Pharmacy & Therapeutics Committee Meeting
Private Dining Room
April 9, 2015 7:00 a.m.

Agenda Items	Individual Responsible	
1. Call to Order	Richard Pesce, MD	
2. Approval of February, 2015 Minutes	Richard Pesce, MD	
3. Therapeutic Interchanges and Formulary Decisions		Page
A. Anti-fungal Class Review	Patrick Ellis, PharmD	5-6
B. EpiPen (epinephrine auto-injector)		
C. Endothelin Receptor Antagonist Class Review		7-8
D. Zerbaxa® (ceftolozane/tazobactam)	Matt Russell, PharmD	9-10
E. Avycaz® (ceftazidime/avibactam)	Eleni Martinez, PharmD	11-12
F. Soliris® (eculizumab) – use criteria, lab testing, etc.	Patrick Ellis, PharmD	13-14
G. Toujeo® (U-300 insulin glargine)		15-17
4. MUE		
A. Miacalcin® injection (calcitonin-salmon)	Patrick Ellis, PharmD	18-20
B. Timing of Antibiotic Administration – Sepsis		21-24
C. Exparel® - orthopedics review		25-26
5. Medication Safety/Quality		
A. ADR Review	Karen Babb, PharmD	27-28
6. Policy, Procedure & Protocols		
A. Pharmacy and Therapeutics Committee – Policy updates	Patrick Ellis, PharmD	29-31
B. Prescription Pad Security	Melissa Roden, RN	
7. Adjournment		

Next Meeting will be TBD in the Private Dining Room

CATHOLIC HEALTH INITIATIVES
Memorial Health Care System

PHARMACY AND THERAPEUTICS COMMITTEE

DATE: February 12, 2015 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. Mark Anderson, M.D. Allen Atchley, M.D. David Dodson, M.D. Michael Harper, M.D. Kevin Lewis, M.D. Michael Stipanov, M.D.	Karen Babb, PharmD Michelle Denham, RN Rodney Elliott, PhT Patrick Ellis, PharmD Lila Heet, PharmD Nan Payne, RN Karen Regal, Supply Chain Rhonda Poulson, RN	Melissa Roden, RN Sandy Vredeveld, DPh Brian Jones, RD Danine Watson, CNO	Diona Brown, RN Vickie Burger, Lab Nathan Chamberlain, M.D. William Oellerich, M.D. Hannah Walker, RN Shannon Harris, RN Scott Harbaugh, Finance	Matthew Russell, PharmD Megan Whittier, PharmD Taylor Austin, student

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 –** On 2/11/15 CHI issued guidance on appropriate Exparel use. Patrick will add this to the April agenda for further discussion.	Information	Pending
Therapeutic Interchanges and Formulary Decisions	The following medications were reviewed: 1. **Inhaled Corticosteroid Formulary** – Patrick reviewed the latest CHI recommendations for formulary consolidation of inhaled respiratory agents. The only outstanding formulary interchange that has not been completed is a conversion to Asmanex HFA (mometasone) as the preferred inhaled corticosteroid agent. The interchange was reviewed and it was recommended to adopt the automatic formulary interchange utilizing Asmanex and all orders for other inhaled corticosteroid agents would be interchanged to a therapeutically equivalent dose of Asmanex HFA. Additionally a request from Dr. Mull was discussed to allow the automatic conversion of any patient receiving non-therapeutic doses of inhaled corticosteroid/beta agonist (once daily dosing) inhalers to be automatically increased to the normal twice daily dosage (Dulera 2 puffs BID). This was recommended for approval by Dr. Pesce. 2. **Akten® (lidocaine ophthalmic gel)** – Topical ophthalmic gel indicated for ocular surface anesthesia during ophthalmologic procedures (cataract surgery, etc.) – requested by Dr. Lindquist. This product provides an alternative to traditional injectable blocks while providing similar although not superior pain control. The gel formulation allows for longer corneal contact time and better anesthetic effect as compared to traditional topical ophthalmic anesthetics. Recommended for approval with restriction to ophthalmology service. 3. **Rapivab® (peramivir)** – Peramivir is the first and only IV antiviral approved for treatment of uncomplicated acute influenza. The CDC still recommends oral Tamiflu as first line therapy for hospitalized patients and that peramivir should only be considered in	1. Formulary interchange approved 2. Approved 3. Approved with restrictions	Complete Complete Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	seriously ill patients who cannot absorb or tolerate oral or enterally administered Tamiflu. It was recommended to add to formulary with the following restrictions: - Patient must be in a critical care/ICU level of care - Cannot or suspect unable to absorb oral/enteral Tamiflu - Ordering restricted to Critical Care and/or Infectious Disease - If initiated therapy will be re-evaluated after 5 days of therapy		Pending
	4. **Pneumonia Vaccination Guidelines** – Patrick reviewed the recently updated pneumonia vaccine recommendations. The new guidelines have changed and now recommend both the PCV13 (Prevnar) and PPSV23 (Pneumovax) vaccine and they should be routinely administered in series to all adults aged ≥ 65 years. In order to achieve optimal immune response with each vaccine it is recommended that the PCV13 vaccine be administered initially with ideally a 1 year window between vaccines depending upon the patient's specific vaccine history. Due to the complexity of the new recommendations and the difficulty in correctly adhering to the new guidelines the following recommendations were made for hospitalized patients: - Remove Pneumovax from the standard admission vaccination assessment & orders and stop routinely vaccinating with the PPSV23 vaccine. - Modify the discharge instructions to encourage patients to discuss pneumonia vaccination with their PCP after discharge. - Communicate with MHP and other local healthcare providers of this hospital process change. - Add Prevnar (PCV13) to formulary and continue to stock a small amount of Pneumovax (PPSV23) for patients who may benefit from immunization during hospitalization. This includes patients with splenectomy and patients with clear vaccination histories whom follow up coordination (additional vaccines, etc.) can be assured.	4. All Recommendations approved	Complete
	5. **Savaysa® (edoxaban) –** Oral inhibitor of factor Xa indicated for stroke prevention in patients with NVAF and for the treatment of DVT & PE. It was recommended to add Savaysa to formulary in order to provide continuity of care for inpatients admitted to the facility on this medication. Dr. Atchley recommended that pharmacy closely monitor patients' renal function while on this medication and recommend transitioning to an alternate agent if CrCl > 95 ml/min due to poor clinical outcomes in the NVAF patient population. Patrick agreed and stated that this medication would be monitored closely along with the other novel oral anticoagulants already on formulary.	5. Approved	Complete
	6. **Prolia® (denosumab)** – RANKL inhibitor indicated for the treatment of osteoporosis. The recommendations and review provided by the Formulary Business Review Committee were reviewed and discussed. Due to no new clinical information indicating superiority as compared to other agents such as Reclast it was recommended to support the Formulary Business Review recommendation of not lifting the current formulary restrictions for Prolia.	6. Lifting of restrictions not approved	Complete
	7. **Caldolor® (IV ibuprofen) –** IV formulation of ibuprofen requested for trial use by Dr. Harper. Dr. Harper reviewed the available clinical data regarding the use of IV ibuprofen in patients with severe sepsis, ARDS, etc. in decreasing physiologic inflammatory effects	7. Approved for trial use with restrictions	

