileum, and colon
Mesalamine	*Apriso*	Capsule	Active	Colon
Mesalamine	*Delzicol*	Capsule	Active	Terminal ileum and colon

Comparison of the Recommended Dosing of the Oral Mesalamine Products		
Drug	Product Strength	Recommended Dosing
Asacol HD	800 mg tablets	Induction: 1.6 g three times daily for 6 weeks
Lialda	1.2 g tablets	Induction: 2.4 to 4.8 grams once daily for 8 weeks Maintenance: 2.4 g daily
Pentasa	250 and 500 mg capsules	Induction: 1 g 4 times daily Maintenance: 1 g 4 times daily
Apriso	375 mg capsules	Maintenance (ulcerative colitis): 1.5 g daily
Delzicol	400 mg capsules	Induction: 800 mg three times daily for 6 weeks Maintenance: 400 mg four times daily

SUMMARY: Each of the above mentioned products are delayed release mesalamine products designed to release the mesalamine at varying locations within the GI tract. *Asacol HD, Lialda, Delzicol,* and *Apriso* are each designed to be released primarily within the colon for either the induction (*Asacol HD, Delzicol, Lialda*) or maintenance (*Lialda, Apriso, Delzicol*) treatment of ulcerative colitits. *Pentasa* is designed to be released throughout the GI tract which is more useful for the treatment of Crohn's disease with more diffuse GI involvement. No significant pricing difference between the products exists as they are all priced within $0.50 of each other when using a price per 400 mg unit.

Based on the changes to the currently available products, it is recommended to modify the current formulary for these agents. This was also discussed with the gastrointestinal specialists and the below are the recommendations for this class of medications:

- **Add *Lialda* to formulary** due to advantage of once daily dosing
- **Add *Delzicol* to formulary** as replacement product for Asacol
- **Substitute *Delzicol* for *Apriso*** orders (*Apriso* 375 mg → *Delzicol* 400 mg)
- ***Pentasa* will remain on formulary**
- **Do not add *Asacol HD*** at this time per GI recommendati

Formulary Review
Topical Antivirals

Agent	MOA	Supply	Indication	Dosing	Price	Considerations
Abreva (docosanol) **OTC** **Manufacturer** GSK	classified as a behenyl alcohol - not virucidal	10% Topical Cream (2 gm)	treatment of herpes labialis due to either HSV-1 or HSV-2	Apply to affected areas 5 times daily until healed (maximum 10 days)	**2 G tube** $14.91	Not considered a true antiviral, shown to have activity against acyclovir-resistant HSV. Study found that docosanol as early treatment showed mean reduction of healing time by 18 hours compared to placebo.[3]
Denavir (penciclovir) **Rx Only** **Manufacturer** New American Therapeutics	inhibits viral DNA synthesis – must be activated intracellularly initially by thymidine kinase - retained *in vitro* inside HSV infected cells for 10-20 hours, compared with 0.7-1 hour for acyclovir	1% Topical Cream (1.5 gm, 5 gm)	treatment of recurrent herpes labialis or herpes facialis due to either HSV-1 or HSV-2	Apply cream at the first sign or symptom of cold sore (eg, tingling, swelling); apply every 2 hours during waking hours for 4 days.	**5 G tube** $311.15	Formulated with propylene glycol. Active metabolite of famciclovir (oral). If initiated within 1 hour of the signs or symptoms of herpes labialis, mean lesion duration is about 0.7-1 day shorter than without treatment.[1]
Zovirax (acyclovir) **Rx Only** **Manufacturer** Valeant	inhibits viral DNA synthesis – must be activated intracellularly initially by thymidine kinase	5% Topical Cream (5 gm) 5% Topical Ointment (30 gm)	treatment of herpes labialis, herpes fibrilis, or herpes genitalis (ointment) caused by HSV-1 or HSV-2	**Cream:** apply to affected area times 5 times daily for 4 days. **Ointment:** apply sufficient quantity to cover lesions every 3 hours, 6 x day for 7 days; initiate at the first sign of symptoms or lesions.	**Zovirax 5% Cream 5 G tube** $451.58 **Zovirax 5% Ointment 30 G tube** $708.80	Cream is formulated with propylene glycol. The most common mechanism of resistance is loss of thymidine kinase activity (cross-resistance with penciclovir but not docosanal). Cream has been shown to reduce lesion healing time by 0.5–0.6 days and the duration of pain by 0.3–0.4 days.[2]

1. Spruance SL, Rea TL, Thoming C, et al. Penciclovir cream for the treatment of herpes simplex labialis. JAMA 1997;277:1374-9.
2. Spruance SL, Nett R, Marbury T, et al. Acyclovir cream for treatment of herpes simplex labialis: results of two randomized, double-blind, vehicle-controlled, multicenter clinical trials. Antimicrob Agents Chemother 46(7):2238–43 (2002 Jul).
3. Habbema L, DeBoulle D, Roders GA, et al. N-Docosanol 10% cream in the treatment of recurrent herpes labialis: A randomized, double-blind, placebo-controlled study. Acta Derm Venereol 1996;76:479-481.

Cost Comparison and Utilization:

Current Formulary Topical Antiviral:	**12-Month Usage:**	**12-Month Expenditure:**
Zovirax (acyclovir) 5% Cream 5 G tube	17 units of 5 gm tube	$7,676.86
Zovirax (acyclovir) 5% Ointment	4 units of 30 gm tube	$2,835.20
		$10,512.06 – total Zovirax expenditures
Alternate Options:	**Comparable Expenditure:**	**Possible Savings:**
Abreva (docosanol) 10% Cream 2 G tube	$313.11	$10,198.95
Denavir (penciclovir) 1% Cream 5 G tube	$6,534.15	$3,977.91

Clinical Trials:
There are no published head to head trials comparing docosanol, acyclovir, and penciclovir in the treatment of herpes labialis.

Zovirax vs. Denavir –
A randomized, double-blind, active comparator study enrolling 248 patients with a diagnosis of herpes simplex facialis/labialis compared penciclovir 1% cream and acyclovir 3% cream. 68 patients were evaluated before treatment and on days three, five, and seven of treatment. No severe adverse events were recorded in either treatment group. There were no significant differences in the efficacy endpoint or cure rate between groups, but a trend towards a shorter time to resolution of all symptoms, cessation of new blisters, and loss of crust was seen with the penciclovir group. In addition, the clinical scores in penciclovir treated patients were significantly lower than those in the acyclovir group on days five and seven. The study used acyclovir cream at a lower strength than the currently available US formulation.

Denavir vs. placebo –
Two randomized, double-blind, parallel group studies were performed with 3,057 patients of which 83% developed clinical lesions. Patients were given either penciclovir 1% cream or placebo for the treatment of recurrent herpes simplex labialis defined as three or more episodes a year that typically manifested as classical lesions. 72 patients self-initiated treatment within one hour of noticing the first signs and symptoms of a recurrence and were required to apply medication six times per day for the first day and every two hours while awake for four consecutive days. The penciclovir group lost lesions 31% faster than the placebo-treated group and experienced 28% faster resolution of lesion pain.

Abreva vs. placebo –
Two identical multicenter, double-blind, placebo-controlled studies were performed with 737 patients who were given either docosanol 10% cream or placebo for the treatment of herpes simplex labialis in the prodrome or erythema stage. 73 patients were treated five times daily until healing occurred (i.e., the crust fell off spontaneously or there was no longer evidence of an active lesion). The median time to healing in the docosanol-treated group was 4.1 days, 18 hours shorter than that of the placebo-treated group. The docosanol group also exhibited reduced times from treatment initiation to cessation of pain and all other symptoms, complete healing of lesion, and cessation of the ulcer or soft crust stage of the lesion. Aborted episodes were experienced by 40% of docosanol patients and 34% of placebo patients. Adverse events with docosanol were mild and similar to those with placebo. The study concluded that docosanol applied five times per day is safe and effective in the treatment of recurrent herpes simplex labialis.

Recommendation:
Based on the current Zovirax usage of 21 units per year, substituting Abreva for each dose of Zovirax would result in a cost savings of $10,198.95/year. **It is the recommendation to use Abreva as the formulary-approved topical antiviral. Although it is not virucidal, Abreva is FDA approved for the same indication as Zovirax - treatment of herpes labialis due to either HSV-1 or HSV-2. Additionally, Abreva offers coverage against acyclovir-resistant HSV, unlike Denavir. Efficacy is comparable among the three agents based on current available literature.**

FORMULARY REVIEW

GENERIC NAME: ROTIGOTINE TRANSDERMAL SYSTEM

PROPRIETARY NAME: *Neupro* (Schwarz)

INDICATIONS: Rotigotine is indicated for the treatment of the signs and symptoms of early-stage and advanced stage idiopathic Parkinson's disease. Rotigotine is also indicated for the treatment of Restless Legs Syndrome (RLS).

CLINICAL PHARMACOLOGY: Rotigotine is a non-ergoline dopamine receptor agonist with activity at the D1, D2, and D3 receptors. Rotigotine is formulated in a matrix-type transdermal patch that provides continuous delivery of rotigotine over 24 hours.

PHARMACOKINETICS: Rotigotine has poor oral bioavailability because of extensive first-pass metabolism via glucuronidation in the gut wall and liver; therefore, the transdermal delivery system is optimal. Following transdermal administration, rotigotine plasma concentrations are detectable in the systemic circulation within 2 to 3 hours after patch application, and peak concentrations are achieved between 15 and 18 hours after application.

ADVERSE REACTIONS: Adverse reactions reported with rotigotine have included nausea, application-site reactions, dizziness, somnolence, insomnia, headache, vomiting, and fatigue. Adverse reactions occur most frequently during the titration phase, declining in frequency during maintenance therapy.

DRUG INTERACTIONS: Rotigotine is neither an inhibitor nor inducer of CYP-450 isozymes 1A2, 2C9, 2C19, or 3A4. It has a low potential to inhibit CYP 2D6 at therapeutic concentrations.

DOSING: Therapy with transdermal rotigotine should be initiated at 2 mg/24 hours for early stage PD and 4 mg/24 hours for advanced stage disease. Based on individual patient response and tolerability, the dose may be increased weekly by 2 mg/24 hours. The lowest effective dose in clinical trials was 4 mg/24 hours. The highest recommended dose is 6 mg/24 hours for early stage and 8 mg/24 hours for advanced stage disease. Doses more than 8 mg/24 hours have not been associated with additional therapeutic benefit and are associated with an increased incidence of adverse reactions. Therapy with rotigotine should be discontinued gradually, with the daily dose reduced by 2 mg/24 hours preferably every other day.