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	such as fever, tachycardia, oxygen consumption, and lactic acidosis. Although the available data has not demonstrated a mortality benefit he believes this may prove to be useful as an adjunct therapy for this patient population. It was recommended for approval on a trial base only and use restricted to Critical Care physicians only for a duration of 48 hrs (10 mg/kg – max 800 mg, Q 6 hrs x 8 doses)		Complete
	8. **Nimbex® (cisatracurium) –** Non-depolarizing neuromuscular blocker that undergoes organ independent metabolism not requiring kidney or liver function for elimination. The current formulary NMB's (rocuronium, vecuronium) can safely be used in patients with renal dysfunction. Their use does present problems if patients also have co-existing liver disease due to their primary hepatic metabolism. Due to the increased per day cost of Nimbex it was recommended to add this drug to formulary and limit its use to patients with multi-system organ failure who are not candidates for therapy with rocuronium or vecuronium.	8. Approved	Complete
	9. **Ofirmev® (IV acetaminophen) –** Per the Februray 2014 P&T decision Ofirmev is currently restricted to use by cardio thoracic surgery only. In November due to the recent price increase this service agreed to remove this from their order sets and has eliminated all usage of this product. It is recommended at this time to designate Ofirmev non-formulary and no longer be stocked by the pharmacy.	9. Approved for formulary removal	
Medication Safety/Quality	• **VTE Core Measure – data review –** Patrick and Nan reviewed the most recent data regarding the hospital's performance with the VTE core measures. The biggest opportunity continues to be with the VTE-1 measure that requires that all patients have either mechanical or pharmacologic prophylaxis (or contraindications to both) by midnight the day after admission. Two proposals were shared. Streamlining of the standard DVT assessment orders to make them more user friendly and to add the mechanical prophylaxis options to standing orders that already have DVT prophylaxis orders included (including sections to document contraindications for both types of prophylaxis). Both of these proposals were approved. Additional discussion occurred around options to create a standardized protocol for all newly admitted patients to have mechanical or pharmacologic prophylaxis unless "opted out" by the admitting physician. This discussion was tabled and it was recommended to possibly route this discussion on to MEC for further discussion.	Order modifications approved	Pending
	• **Antithrombotic Reversal/Surgical Management Recommendations –** Patrick shared with the group that the updated reference cards including Edoxaban will be distributed soon to physicians and other clinical staff at both campuses.	Information	Complete
Policy, Procedure & Protocols	• **Look-Alike, Sound-Alike Policy –** Policy requires annual review and Patrick explained that recent changes were made to incorporate errors that occurred due to similar named products.	Approved	Complete
Nutrition Support Team	• **Diet Manual –** Brian reviewed that a new diet manual (Sodexo Hospital Diet Manual) will now be used as a supplement for menu planning purposes. The updated policy was shared with the committee.	Approved	Complete

There being no further business, the meeting was adjourned at 8:00 A.M. The next P&T meeting is April 9, 2015.

Anti-fungal Formulary Class Review
Pharmacy and Therapeutics Summary Document

Recommendations:
Based on a review of efficacy, safety, and cost, the antifungal class formulary should consist of a group of preferred agents as listed in the following table and further described in the below text.

Azole antifungals:
Fluconazole is the drug of choice for most forms of candidiasis with some exceptions depending on the Candida species. It is well tolerated, available in oral and IV formulation, has good CNS penetration, and is available as a generic at relatively low cost. However, fluconazole does have a narrower spectrum of activity than some of the other available azole antifungals and the other azoles may be considered for the treatment of more specific and less common fungal pathogens as described below. Itraconazole is the drug of choice for histoplasmosis and some forms of blastomycosis, and has in vitro activity against Aspergillus. Posaconazole is active against a wide range of fungi refractory to other antifungal treatments including: aspergillosis, mucorales, fusariosis, histoplasmosis, refractory candidiasis, refractory cryptococcosis, and refractory chromoblastomycosis. Voriconazole is the preferred treatment for most species of *Aspergillus*. The use of itraconazole, posaconazole, and voriconazole may be considered in certain clinical scenarios as described above when clinically indicated. Ketoconazole use may be reserved for off-label treatment of refractory prostate cancer only and is not usually utilized for treatment of fungal infections.

Echinocandin antifungals
The spectrum of activity for each echinocandin is similar between the three available products. However, there is a difference in FDA approvals between the available products. This class of antifungals is predominantly used for the treatment of candidemia. However, they also play a role in the treatment of a multitude of other fungal infections and are also useful in patients who are moderately to severely ill with serious illness and recent azole exposure. Despite the differences in FDA approved indications the available data suggests that these agents are interchangeable and that significant therapeutic differences do not exist within this class of antifungals. Therefore, it is recommended that micafungin be the preferred formulary echinocandin due to it being the most cost effective medication within this class.

Lipid based amphotericins
Abelcet (amphotericin lipid complex) and Ambisome (amphotericin b liposomal) are largely considered interchangeable based on both clinical efficacy and FDA approved indications. Ambisome is currently the most cost effective of the lipid based products and is recommended to be the preferred formulary product.

Other products (nystatin, terbinafine, griseofulvin, flucytosine)
Of the remaining antifungal agents it is recommended that nystatin be utilized for the treatment of oral thrush and flucytosine be utilized as part of combination antifungal therapy when clinically indicated (*Cryptococcus, etc.)*. It is recommended to not utilize griseofulvin or terbinafine on hospital formularies. Patients that are taking these medications prior to admission may continue to utilize own supply after identification by pharmacist per facility policy.

Class	Recommend formulary agents	Recommended non-formulary agents
Azoles	Fluconazole Itraconazole[*] Voriconazole[*] Posaconazole[*,@]	Ketoconazole[#]
Echinocandins	Micafungin[*]	Caspofungin Anidulafungin
Polyenes	Nystatin Amphotericin B liposomal[*]	Amphotericin B lipid complex Amphotericin B Cholesteryl sulfate
Miscellaneous	Flucytosine[*]	Terbinafine Griseolfulvin

[*] Use should be restricted based on indications and/or to infectious diseases specialist
[@] Delayed release tablets preferred over the oral suspension, however the oral suspension should still be available for patients with difficulty swallowing.
[#] Ketoconazole use for treatment of advanced prostate cancer may be considered but non-formulary for treatment of fungal infections

AMBISOME – Indication Specific Dosing

Indication	Ambisome
Candidal endocarditis	3-5mg/kg/day with or without flucytosine 25 mg/kg 4 times daily
Candidal endopthalmitis	5 mg/kg/day
Candidal meningitis	5 mg/kg/day with flucytosine 25mg/kg 4 times daily
Candidemia, histoplasmosis, or other non-invasive candida infections	3 mg/kg/day
C. krusei candidemia	5 mg/kg/day
Cryptococcal meningitis (HIV-positive)	6 mg/kg/day or 4-6 mg/kg/day with Flucytosine 25 mg/kg 4 times daily
Fungal sinusitis (unless causative organism is Aspergillus spp Pseudallescheria boydii for which azole is preferred)	5 mg/kg/day
Neutropenic fever or candidemia in neutropenic patient	3-5 mg/kg/day
Systemic fungal infections (Aspergillus, Candida, Cryptococcus)	5 mg/kg/day

Drug Class Review
Endothelin-Receptor Antagonists

1.	**Current Drugs in Class**:	Bosentan	Ambrisentan	Macitentan
2.	**Brand Names (approved date):**	Tracleer® (2001)	Letairis® (2007)	Opsumit® (2013)
3.	**Patent Expiration:**	11/20/2015	07/29/2018	04/18/2029

4. **Current Formulary:**
Bosentan (Tracleer®)

5. **Indication:**
Endothelin-Receptor Antagonists are approved for treatment in patients with pulmonary arterial hypertension (PAH) WHO Group 1 by slowing disease progression and improving exercise tolerance.

6. **Clinical pharmacology:**
Endothelin-1 (ET-1) is a potent pulmonary vasoconstrictor and causes smooth muscle contractions mainly via ET_A receptors. Upregulation of ET-1 system and ET_A and ET_B receptors has been observed in patients with PAH. Endothelin-Receptor Antagonists (ERAs) block ET-1 from binding to endothelin receptors, ET_A and ET_B (Ambrisentan – selective for ET_A), on vascular endothelium and smooth muscle cells.