PRODUCT AVAILABILITY and COST: 2 mg patch - $4.89; 4 mg patch - $14.37

CONCLUSION: Rotigotine transdermal will offer a non-oral alternative to pramipexole and ropinirole for the therapy of Parkinson disease. This medication was requested by Dr. Freedman as an alternative to oral therapy for patients who are not candidates for oral therapy. Dr. Freedman expects only 2-3 patients per month who will need therapy with this medication and it was agreed to only carry the 2 mg and 4 mg patches to help minimize the amount of product on hand.

FORMULARY REVIEW

GENERIC NAME: Vilazodone

PROPRIETARY NAME: Viibryd

INDICATIONS: Vilazodone is indicated to treat major depressive disorder in adults.

CLINICAL PHARMACOLOGY: Vilazodone is a selective serotonin reuptake inhibitor/ 5-HT1A partial agonist. It displays minimal or no effect on the reuptake of norepinephrine or dopamine. It has selective affinity for the 5-HT1A receptors; partial agonism at these receptors minimizes receptor overstimulation in the presence of an excess of serotonin. Because of this particular mechanism of action, vilazodone has been termed a serotonin partial agonist—reuptake inhibitor (SPARI).

Buspirone is an example of another antidepressant with partial agonism at the 5-HT1A receptor. Medications like this offer the desired antidepressant effect with fewer potential side effects.

PHARMACOKINETICS: Vilazodone is highly protein bound (96%-99%). It is hepatically metabolized by CYP3A4 (major), 2C19 (minor), and 2D6 (minor). Vilazodone is 72% bioavailable with food; AUC may be decreased by up to 50% in the fasting state. Half-life is around 25 hours with a time to peak serum concentration at 4-5 hours. The presence of mild or moderate renal or hepatic impairment does not affect the clearance of vilazodone.

ADVERSE REACTIONS: The most common adverse reactions include GI symptoms such as diarrhea and nausea. Less common reactions include heart palpitations, dizziness, insomnia, sexual dysfunction, xerostomia, arthralgia, blurred vision, and night sweats.

PIVOTAL STUDIES: Efficacy data supporting the efficacy of vilazodone were obtained from 2 randomized, double-blind, placebo-controlled trials lasting a total of 8 weeks each and included 869 adults age 18-70. In both trials, vilazodone provided superior improvement in depressive symptoms compared to placebo. A longer open-label study lasting for 1 year also concluded that vilazodone was safe and well tolerated by adults with MDD.

CONTRAINDICATIONS: Vilazodone is contraindicated in patients treated with MAOI's within the previous 14 days. Initiation of vilazodone should not occur in patients receiving linezolid or IV methylene blue.

BLACK BOX WARNING: Studies have shown an increased risk of suicidal thinking and behavior in children, adolescents, and young adults when compared to placebo.

DRUG INTERACTIONS: Vilazodone may increase the risk of bleeding in patients taking NSAIDs, aspirin and other agents affecting coagulation. Other antidepressants as well as linezolid and methylene blue may increase serotonin levels and could lead to serotonin syndrome.

MONITORING: Monitor patient for changes in mental status, particularly for depression, suicidal ideation, anxiety, mania, panic attacks, and serotonin syndrome.

DOSING: Initial dosing should be 10 mg by mouth once daily for 7 days, and then increase to 20 mg by mouth once daily for 7 days. The target dose is 40 mg by mouth once daily. Vilazodone should not be stopped abruptly. Dosing should not exceed 20 mg/day if administered concomitantly with strong 3A4 inhibitors such as erythromycin.

COST: Viibryd cost $4.35 per dose for all strengths (10, 20, and 40 mg).

CONCLUSION: Vilazodone's mechanism of action increases release of serotonin similar to SSRI's and also stimulates the 5-HT1A receptor via partial agonism similar to buspirone. Because of this dual

mechanism, it is hopeful that it will elicit the desired antidepressant effect while decreasing the potential for adverse effects.

Due to the unique mechanism of action of this agent and a lack of similar drugs on formulary it is not an ideal agent to be considered for a formulary interchange at this time. Therefore, it is recommended to add this agent to formulary in order to provide continuity of therapy for patients admitted on this treatment as a home medication.

PHENERGAN – PHLEBITIS

(FEBRUARY – MARCH 2013)

FEBRUARY

DATE	ACCOUNT #	AGE	# DOSES	PHLEBITIS GRADE	INDICATION
2/6/2013	36469927	56	16	2	Acute Pancreatitis
2/6/2013	36469528	50	43	1	Cancer patient (nausea)
2/10/2013	36469528	50	43	1	Cancer patient (nausea)
2/16/2013	36533871	37	1	2	Hypertensive urgency/headache
2/18/2013	36534478	61	10	1	Gastritis
2/18/2013	36518375	34	34	1	Abdominal pain/nausea (*C.diff)*
2/20/2013	36533692	76	10	1	Post-op nausea (orthopedic surgery)
2/20/2013	36542039	52	9	1	Post-op nausea (abdominal surgery)
2/23/2013	36550970	29	13	2	Abdominal pain/nausea (*C.diff)*

MARCH

DATE	ACCOUNT #	AGE	# DOSES	PHLEBITIS GRADE	INDICATION
3/20/2013	36702761	45	31	3-4	Abdominal pain/nausea (Crohn's exacerbation)
3/24/2013	36753919	55	28	1	Abdominal pain/nausea (diverticulitis)
3/27/2013	36711981	29	20	1	Refractory nausea/vomiting
3/29/2013	36753919	55	28	1	Abdominal pain/nausea (diverticulitis)
3/31/2013	36760087	45	36	1	Abdominal pain/nausea (Crohn's exacerbation)

PICC PLACED FOR PHENERGAN ADMINISTRATION

DATE	ACCOUNT #	AGE	# DOSES		INDICATION
2/6/2013	36470071	36	31	PLACED PICC LINE	Chronic gastroparesis
2/6/2013	36469528	50	43	PLACED PICC LINE	Cancer patient (nausea)
3/24/2013	36720247	51	6	PLACED PICC LINE	Inflammatory bowel disease (nausea)
3/25/2013	36759003	42	28	PLACED PICC LINE	Abdominal pain/nausea (Crohn's & *C.diff*)

IV PROMETHAZINE
USAGE SUMMARY (MARCH 2013)

Total doses administered: 2311

- 766 patients
- Average – 3 doses/patient

Cumulative doses	# Patients	% Patients	% Total doses
1	520	68%	23%
2	99	13%	8%
3	30	4%	4%
4-9	66	9%	16%
≥ 10	48	6%	49%

Distribution of doses per nursing unit

Nursing Unit	Total doses	% Total doses
5 South	493	21%
1 CE/ 1 NO/ 1 SO	348	15%
Unit 3 (Hixson)	211	9%
ED (Glenwood)	189	8%
4 South	168	7%
4 East	162	7%
ED (Hixson)	121	5%
2 CE/2 SO	102	4%
PACU	77	3%
Unit 2 (Hixson)	62	3%
3 SO	53	2%
MIC	34	1%
CCU	22	1%
SIC	18	1%

Documented promethazine related phlebitis (Feb – Mar)

- 16 patients
- Average doses of promethazine per patient – 20 doses
  - 1 patient received only 1 dose

Summary:
Based on the above utilization review, the majority of all patients receiving IV promethazine receive no more than 2 total doses (81%). However, although only 6% of patients receive 10 or more total doses these doses represent 49% of all doses administered based on drug utilization data. Additionally, according to the phlebitis data provided by the IV team there is a clear correlation with repeated administration and the risk of developing phlebitis based on the average number of doses received by those patients who developed phlebitis (20 doses). The majority of the IV promethazine orders for patients who developed phlebitis were from standard admission or post-operative order sets.

Adverse Drug Reaction Summary
2nd Quarter (FY13)
October-December 2012

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: 100 (25%)
Prior to hospitalization: 292 (75%)
Total: 393

Category 1: 238
Category 2: 154
Category 3: 0

Inpatient ADRs:

Antibiotics: 8%. Vancomycin contributed to 7%. Reactions included acute kidney injury, hypotension, nausea, rash, and itching.

Anticoagulants: 7%. Warfarin contributed to 80%. Only 4 of these ADRs occurred as an inpatient. Reactions included GI bleed liver hematoma, GI bleed, and hematuria.

Narcotics: 6%. Reactions included over sedation, hallucinations, confusion, nausea, constipation, and itching.

Steroids: 68%. Most common reaction was hyperglycemia.

Total ADRs:

Antibiotics: 35%, with 13% of those being Bactrim®
Anticoagulants: 8% with 80% being Warfarin
Chemo: 13%
Narcotics: 24%
Steroids: 17%

Adverse Drug Reaction Summary
3rd Quarter (FY13)
January - March 2013

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: 221 (37.6%)
Prior to hospitalization: 366 (62.3%)
Total: 587

Category 1: 281
Category 2: 306
Category 3: 0

Inpatient ADRs:

Antibiotics: 7.2%. Vancomycin contributed to 43% of these reactions with the majority of these being transient increases in serum creatinine.

Anticoagulants: 3.2%. Only 7 of these ADRs occurred as an inpatient. Warfarin and heparin each contributed to 3 of these ADRs and reactions included rectal bleeding, hematuria and unspecified acute blood loss. (1) case of rectal bleeding reported secondary to rivaroxaban use in a patient with impaired renal function.

Narcotics: 9.5%. Hydromorphone and morphine related ADRs were the most commonly reported. Reactions included oversedation, hallucinations, confusion/encephalopathy, rash and respiratory depression. (2) cases required intubation due to over-sedation secondary to IV morphine.

Steroids: 29.8%. Most common reaction was hyperglycemia.