7. Contraindications, Warning and Precautions:

a. Contraindications:
   i. All three agents are contraindicated in women who are or may become pregnant.
   ii. Bosentan is contraindicated in patients with concomitant use with cyclosporine A or glyburide and hypersensitivity to bosentan or any component of the product.
   iii. Ambrisentan is contraindicated in patients with idiopathic pulmonary fibrosis.
   iv. No additional contraindications for Macitentan.

b. Warnings and Precautions
   i. All three ERAs have Boxed warning for Embryo-fetal toxicity and a REMS for outpatient and inpatient dispensing. Bosentan has additional Boxed warning and REMS for hepatotoxicity.
   ii. With bosentan, monthly liver function test is required.
   iii. Adverse event profiles are similar among the three agents. Commonly seen adverse effects in clinical trials include hepatotoxicity, fluid retention, decrease in Hgb and Hct and anemia. Macitentan should not be initiated with severe anemia. Impaired spermatogenesis has been observed with bosentan and ambrisentan but not with macitentan (Counseling still recommended).

8. Monitoring parameters:

a. Bosentan – Serum transaminase (AST and ALT) and bilirubin should be monitored at baseline and monthly thereafter. Hemoglobin and Hematocrit should be measured at baseline and monthly for 3 months, and every 3 months thereafter. Liver injury (e.g. abdominal pain, fatigue, fever, jaundice, and nausea/vomiting) should be monitored. Pregnancy should be tested monthly.
b. Ambrisentan – Significant peripheral edema should be monitored. Monitor liver injury and if injury suspected, liver enzymes should be measured. Pregnancy should be tested monthly.
c. Macitentan – Significant peripheral edema should be monitored and liver enzymes should be measured if clinically appropriate. Monitor for clinical signs and symptoms of liver injury. Hemoglobin and Hematocrit level should be measured if clinically appropriate. Pregnancy should be tested monthly.

	Bosentan	Ambrisentan	Macitentan
FDA indication	PAH, WHO Group 1; functional class II – III	PAH, WHO Group 1; functional class II – III	PAH, WHO Group 1; functional class unspecified
Recommended dosage	62.5 mg orally twice daily for 4 weeks; then increase to 125 mg twice daily	5 mg orally once daily; consider increasing to 10mg once daily if tolerated	10 mg orally once daily
Dosing consideration	In patients <40 kg and > 12 years of age and older: initial and maintenance dose is 62.5 mg twice daily. Need to adjust dose if ALT/AST level > 3x ULN; discontinue if levels >5x ULN; do not rechallenge if levels >8x ULN	Not recommended in patients with moderate or severe hepatic impairment	None
Drug interaction	Bosentan decreases effects of contraceptives. Discontinue bosentan 36 hours prior to ritonavir; restart after ≥10 days	Cyclosporine can increase ambrisentan serum level	Manufacturer recommends to avoid concomitant use with strong CYP3A4 inhibitors/inducers

9. Conclusion:

Macitentan is a new addition to ERAs, which was recently approved in 2013. ERAs, along with calcium channel blockers, phosphodiesterase type 5 inhibitors and prostanoids, are one of the treatment options in patients with PAH. Currently, The American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) does not recognize a specific agent or drug class as superior for treatment of PAH.

Bosentan is the first ERA that was approved for treatment of PAH. It is a dual antagonist of ET_A and ET_B receptors and showed an improvement in exercise tolerance and reduction of disease progress in patients with PAH. Ambrisentan has a theoretical advantage of blocking ETA receptors selectively, its clinical efficacy is similar to that of bosentan. Although there is no published studies investigating the safety and efficacy of macitentan as compared with other agents, macitentan seems to have a similar profile to that of bosentan and ambrisentan. Potential advantages of macitentan compared to previous two agents include fewer absolute contraindications, potential use in patients with hepatic impairments, and once daily dosing frequency.

10. Therapeutic Interchange and Cost:

Medication	Cost Per Day	Cost Per 30 Day Supply	Patent Expiration
Tracleer 62.5 mg	$ 328.8	$ 9,864	Nov 2015
Tracleer 125 mg	$ 328.8	$ 9,864	
Letairis 5 mg	$ 294.76	$ 8,842.73	July 2018
Letairis 10 mg	$ 294.76	$ 8,842.73	
Opsumit 10 mg	$ 270.64	$ 8119.05	April 2029

11. Recommendation:

Efficacy and safety of macitentan seems to have a comparable profile compared to that of other two ERA agents. However, the drug was evaluated in only 1 clinical trial. Additionally, clinical studies comparing all three agents are currently lacking. Due to the REMS requirements for each medication, patients must be enrolled in the REMS program specific to each medication and thus patients must be maintained on their home therapy and not switched to alternate therapies while hospitalized.

Opsumit may have potential benefits including fewer contraindications, simplified dosing regimen, and potential use in patients with moderate/severe hepatic impairments. It also seems to provide a financial saving solely based on medication purchasing data. Limiting factors of Opsumit usage are its limited clinical data and experiences in practice. Tracleer was approved in 2001 and its generic form should be available in November, 2015. At this point, Opsumit should remain as a treatment option in patients who cannot tolerate Tracleer.

FORMULARY REVIEW

GENERIC NAME: CEFTOLOZANE/TAZOBACTAM

PROPRIETARY NAME: ZERBAXA (Cubist Pharmaceuticals)

INDICATIONS: Ceftolozane/tazobactam is indicated for the treatment of complicated intra-abdominal infections in combination with metronidazole and complicated urinary tract infections, including pyelonephritis.

Pathogen/ Isolate Source	Minimum Inhibitory Concentrations (mcg/mL)			Disk Diffusion Zone Diameter (mm)		
	S	I	R	S	I	R
Enterobacteriaceae	≤ 2/4	4/4	≥ 8/4	-	-	-
Pseudomonas aeruginosa	≤ 4/4	8/4	≥ 16/4	≥ 21	17-20	≥ 16
Streptococcus anginosus Streptococcus constellatus & salivarus	< 8/4	16/4	≥ 32/4	-	-	-
B. fragilis	≤ 8/4	16/4	≥ 32/4	-	-	-

S = susceptible, I = intermediate, R = resistance

CLINICAL PHARMACOLOGY: Ceftolozane is structurally similar to ceftazidime and belongs to the cephalosporin antibacterial class. Its bactericidal mechanism is through binding to penicillin-binding proteins, preventing cell wall biosynthesis. Tazobactam has minimal activity against bacteria, but acts as an irreversible inhibitor of some beta-lactamases, thus extending ceftolozane's spectrum of activity.

PHARMACOKINETICS: The C_{max} and AUC of ceftolozane/tazobactam increase in proportion to dose, making the half-life dose dependent (generally ~3 hours). Plasma levels are not raised significantly following multiple intravenous infusions of up to 2g/1g given every 8 hours for up to 10 days in healthy adults with normal renal function. Protein binding of ceftolozane is approximately 16-21% with tazobactam binding up to 30%. The penetration ratio of ceftolozane into the ELF compared to plasma is ~0.48. Ceftolozane is not appreciably metabolized and is readily eliminated in the urine as unchanged drug via renal excretion. Tazobactam is hydrolyzed to its inactive metabolite, M1, and undergoes similar elimination.

ADVERSE REACTIONS: The most common adverse reactions reported in the clinical trials were nausea, diarrhea, headache, and pyrexia.

COMPARATIVE SAFETY & EFFICACY: In the double-blind phase III ASPECT-cIAI trial, adults hospitalized with complicated intra-abdominal infections (appendicitis, cholecystitis, diverticulitis, gastric/duodenal perforation, perforation of the intestine, and other sources of intra-abdominal abscesses) were randomized to receive ceftolozane/tazobactam (1g/0.5g every 8 hours) plus metronidazole (500mg every 8 hours) versus meropenem (1g every 8 hours) for 4-14 days of therapy. The study medication and metronidazole were non-inferior to meropenem in regards to cure rate, 83%vs 87.3% in the intention-to-treat population.