Total ADRs:

Antibiotics: 10.7%, with 25% of those being Bactrim®
Anticoagulants: 10.7% with 81% being warfarin
Chemotherapy: 10.3%
Narcotics: 10.2%
Steroids: 16%

Antithrombotic Reversal & Surgical Management Recommendations*

Drug Class	*Non-Urgent*	*Urgent - Bleeding or immediate surgery necessary*	*Comments*
Unfractionated Heparin	• Infusion: Stop infusion 4 – 6 hours prior to procedure • SQ doses: Hold the evening dose prior to the procedure	• Protamine sulfate	• aPTT can be utilized to determine degree of anticoagulation
Low Molecular Weight Heparins	• The last dose should be given 24 hours before the procedure. *i.e., enoxaparin at a dose of 1 mg/kg ONCE 24 hrs prior to surgery if dose was 1mg/kg BID*	• Wait 12-24 hours if possible • Consider protamine sulfate if delay not possible for high bleeding risk procedure (only partially reverses LMWH)	• Elimination can be further delayed in patients with acute or chronic kidney disease • Anti Xa assay can be used to assess degree of anticoagulation
Indirect Factor Xa Inhibitor			
Arixtra® (fondaparinux)	• Hold 36-48 hours prior to procedure	• No specific antidote • rVIIa – limited data available *consider low dose (1 mg) and assess response*	• Elimination can be further delayed in patients with acute or chronic kidney disease
Vitamin K Antagonist			
Warfarin	• Stop 5 days prior to procedure • Check INR 1-2 days prior, and if INR greater than 1.5, give Vitamin K 1-2 mg PO • May consider bridge therapy with LMWH in high risk patients	• If procedure can be delayed 6-24 hours, Vitamin K 5-10 mg PO/IV • If procedure cannot be delayed, give FFP or PCC prior to procedure. If PCC used give Vitamin K 10 mg IV to sustain anticoagulation reversal	• PCC dosing: Dose based on INR: 2 – 3.9 → 25 units/kg (max dose: 2500) 4 – 5.9 → 35 units/kg (max dose: 3500) ≥ 6 → 50 units/kg (max dose: 5000)

***This is intended to provide the clinician with possible strategies for patient management and does not establish a fixed set of guidelines that preempt physician judgment. Consider risk of thrombosis when reversal agents utilized.**

Antithrombotic Reversal & Surgical Management Recommendations*

Drug Class	*Non-Urgent*	*Urgent - Bleeding or immediate surgery necessary*	*Comments*
Thrombin Inhibitor			
Pradaxa® (Dabigatran)	• Hold for 1-2 days prior to procedure for CrCl greater than 50 ml/min • Hold for 3-5 days prior to procedure for CrCl less than 50 ml/min	• No specific antidote • rVIIa – limited data available *consider low dose (1 mg) and assess response* • Hemodialysis	• aPPT or PT can be used to rule out substantial residual effect • PCC likely not effective
Factor Xa Inhibitors			
Xarelto® (Rivaroxaban)	• Hold for at least 24 hours prior to procedure with normal renal function (>90 ml/min). Consider holding 2-3 days for patients with CrCl 30-90 ml/min.	• No specific antidote • PCC – *25 units/kg and assess response (limited clinical data)* • Not Dialyzable	PT can be used to rule out substantial residual effect. Normal value may rule out clinically relevant residual anticoagulant effect. PT not intended to be used for dosage adjustment.
Eliquis® (Apixaban)	• Hold for at least 48 hrs prior to procedures with high risk of bleeding; 24 hrs prior to procedures with low risk of bleeding. Consider holding 2-3 days for any patient with CrCl < 60 ml/min regardless of procedure type or 3 or more days if CrCl < 50 ml/min.	• No specific antidote • PCC – *25 units/kg and assess response (limited clinical data)* • Not Dialyzable	PT can be used to rule out substantial residual effect. Normal value may rule out clinically relevant residual anticoagulant effect. PT not intended to be used for dosage adjustment.
Anti-platelets Agents	Hold 5 days prior to procedure* o Plavix® (clopidogrel) o Brilinta® (ticagrelor) Hold 7 days prior to proc.* o Effient® (prasugrel) o Aggrenox® (ASA/dyprid.)	• Consider platelet transfusion	• Caution advised in patients with cardiac stents • Abrupt discontinuation can increase risk of acute stent thrombosis

***This is intended to provide the clinician with possible strategies for patient management and does not establish a fixed set of guidelines that preempt physician judgment. Consider risk of thrombosis when reversal agents utilized.**

Procalcitonin Use Evaluation
Memorial Hospital
May 2013

From January through April of 2013, the utility of procalcitonin (PCT) to reduce antimicrobial exposure in patients with lower respiratory tract infections (LRTI) and sepsis was evaluated. PCT has been evaluated as a biomarker to assist the clinician in the diagnosis and treatment of bacterial infections.

Methods:

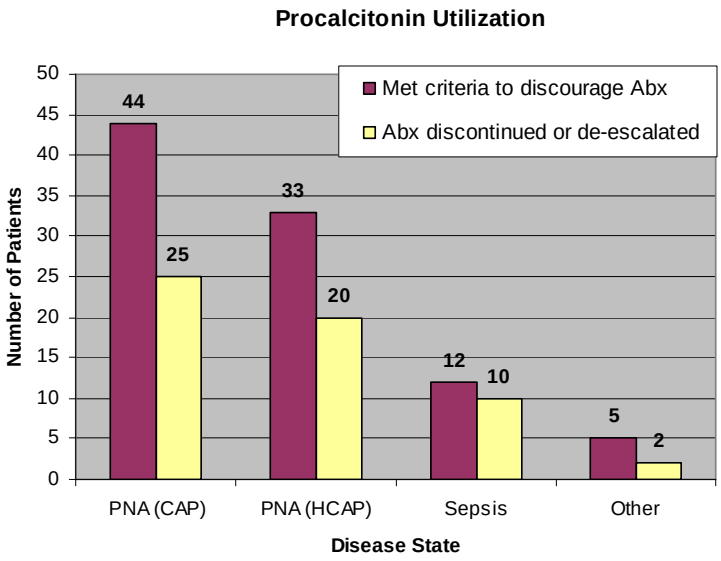
All patients with at least one PCT drawn between August 1st, 2012 and December 16th, 2012 were evaluated for inclusion to the study.