In the double-blind phase III ASPECT-cUTI trial, adults hospitalized with complicated urinary tract infections, including pyelonephritis, were randomized to receive ceftolozane/tazobactam (1g/0.5g every 8 hours) to levaquin (750mg daily) for 7 days of therapy. A statistically significant difference in favor of the study medication was observed in regards to composite microbiological and clinical cure rates in the modified intention-to-treat population, 76.9% vs 68.4%. This observation was noted to be likely due to the pathogens non-susceptible to levaquin at baseline.

A randomized, open-label phase III trial directly comparing ceftolozane/tazobactam (3g every 8 hours) vs pipercillin/tazobactam (4.5g every 8 hours) in adults hospitalized with ventilator associated pneumonia (VAP) was initiated in July 2013 and terminated in November 2013 for reasons unknown. Currently a similar prospective, double-blind, randomized, phase III study is being conducted to compare ceftolozane/tazobactam (3g every 8

hours) vs meropenem (1g every 8 hours) in the setting of VAP. Additionally, an open-label phase I trial examining the pharmacokinetics and lung penetration of ceftolozane/tazobactam in critically ill patients is underway. The higher dosing strategy utilized in these trials stems from ELF/plasma AUC ratio data derived from a phase 1, open-label study showing lower concentrations of ceftolozane/tazobactam in the ELF vs plasma up to 6 hours post infusion.

COMPARATIVE IN VITRO SUSCEPTIBILITY: Ceftolozane/tazobactam lacks broad anaerobic coverage compared to pipercillin/tazobactam and has equally unreliable efficacy against ESBL-producing gram negative bacilli. Ceftolozane/tazobactam has been shown to be susceptible to more resistant strains of pseudomonas aeruginosa, including pipercillin/tazobactam, meropenem, and pan-resistant phenotypes, however, most in vitro data behind the potential use of ceftolozane/tazobactam in this setting support a proposed MIC $\leq$ 8 mg/mL. As the FDA has approved a lower breakpoint (MIC $\leq$ 4 mg/mL) for this specific situation, empirical coverage with pipercillin/tazobactam would be preferable to ceftolozane/tazobactam until an E-test verifying MIC and susceptibility data are available.

CONTRAINDICATIONS: Ceftolozane/tazobactam is contraindicated in patients with known serious hypersensitivity to this agent, pipercillin/tazobactam, or other members of the beta-lactam class.

WARNINGS AND PRECAUTIONS: Caution should be used in patients with baseline CrCl: 30 to $\leq$ 50 mL/min as decreased efficacy was demonstrated in this population. Clostridium difficile-associated diarrhea has been reported with almost all systemic antibacterial agents, including ceftolozane/tazobactam.

DRUG INTERACTIONS: No significant drug-drug interactions are likely between ceftolozane/tazobactam and substrates, inducers, or inhibitors of cytochrome P450 enzymes.

DOSING:

Indication(s): Complicated Intra-abdominal or Urinary Tract Infection	
CrCl > 50 mL/min	1g/0.5g every 8 hours
CrCl: 30-50 mL/min	500mg/250mg every 8 hours
CrCl: 15-29 mL/min	250mg/125mg every 8 hours
HD	500mg/250mg x 1 then 100mg/50mg every 8 hours
Indication: Pneumonia (Off-label Use)	
CrCl > 50 mL/min	2g/1g every 8 hours
CrCl: 30-50 mL/min	1g/0.5g every 8 hours
CrCl: 15-29 mL/min	500mg/250mg every 8 hours

(Doses are given over 60 minute infusions. On hemodialysis days, administer as closely to after dialysis as possible)

COST & COMPARISON TO SIMILAR AGENTS –
Pipercillin/tazobactam – 3g/0.375g three times daily: $10.35
Meropenem – 500mg four times daily: $15.72
Meropenem – 1g three times daily: $23.58
Ceftolozane/tazobactam – 1g/0.5g three times daily: $237.21

INCIDENCE OF CARBAPENEM RESISTANT PSEUDOMONAS: 59 isolates (calendar year 2014)

CONCLUSION: Ceftolozane/tazobactam is a novel combination of a cephalosporin with a beta-lactamase inhibitor that is FDA approved for the treatment of complicated UTIs or intra-abdominal infections (with the addition of metronidazole). As this antibiotic offers no distinct advantages over pipercillin/tazobactam with the exception of potentially treating very resistant pseudomonas aeruginosa strains, it is recommended at this time to add ceftolozane/tazobactam to formulary with restriction to ID physicians or proven cases of susceptibility in the setting of multi-drug resistance on a case-by-case basis.

FORMULARY REVIEW

GENERIC NAME: CEFTAZIDIME-AVIBACTAM

PROPRIETARY NAME: AVYCAZ (Forest Pharmaceuticals Inc)

INDICATIONS: Ceftazidime/avibactam is indicated for the treatment of complicated intra-abdominal infections (cIAI), in combination with metronidazole caused by the following susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Providencia stuartii, Enterobacter cloacae, Klebsiella oxytoca,* and *Pseudomonas aeruginosa*. It is also indicated for the treatment of complicated urinary tract infections (cUTI), including kidney infections (pyelonephritis) caused by the following susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Citrobacter freundii, Proteus* spp., and *Pseudomonas aeruginosa.* **As only limited clinical safety and efficacy data are currently available, reserve this antibiotic for use in patients who have limited or no alternative treatment options.**

Pathogen/ Isolate Source	Minimum Inhibitory Concentrations (mcg/mL)		Disk Diffusion Zone Diameter (mm)	
	S	R	S	R
Enterobacteriaceae	≤ 8/4	≥ 16/4	≥ 21	≤ 20
Pseudomonas aeruginosa	≤ 8/4	≥ 16/4	≥ 18	≤ 17

S = susceptible, R = resistance

CLINICAL PHARMACOLOGY:
Ceftazidime is a cephalosporin antibacterial drug with *in vitro* activity against certain gram-negative and gram-positive bacteria. Its bactericidal action is mediated through binding to essential penicillin-binding proteins, preventing cell wall biosynthesis. Avibactam is a non-beta lactam beta-lactamase inhibitor that increases the spectrum of activity of ceftazidime against resistant microorganisms by inactivating certain beta-lactamases. Avibactam inhibits the activity of Ambler class A, which includes ESBL and KPC, class C, which includes AmpC, and some class D enzymes, including oxacillinases. It is not active against metallo-β-lactamases due to the absence of the active-site serine residue.

PHARMACOKINETICS: The Cmax and AUC of ceftazidime increase in proportion to dose, making the half-life dose dependent (around 3 hours). Avibactam produces linear pharmacokinetics across the dose range studied (50 mg to 2000 mg) for single intravenous administration. Plasma levels are not raised significantly following multiple intravenous infusions of ceftazidime/avibactam 2.5 grams (2 grams ceftazidime and 0.5 grams avibactam) administered every 8 hours for up to 11 days in healthy adults with normal renal function. Less than 10% of ceftazidime is protein bound and the degree of protein binding is independent of concentration. The binding of avibactam to human plasma proteins is also low (5.7% to 8.2%) based on *in vitro* studies. Ceftazidime and avibactam are not appreciably metabolized and are mostly eliminated as unchanged drug via renal excretion.

ADVERSE REACTIONS: The most common adverse reactions include vomiting, nausea, constipation and anxiety. Decreased efficacy, seizures and other neurologic events were seen in patients with poor kidney function (renal impairment). Serious skin reactions and anaphylaxis may occur in patients with penicillin allergies.