Algorithms derived from the ProHOSP and PRORATA trials were used to guide therapy and make antibiotic recommendations.

Results:

- 183 patients reviewed that had at least 1 PCT drawn
- 45 patients excluded:
  - Primary infection was localized infection
  - Patient was transferred from Memorial Hixson
  - Patient expired or discharged to hospice
- 138 patients met inclusion/exclusion criteria
  - Average age – 67.2
  - Male – 65 (47%)
  - Female – 73 (53%)

	Total	**PCT within 24 hr of infxn presentation**	Percent of total	**Met PCT algorithm criteria to discourage antibiotics**	Percent of total	**Abx narrowed or d/c'd**	Percent that met criteria	Percent of total
All LRTI	108	61	56.48%	77	71.30%	45	58.44%	41.67%
PNA (CAP)	62	41	66.13%	44	70.97%	25	56.82%	40.32%
PNA (HCAP)	46	20	43.48%	33	71.74%	20	60.61%	43.48%
Sepsis	18	4	22.22%	12	66.67%	10	83.33%	55.56%
Other	12	5	41.67%	5	41.67%	2	40.00%	16.67%
Total	138	70	50.72%	94	68.12%	57	60.64%	41.30%



Community acquired pneumonia subgroup analysis:

	Number of patients that met criteria	Average days of therapy
Abx discontinued or de-escalated	25	3.1
Abx NOT discontinued or de-escalated	19	4.6*

* = Does not include Abx given upon discharge

Discussion:

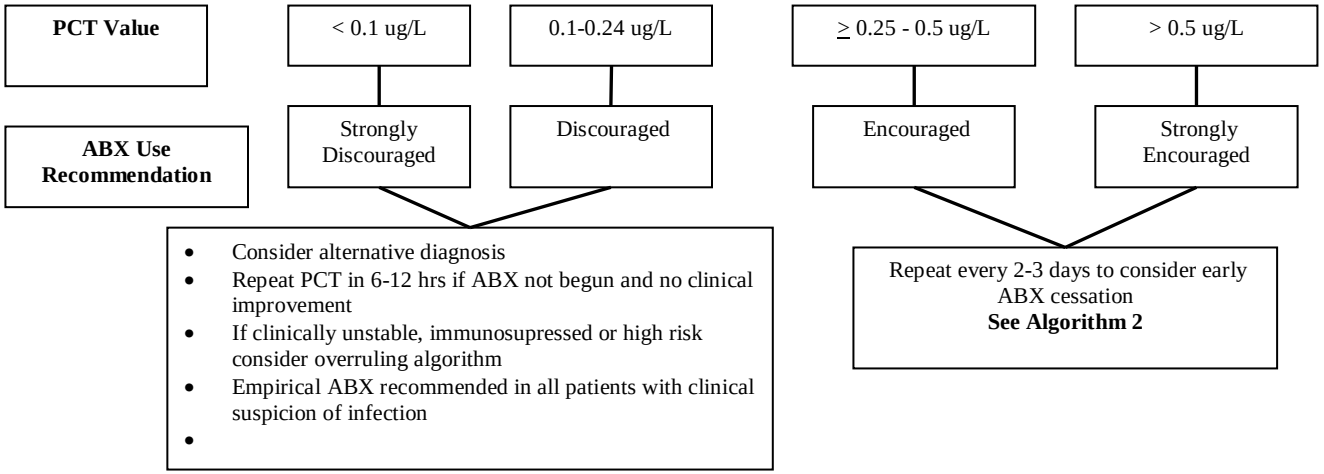
Overall, 41.3% of all included patients (57/138) had their antibiotic course shortened due to procalcitonin. Of the patients that met our PCT algorithm for discouraging antibiotics, 60.6% had their antibiotic course shortened.

Some potential limitations of this study include the potential for selection bias since there was no randomization or control group. Secondly, procalcitonin is new to our facility and our physicians so many providers were unfamiliar with the assay. Finally, I did not evaluate re-admission rates or mortality.