COMPARATIVE SAFETY & EFFICACY: In the randomized, active-controlled, double-blind, multicenter, phase II trial for complicated intra-abdominal infections, adults with confirmed cIAI infection (including infection in the appendix, stomach/duodenum, colon or small bowel, gall bladder, liver or spleen) requiring surgical intervention and antibiotics were randomized 1:1 to receive intravenously either ceftazidime/avibactam (2g/0.5g every 8 hours) plus a separate infusion of metronidazole (500mg every 8 hours) or meropenem (1g every 8 hours) plus placebo every 8 hours for a minimum of 5 days and a maximum of 14 days. Favorable clinical response rates (complete resolution or significant improvement of the signs and symptoms of infection 2 weeks after the last treatment dose) were not significantly different between the two groups, 91.2 % (62/68) in ceftazidime/avibactam plus metronidazole arm and 93.4 % (71/76) in meropenem arm, (p = 0.60). For patients found to have one or more ceftazidime-resistant pathogens, a favorable microbiological response was achieved in 96.2% (25/26) of patients in the ceftazidime/avibactam plus metronidazole arm and 94.1 % (16 /17) of patients in the meropenem arm.

In the prospective, randomized, double-blind, multicenter phase II trial for complicated urinary tract infections, adults with pyelonephritis or other cUTI were randomized 1:1 to receive intravenously either ceftazidime/avibactam (500mg/125mg every 8 hours) or imipenem/cilastatin (500mg every 6 hours). Patient meeting pre-specified improvement criteria (afebrile for 24 hours, resolution of nausea and vomiting, improved signs and symptoms) after 4 days could be switched to oral ciprofloxacin. Patients were treated for a total of 7-14 days. Favorable microbiological response rates (eradication of pathogens in the urinary tract and no pathogens in the blood at a follow-up 5–9 days after completion of therapy) were not significantly different between the two groups,

70.4 % for the ceftazidime/avibactam arm and 71.4 % for the imipenem/cilastatin arm, (95 % CI difference of -27.2 % to 25.0 %). For patients found to have one or more ceftazidime-resistant pathogens, a favorable microbiological response was achieved in 85.7% (6/7) of patients in the ceftazidime/avibactam arm and 81.8 % (9 /11) of patients in the imipenem/cilastatin arm. Adverse effects were lower for the ceftazidime/avibactam arm than the imipenem/cilastatin arm, 67.1% and 76.1% respectively.

Both trials included a small number of participants and neither was statistically powered to demonstrate non-inferiority.

COMPARATIVE IN VITRO SUSCEPTIBILITY:
Ceftazidime/avibactam has demonstrated clinical efficacy similar to that of the carbapenems, plus extended susceptibility to some enzymes that confer resistance to carbapenems. It has demonstrated *in vitro* activity against Enterobacteriaceae in the presence of some beta-lactamases and extended-spectrum beta-lactamases (ESBLs) such as KPCs, AmpC, and certain oxacillinases. It also demonstrated *in vitro* activity against *P. aeruginosa* in the presence of some AmpC beta-lactamases, although the treatment of MDR *pseudomonas* is variable per these studies and susceptibility with E-testing would need to be confirmed.

CONTRAINDICATIONS: Ceftazidime/avibactam is contraindicated for patients with known serious hypersensitivity to ceftazidime, avibactam or other members of the cephalosporin class.

WARNINGS AND PRECAUTIONS: Caution should be used in patients with baseline CrCL of 30 to 50 mL/min as decreased efficacy was demonstrated in this population. Seizures and other neurologic events may also occur in patients with renal impairment. Clostridium difficile-associated diarrhea has been reported with almost all systemic antibacterial agents, including ceftazidime/avibactam. Additionally, hypersensitivity reactions may occur in patients with a history of penicillin allergy.

DRUG INTERACTIONS: *In vitro*, avibactam is a substrate of OAT1 and OAT3 transporters. As a potent OAT inhibitor, probenecid inhibits OAT uptake of avibactam by 56% to 70% *in vitro* and, therefore, has the potential to decrease the elimination of avibactam when co-administered. It does not inhibit or induce the major cytochrome P450 isomers.

DOSING & COST:

Estimated Creatinine Clearance (mL/min)[1]	**Recommended Dosage Regimen for AVYCAZ** Infuse each dose intravenously over 2 hours
greater than 50	2.5 grams (2 grams/0.5 grams) every 8 hours
31 to 50	1.25 grams (1 grams/0.25 grams) every 8 hours
16 to 30	0.94 grams (0.75 grams/0.19 grams every 12 hours
6 to 15[2]	0.94 grams (0.75 grams/0.19 grams) every 24 hours
Less than or equal 5[2]	0.94 grams (0.75 grams/0.19 grams) every 48 hours
1. As calculated using the Cockcroft-Gault formula. 2. Both ceftazidime and avibactam are hemodialyzable; thus, administer ceftazidime/avibactam after hemodialysis on hemodialysis days.	

Recommended duration of treatment:
- cIAI: 5 to 14 days
- cUTI including pyelonephritis: 7 to 14 days

Cost: $271.52 per vial (2 grams/0.5 grams)

INCIDENCE OF CARBAPENEMASE PRODUCING ENTEROBACTERIACEAE: 20 isolates (calendar year 2015)

CONCLUSION: Ceftazidime/avibactam is a novel combination of a cephalosporin with a beta-lactamase inhibitor that is FDA approved for the treatment of complicated UTIs and complicated intra-abdominal infections (with the addition of metronidazole). However, most use will likely be for the treatment of resistant organisms due to production of certain beta lactamase enzymes. This antibiotic offers a significant advantage over other beta lactams and beta-lactamase inhibitor combination products because it can be used for the treatment of infections caused by resistant organisms that produce ESBL, certain carbapenemases, including KPC and/or AmpC beta-lactamases. Additionally, ceftazidime-avibactam may be of clinical benefit in patients with resistant *P. aeruginosa* infections but an E-test would be needed to confirm susceptibility. Therefore, it is recommended at this time to add ceftazidime/avibactam to formulary with restriction to ID physicians and other clinically appropriate situations based on culture data and review by the antibiotic stewardship team.

FORMULARY REVIEW

GENERIC NAME: ECULIZUMAB

PROPRIETARY NAME: *SOLIRIS* (Alexion)

INDICATIONS: Eculizumab is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis and for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

CLINICAL PHARMACOLOGY: Eculizumab is a recombinant humanized monoclonal immunoglobulin antibody against terminal complement protein C5 that inhibits terminal complement activation. Eculizumab binds to the complement protein C5 with high affinity, inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. Eculizumab inhibits terminal complement-mediated intravascular hemolysis in patients with PNH. In aHUS, impairment in the regulation of complement activity leads to uncontrolled terminal complement activation, resulting in platelet activation, endothelial cell damage and thrombotic microangiopathy.

PHARMACOKINETICS: Doses of 600 mg weekly and 900 mg every other week maintained trough levels of eculizumab above 35 mcg/mL in the majority of patients. The pharmacokinetics of eculizumab have not been assessed in special populations defined by gender, race, age, or the presence of renal or hepatic function impairment.

ADVERSE REACTIONS: The most common adverse reactions observed in eculizumab-treated patients have included headache, nasopharyngitis, back pain, and nausea. Hypersensitivity reactions, including anaphylactoid reactions, are possible.

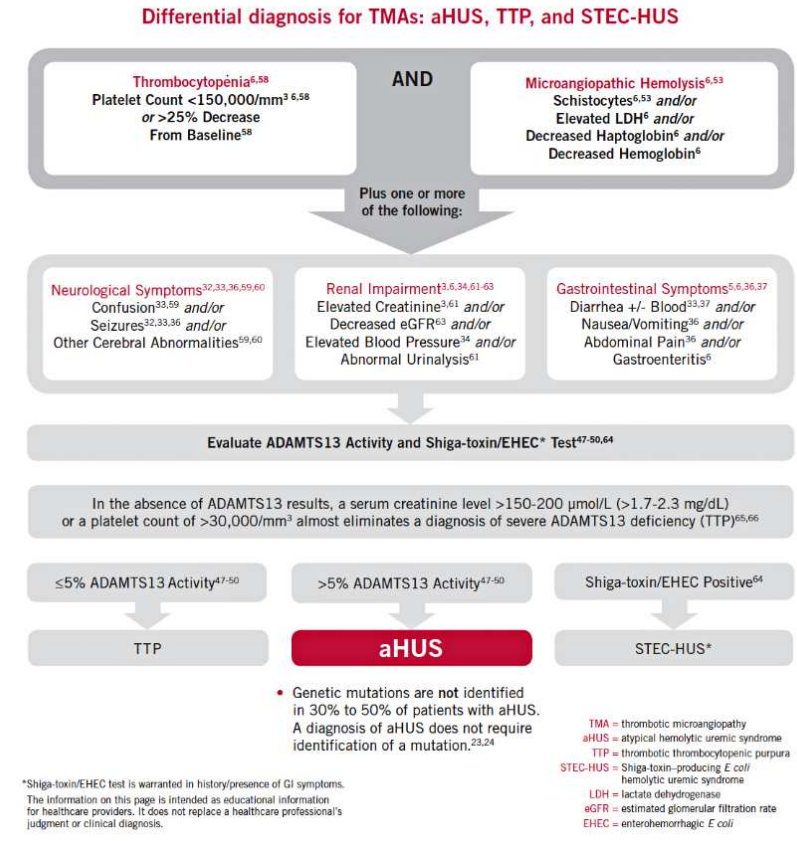
BLACK BOX WARNING: Life threatening and fatal meningococcal infections have occurred in patients treated with Solirs. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Due to this risk a REMS program has been established to control the prescribing and distribution of Soliris. Healthcare providers who prescribe Soliris must be specifically certified as part of the required FDA mandated REMS program.

DRUG INTERACTIONS: Drug interaction studies have not been conducted with eculizumab, and to date, no drug interactions have been described with eculizumab.

DOSING & COST:
PNH: 600 mg weekly x 4 weeks, followed 1 week later with 900 mg, then 900 mg Q 2 weeks thereafter.
aHUS: 900 mg weekly x 4 weeks, followed 1 week later with 1200 mg, then 1200 mg Q 2 weeks thereafter.

$6,086.66 per each 300 mg vial

TMA Diagnostic Pathway



FORMULARY REVIEW

GENERIC NAME: GLARGINE U-300 (300 units/ml)

PROPRIETARY NAME: *TOUJEO* **® (**Sanofi)

BACKGROUND: The U.S. Food and Drug Administration recently approved Sanofi's Toujeo® (glargine, U-300) insulin, a once daily, long acting basal insulin to treat type 1 and 2 diabetes. The company will lose its patent protection on Lantus® (glargine, U-100) this year which will likely result in a biosimilar product being available later this year. U-300 is a new formulation based on the insulin glargine molecule but has a flatter, more prolonged pharmacokinetic profile than Lantus® and offers the benefit of a smaller volume of injected dose.

INDICATIONS: Toujeo® Solostar (300 units/mL) is a long-acting insulin analog indicated to improve glycemic control in adults with diabetes mellitus, both type 1 and type 2. Toujeo®® is not approved or recommended for treatment of DKA or HHS.

CLINICAL PHARMACOLGY: Toujeo®® is a new, more concentrated formulation of insulin glargine. The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production.

PHARMACOKINETICS: Insulin glargine is administered via the subcutaneous route only. Insulin distributes widely throughout the body. A small portion is inactivated by peripheral tissues, but the majority is metabolized by the liver and kidneys. Insulin is filtered and reabsorbed by the kidneys; the plasma half-life of human endogenous insulin is approximately 5-6 minutes.

On average, the onset of glucose lowering activity after a single dose of Toujeo® 0.4, 0.6, 0.9 units/kg developed over 6 hours and mean serum insulin concentrations declined to the lower limit of quantitation by 16, 28, and > 36 hours, respectively. Steady state insulin concentrations are reached by at least day 5 of once daily subcutaneous administration of 0.4-0.6 units/kg. At steady state, the 24 hour glucose lowering effect of Toujeo® was approximately 27% lower and had a different distribution profile than an equivalent dose of Lantus®. The glucose lowering effect increased with each daily administration of Toujeo®.

COMPARATIVE EFFICACY: The efficacy of Toujeo® was studied in four, phase III, multi-centered, open-label, randomized clinical trials.

Edition I compared U300 with U100 (Lantus®) in 807 patients with type 2 diabetes, who were on basal insulin plus meal-time insulin at baseline. Participants had a mean age of 60 years, diabetes duration 16 years, BI 36.6 kg/m^2 , and HbA1c of 8.15%. The primary endpoint of improvement in HbA1c from baseline was equivalent between regimens; least square mean difference -0.00% (95% CI -0.11 to 0.11). Fewer participants reported one or more nocturnal hypoglycemic incidence in the U-300 vs the Lantus® group (36 vs 46%; RR 0.79 {95% CI 0.67-0.93}; P < 0.005).

Edition II compared U300 with U100 (Lantus®) in 811 patients with type 2 diabetes, who failed to control their blood glucose levels on basal insulin and oral medications. Patients were randomized 1:1 ratio to either Lantus® (n= 407) or Toujeo® (n=404) once daily in the evening, while continuing oral anti-diabetic agents. Baseline characteristics were similar between groups: mean age 58.2 years, duration of diabetes: 12.6 years; BMI: 34.8 kg/m^2; HbA1c: 8.24%; baseline insulin dose: 0.67 U/kg at baseline. The primary endpoint of improvement in HbA1c for baseline was met [least square mean change -0.57% (0.09) and -0.56%, respectively; difference -0.01% (95% CI: -0.14 to 0.120]. The percentage of participants with severe or confirmed (defined by plasma glucose ≤70 mg/dL) nocturnal hypoglycemia from month 3 to 6 was significantly lower with U300 vs. Lantus® [21.6% vs. 27.9%; relative risk (RR) 0.77 (95% CI: 0.61 to 0.99); p=0.038]. Over the 6-month treatment period, the incidence of any nocturnal hypoglycemia (% of participants with ≥1 event) was lower with U300 vs. Lantus® [30.5% vs. 41.6%; RR 0.73 (95% CI: 0.60 to 0.89)] as was the incidence of any hypoglycemic event at any time of the day (over a 24hour period) [U300: 71.5%; Lantus®: 79.3%; RR 0.90 (95% CI: 0.84 to 0.97)]. This result was also obtained across the entire 6-month study period, including the first 8 weeks of the trial

Edition III compared U300 with U100 (Lantus®) in 878 patients with type 2 diabetes not previously treated with insulin and uncontrolled on oral medications. The primary endpoint of improvement in HbA1c from baseline was met (-1.42%, [95% CI: -1.511 to -1.326] in the U-300 group and (-1.46% [95% CI: -1.555 to -1.367} in the Lantus® group). The rates of severe or nocturnal hypoglycemia, month 3 to month 6 were lower with U300 (15.5% for U300 vs. 17.4% for Lantus®), but unlike EDITION I and II, the reduction was not statistically significant. Overall incidence of any documented hypoglycemia during the entire 6-month treatment

period was numerically lower in the U300 group than in the Lantus®® group (49.9% vs. 55.3%; no statistical analysis was performed.)

Edition IV compared U300 with U100 (Lantus®) in 549 patients with Type 1 DM treated with basal and mealtime insulin. Mean age was 47.3 years and mean duration of diabetes was 21 years. 57% were male. 85.1% were Caucasian, 4.7% Black or African American. 4.7% were Hispanic. 32.2 percent of patients had GFR>90 mL/min/1.73m2. The mean BMI was approximately 27.6%. Primary endpoint showed similar reduction in HbA1c from baseline at 6 months (-0.40% [95% CI: -0.501 to -0.299] in the U300 group, and -0.44% [95% CI: -0.543 to - 0.344] in the Lantus® group). Confirmed and severe nocturnal hypoglycemia from month 3 to 6 was not pre-specified as a main secondary endpoint per study protocol. Patients treated with U300 used 17.5% more basal insulin than patients treated with Lantus®.