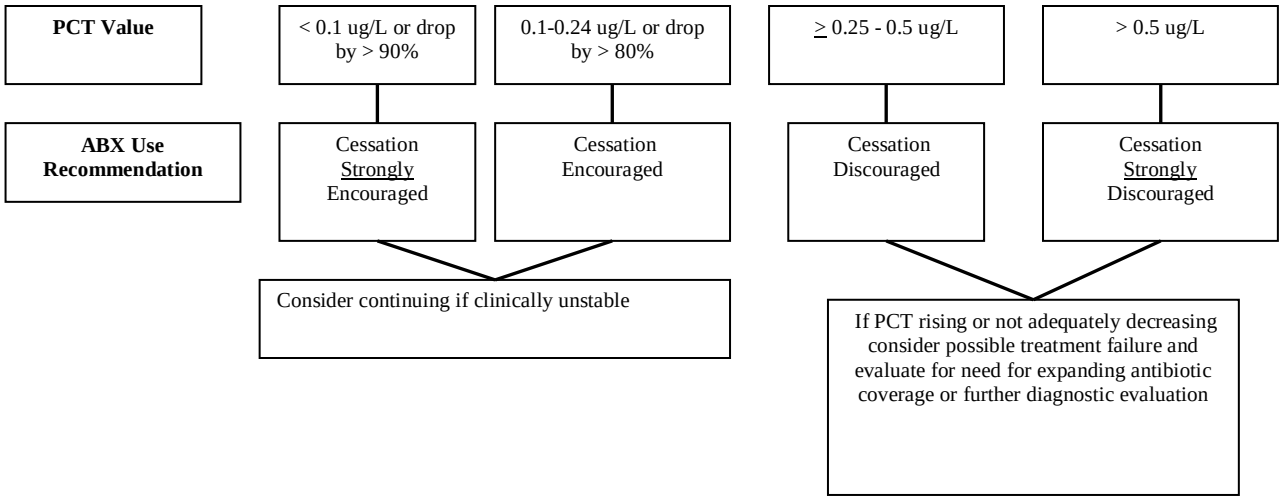
Conclusion:

Procalcitonin use in conjunction with clinical judgment can be beneficial to reduce antibiotic utilization. Provider understanding and acceptance is vital to the success of procalcitonin as a clinical tool for antimicrobial stewardship. I feel there are two scenarios in which procalcitonin has the most impact. First, patients admitted with possible CAP vs. COPD or CHF exacerbation to determine if antibiotics are needed. Secondly, HCAP or sepsis patients a procalcitonin drawn every 2-3 days to determine when antibiotics should be discontinued.

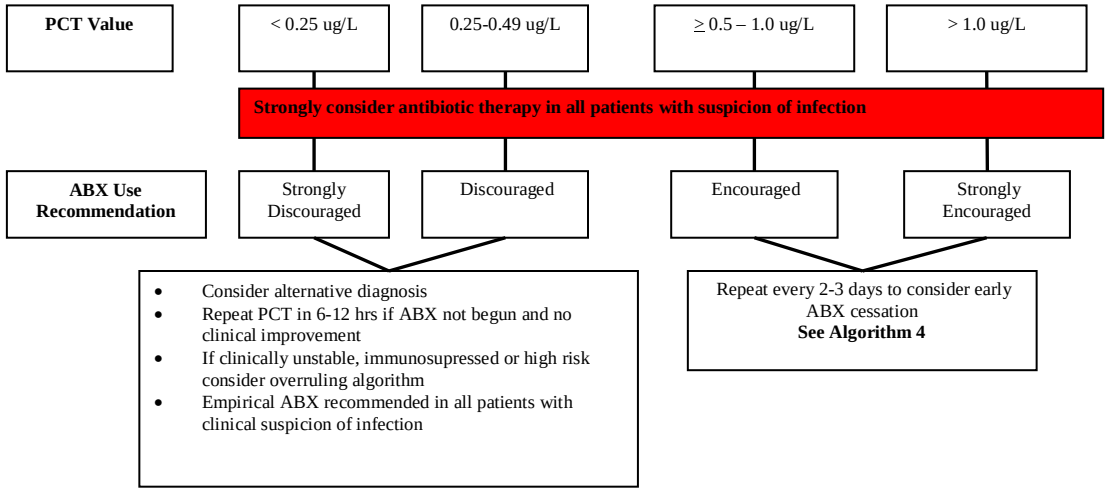
LRTI Initial Antibiotic Use Algorithm (#1)



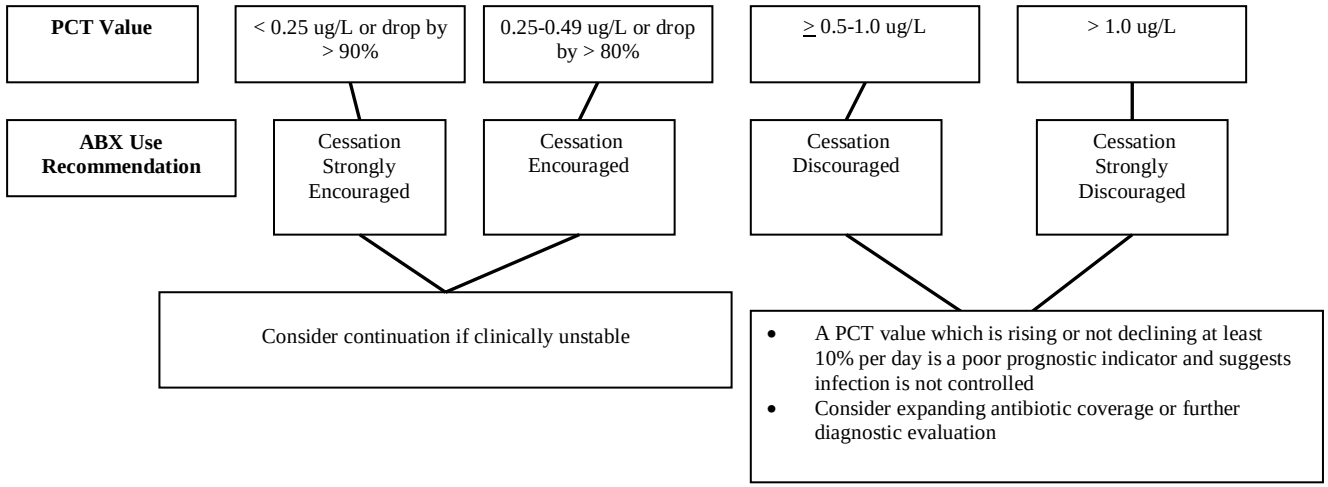
LRTI PCT Follow up Algorithm (#2)



Sepsis Initial Antibiotic Use Algorithm (#3)



Sepsis Follow-up PCT Antibiotic Use Algorithm (#4)



Warfarin Urgent Reversal
Prothrombin Complex Concentrate (PCC)
Kcentra™

- Indications
  - Life Threatening Bleeding
  - Serious Bleeding and Rapid Reversal Needed (surgery within 12 hours)
  - Serious Bleeding and Patient Intolerant to High Volumes of Fluid (i.e. FFP)

- Hold Coumadin and Give Vitamin K 10 mg IVPB immediately x 1 dose.

- Circle Appropriate Dose Based on Weight and INR.

Pre-treatment INR	2 - < 4	4 – 6	> 6
Dose of PCC: Units (Factor IX) / Kg (body weight)	25 units/kg	35 units/kg	50 units/kg
Maximum dose (units of Factor IX)	2500 units	3500 units	5000 units
Duration of Infusion	15 minutes	20 minutes	25 minutes

*Maximum Body Weight: 100 kg
*Dose will be rounded to the nearest vial size.

- Follow Up INR in 1 hour and 12 hours.

- Repeat Dosing is NOT recommended.

- Contraindications
  - Disseminated Intravascular Coagulation
  - Heparin Induced Thrombocytopenia

- Precautions
  - There is an increased risk of thrombosis in patients with previous thrombolic event.
  - PCC is made from human blood and may carry a risk for transmitting infectious agents.
  - High doses of Vitamin K can cause warfarin resistance.
  - Vitamin K IV may rarely cause anaphylactic reactions.

Title: **Renal Dosing Adjustments**		
		Page 1 of 1
Policy Number: PHRM – POL- 0579	***Date Last Revised:*** 6/13	***Valid Until:*** 6/16
Department(s) Affected: Pharmacy	***Review Period:*** every 3 years	
Signature(s):		

OUTCOME:

To ensure appropriate medication dosing based on patient's renal function and optimize pharmacodynamics and pharmacokinetic properties of renally eliminated medications while decreasing toxicities associated with inappropriate dosing.

POLICY:

Pharmacists may automatically adjust the dose of renally eliminated antimicrobials, anticoagulants, and other medications as approved per the Pharmacy and Therapeutics committee after evaluation of a patient's renal function. In instances where a renal dosage change is warranted, but the medication is not included for automatic dosage adjustment, the pharmacist may contact the prescriber with the recommended dosage change.

PROCEDURE:

1. A pharmacist may evaluate a patient's medication profile for renally eliminated medications. If relevant renal labs have not been ordered within 24 hours of the medication order, the pharmacist may order a basic metabolic profile (BMP) in order to complete this evaluation.

2. During the evaluation, the pharmacist may assess the doses of renally eliminated medications. Based on the patient's calculated creatinine clearance and clinical status, the pharmacist may make necessary adjustments. In instances where a renal dosage adjustment is warranted, but the medication is not approved for automatic adjustment, the pharmacist may contact the prescriber recommending a dosage change.

3. When an automatic dosage adjustment is made, the pharmacist will write the new order as "Per Therapeutics Committee." The pharmacist will also write a brief progress note communicating the patient's relevant clinical history and the therapeutic rationale of the dosage change.

4. The pharmacist will follow up on dosage adjustments as appropriate, evaluating subsequent changes in patient's renal function and clinical status. If relevant renal labs have not been ordered within 48 hours after a dosage adjustment, the pharmacist may order a basic metabolic profile (BMP).

5. If any dosage adjustment made by a pharmacist is subsequently changed by a prescriber, the pharmacist will make not further automatic adjustments on that medication during the current admission, unless otherwise directed.

Pharmacist Ordering of Lab Values
Proposed Additions

Background:
As part of the *Medication Orders – Pharmacist Review* policy, pharmacists are authorized to initiate the ordering of necessary laboratory tests in consideration of patient safety and improved patient care. The laboratory tests that may be ordered are as defined by the Pharmacy and Therapeutics committee.

Previously approved laboratory tests/drug levels: theophylline, digoxin, INR

Proposed additions:
Recent patient safety events have highlighted the need for additions to this P&T managed protocol. The following are the proposed additions to this policy/protocol:

- Vancomycin levels
  - *patients not being managed by pharmacokinetic service*
- Phenytoin levels
- Serum creatinine
  - *to assess appropriate dosing of renally eliminated medications*