In all of the above mentioned studies, no difference in other adverse events were observed between U300 and Lantus®.

CONTRAINDICATIONS: Toujeo® is contraindicated in patients with hypersensitivity to Toujeo® or one of its excipients.

WARNINGS AND PRECAUTIONS: Never share Toujeo® SoloStar insulin pens between patients, even if the needle is changed. Hypoglycemia or hyperglycemia may occur with changes in insulin regimen, patients should monitor blood glucose often. Inadvertent use of the 300 units/mL concentration in place of the 100 units/mL could result in severe over dosage and hypoglycemia, care should be taken to observe the difference in strengths. Fluid retention and acute exacerbation of heart failure has occurred with concomitant use glargine insulin and thiazolidinediones (TZDs), consider dose reduction or discontinuation of TZD if heart failure occurs.

PREGNANCY and LACTATION: Insulin glargine is classified in FDA pregnancy risk category C. There are no adequate, well-controlled clinical studies of the use of insulin glargine in pregnant women. The extent of excretion of insulin glargine into breast milk is unknown; however, many drugs, including human insulin, are excreted into breast milk which then gets degraded by the gastrointestinal tract and likely not absorbed by a breast feeding infant.

ADVERSE REACTIONS (> or equal to 5%)
Hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema and weight gain

DRUG INTERACTIONS:

- Drugs that may increase the risk of hypoglycemia, closely monitor blood glucose:
  antidiabetic agents, ACE-inhibitors, ARBs, fibrates, fluoxetine, salicylates, somatostatin analogues, and sulfonamide antibiotics.
- Drugs that may decrease the blood glucose lowering effect: atypical antipsychotics, corticosteroids, diuretics, estrogens, niacin, protease inhibitors, and thyroid hormones.
- Drugs that may increase or decrease the blood glucose lowering effect: alcohol, betablockers, clonidine, and lithium salts.
- Anti-adrenergic drugs (e.g. beta blockers, clonidine, guanethidine, and reserpine) signs and symptoms of hypoglycemia may be reduced or absent.

DOSING:

TYPE 1**:** Initial: administer one-third to one-half of the total daily insulin requirements/dose subcutaneously once daily.

TYPE 2: In insulin naïve patients, 0.2 units/kg/dose subcutaneously once daily

The total daily dose ranges from 1-80 units. Titrate dosage every 3-4 days to achieve blood glucose control and A1C goals. The dose should be given at the same time every day, at any time. Expect that patients previously controlled on Lantus® will require a higher daily dose of Toujeo® to maintain the same level of glycemic control.

Conversion from Toujeo to 100 unit/ml basal insulin
In clinical trials patients on Toujeo were switched back to basal insulin 100 u/ml on a 1:1 basis and followed for 4 weeks. During week 1 post treatment for subjects previously on Toujeo, basal insulin doses were slightly reduced (reduced by up to 4 units [0.05 U/kg]). At the end of the 4 week post treatment follow-up period, the basal insulin dose slightly increased again (change from end of Toujeo treatment -2.29 units for basal insulin 100 unit/ml).

DOSAGE FORMS: 300 units/mL insulin glargine in 1.5 mL SoloStar disposable prefilled pen. Toujeo pen contains 450 units of Toujeo and each dose of Toujeo is one third the injection volume for the same dose of Lantun (glargine 100 units/ml). The Toujeo pen has been specially designed for Toujeo, therefore no dose conversion is required.

STORAGE INFORMATION:

	Not in-use (unopened)	In-use (opened)
1.5 mL Toujeo® Solostar disposable prefilled pen	Store in refrigerator, (36°F - 46°F (2°C - 8°C) Discard after the expiration date	28 days Room temperature only (Do not refrigerate)

COST: $106.54 per pre-filled insulin pen (450 units per syringe – 1.5 ml syringe; 300 units/ml)
Levemir cost: $105.80 per vial (1000 units per vial – 10 ml vial; 100 units/ml)

CONCLUSION:
Toujeo®, manufactured by Sanofi as the higher concentrated alternative to Lantus® insulin, will be released in April 2015 formulated as a prefilled pen. In the results of several phase three clinical trials, Toujeo® performed similarly to Lantus® in lowering blood glucose levels over a six month period, with a lower rate of nocturnal hypoglycemia. However, Toujeo® required 10-17.5% higher daily doses to achieve the same level of glucose control as Lantus®. In addition, there is a significant risk to patient safety in stocking U-100 products and U-300 products. Specific safety measures would need to be put in place to prevent an error in using one agent over the other and even with that in place; it is likely that errors will still occur. Although Toujeo® appears to be a promising new option for diabetic treatment the error potential and the lack of substantial clinical benefit leads to the conclusion that there is no significant benefits to its use over insulin glargine that would outweigh the extra costs incurred.

RECOMMENDATION:
1. Do not add Toujeo® to CHI drug formularies.
2. Continue to interchange patients on Lantus® and when available, Toujeo® to Levemir® for inpatients within CHI hospitals.
3. Assign non-formulary status at all CHI hospitals.
4. Assign non-stock status at wholesaler level for all CHI hospital accounts.

Calcitonin (Salmon) Medication Use Evaluation
Memorial Health System

A medication use evaluation was conducted to determine calcitonin usage trends at Memorial Hospital. A dramatic price increase of injectable calcitonin occurred in the previous year and based on normal usage will result in a significant increased annual expense for this product (see below for cost details). The purpose of this evaluation was to evaluate hypercalcemia management and identify opportunities to reduce inappropriate use of calcitonin while still properly managing hypercalcemic episodes. Data from 47 cases (43 patients) where ≥1 dose of calcitonin was administered were evaluated from calendar year 2014.

Cost – historical and current: $64.75 per vial (July 2014); $1,893 per vial (current price)
Estimated annual cost: $344,526 ($332,742 annual increase)

Background:
Hypercalcemia is a disorder commonly encountered in clinical practice. In severe cases of hypercalcemia, cardiovascular or renal complications may occur. Although there are diverse causes of hypercalcemia, the most common causes include malignancy and primary hyperparathyroidism. The indications for the treatment of acute hypercalcemia largely depend on the severity of the condition, acuity of development, and presence or absence of symptoms. Management of hypercalcemia should start with careful investigations of patient history, physical examination, ECG monitoring, and pertinent lab values. Currently available treatment options of hypercalcemia include fluid resuscitation, loop diuretics, bisphosphonates, glucocorticoids and calcitonin.

Treatment of hypercalcemia:

Severity	Clinical presentation	Treatment Options Preferred	Alternative Treatment Options	Comments
Mild **[Ca^{2+}]: 10 – 12 mg/dL**	▪ Cognitive impairments, abdominal pain, fatigue or muscle weakness	▪ Observation ▪ Hydration (oral) ▪ Increase mobility ▪ Discontinue offending agents	▪ N/A	▪ Asymptomatic or mildly symptomatic hypercalcemia do not require immediate treatment
Moderate **[Ca^{2+}]: 12 – 14 mg/dL**	▪ Cognitive impairments, abdominal pain, fatigue or muscle weakness	▪ Follow the same precautions as described in Mild hypercalcemia ▪ *Acute Ca^{2+} rise with symptomatic changes requires aggressive treatment*	▪ 0.9% NS 4 - 6 L in 24 hours *After rehydration,* ▪ Pamidronate 30 - 90 mg at 20 mg/h or Zoledronic acid (ZA) 4 mg over 15 min ▪ Furosemide IV 10 - 20 mg *if necessary*	▪ Usually well-tolerated chronically and may not require immediate treatment ▪ Prior to saline and diuresis treatment, determine and monitor fluid status in patients with heart or renal impairments. ▪ Bisphosphonate maximum effect occurs in 2-4 days
Severe **[Ca^{2+}]: > 14 mg/dL**	▪ May see life-threatening symptoms; ECG changes, pancreatitis	▪ 0.9% NS 4 - 6 L in 24 hours *After rehydration,* ▪ Pamidronate 30 - 90 mg at 20 mg/h or Zoledronic acid (ZA) 4 mg over 15 min ▪ Calcitonin 4 units/kg 6 - 12 hours for 24 hours ▪ Furosemide IV 10 - 20 mg *if necessary*	▪ Denosumab SQ 60 mg (in severe, symptomatic hypercalcemia of malignancy refractory to ZA)	▪ Require treatment regardless of symptoms ▪ Calcitonin is most beneficial in patients with symptoms and calcium >14 mg/dL ▪ Calcitonin - tachyphylaxis limits usefulness to ~ 48 hrs

Results:

Total hypercalcemia cases	**32**/47	Notes
▪ Mild ▪ Moderate ▪ Severe	▪ 7 cases (22%) ▪ 13 cases (41%) ▪ 12 cases (37%)	
Calcitonin as 1st line	**18**/32	Notes
▪ Mild ▪ Moderate ▪ Severe	▪ 6 cases ▪ 8 cases ▪ 4 cases	50% of the patients with mild-moderate hypercalcemia had a recent dose of bisphosphonate prior to hospitalization OR were not candidates for bisphosphonate due to renal insufficiency.
Bisphosphonate as 1st line	**9**/32	Notes
▪ Mild ▪ Moderate ▪ Severe	▪ 1 cases ▪ 5 cases ▪ 3 cases	In total of 20 cases, bisphosphonate was not given (3 mild, 5 moderate, and 12 severe cases).
Combined therapy as 1st line	**5**/32	Notes
▪ Mild ▪ Moderate ▪ Severe	▪ 0 case ▪ 0 case ▪ 5 cases	
Underlying Causes of Hypercalcemia	-	Notes
▪ Malignancy ▪ Hyperparathyroidism ▪ Other	▪ 17 cases ▪ 4 cases ▪ 11 cases	*Other* included immobilization, excessive Ca^{2+} intake, dehydration, AKI, sarcoidosis, adrenal insufficiency and unknown causes.
Other Indications	**-**	Notes
▪ Compression Fracture (pain) ▪ Bone fracture (pain)	▪ 9 cases ▪ 6 cases	
Total Dose (Unit) Used	**35318 units**	Notes
▪ Mild ▪ Moderate ▪ Severe ▪ Compression fracture/bone fracture	▪ 7100 units ▪ 13612 units ▪ 8406 units ▪ 6200 units	Compression fracture/bone fracture doses all ordered by hospitalists
Average doses administered per patient	**Doses per patient**	Notes
▪ Mild ▪ Moderate ▪ Severe ▪ Compression fracture/bone fracture	▪ 4.9 ▪ 5 ▪ 3 ▪ 2.8	Notable outlier: patient with moderate hypercalcemia secondary to hyperparathyroidism treated with 24 total doses (hospitalist).

Summary & Conclusion:

Overall data summary:

Approximately 70% of patients prescribed calcitonin in the hospital were utilized for treatment of mild, moderate, or severe hypercalcemia. Overall, calcitonin was used more frequently as a 1st line treatment than bisphosphonate or combination therapy. The most commonly seen underlying cause of hypercalcemia was malignancy. Thiazide diuretic use was implicated as a possible precipitating cause of hypercalcemia in 4 patients requiring calcitonin therapy. There were 15 cases where calcitonin was administered for patients with recent compression fracture or other recent fracture.

Use in mild & moderate hypercalcemia:
The data shows that in patients with mild to moderate hypercalcemia use of calcitonin was limited mostly to patients with hypercalcemia of malignancy and hyperparathyroidism. In most situations calcitonin was used initially due to the patient recently receiving a bisphosphonate as an outpatient or in patients with existing renal dysfunction for whom initial therapy with a bisphosphonate may not be appropriate. However, approximately 50% of the patients with mild to moderate hypercalcemia were initially treated with calcitonin and potentially could have been treated with a bisphosphonate instead as an initial treatment. The length of therapy was variable for this patient population although the longer durations of therapy were most often associated with hospitalist prescribers.

Use in severe hypercalcemia:
Severe cases ($[Ca^{2+}]$ > 14 mg/dL) composed 38% of hypercalcemic cases. The use of calcitonin in patients with severe hypercalcemia appears to be largely appropriate per the available treatment guidelines and either combination therapy (bisphosphonate + calcitonin) or initial therapy with bisphosphonate was utilized prior to calcitonin. The situations in which calcitonin was used initially as monotherapy were all appropriate due to each of these patients presenting with acute renal failure and not initially candidates for bisphosphonate therapy.

Use in non hypercalcemic patients (compression fracture/bone fracture):
Approximately 32% of patients prescribed calcitonin were utilized for patients NOT presenting with hypercalcemia. The majority of this use was for patients with recent osteoporotic vertebral compression fractures. There is some data available that suggests that when utilized for 2-4 weeks post fracture that calcitonin provides a benefit in regards to pain control. Additionally, although some of these patients only received 1-2 doses of calcitonin many received multiple days of therapy for this off label indication. Calcitonin prescribing for this indication was ordered entirely by hospitalist physicians.

Conclusion:
Calcitonin rapidly lowers calcium level upon its administration. However, it is considered to be less efficacious compared to bisphosphonates. Its hypocalcemic effect usually diminishes after 1 or 2 days of administration. Due to its unique characteristics, calcitonin is considered most beneficial when used in symptomatic patients with severely elevated calcium (>14 mg/dL) whose condition is not controlled with general measures (rehydration and loop-diuretic diuresis). Bisphosphonates are also a potent agent in managing hypercalcemic episodes especially in patients with malignancy. These agents normally lower calcium level within 2 to 3 days of initiation and provides sustained normo-calcemic effects. Although it is known to be well-tolerated, however, use in patients with renal impairment (CrCl < 35 mL/min) is contraindicated.

Potential opportunities to reduce calcitonin use while properly managing patients have been identified. Due to the recent significant price increase for calcitonin it is essential that the use of calcitonin injection is appropriate to ensure cost effective treatment of patients with hypercalcemia. This MUE has shown that although much of the use of calcitonin were appropriate some opportunities to reduce use do exist. Some patients with mild to moderate hypercalcemia could have potentially received initial therapy with a bisphosphonate rather than receiving calcitonin as the initial treatment choice. Additionally, due to the reduced effect that is seen with prolonged calcitonin administration the duration of use should be monitored closely for all patients receiving calcitonin and decisions to potentially discontinue therapy should be considered following 2 days of therapy.

The use of calcitonin in non-hypercalcemic patients need to be closely re-evaluated to determine if this is a cost effective therapy in light of the recent price increase for this agent. Due to the lack of large, well designed studies demonstrating benefit in this population the use of injectable calcitonin for patients with recent fractures should be re-examined and education provided to these prescribers.

Antibiotic Administration Times: Septic Patients in the ED

Overview

- Surviving Sepsis Guidelines – Antibiotic Therapy
  - Begin IV antibiotics within one hour.
  - Use broad spectrum coverage initially.
    - Reassess coverage within 72 hours and narrow based on C&S results
  - Continue broad spectrum coverage in neutropenic patients & patients with MDR infections, regardless of C&S results.
    - Consider combination therapy

SIRS:
Temperature > 100.4ºF or < 96.8ºF
HR > 90 bpm
RR > 20 rpm OR $PaCO_2 \leq 32$ mmHg
WBCs ≥ 12k or ≤ 4k

SEPSIS = ≥ 2 SIRS criteria + documented or suspected infection

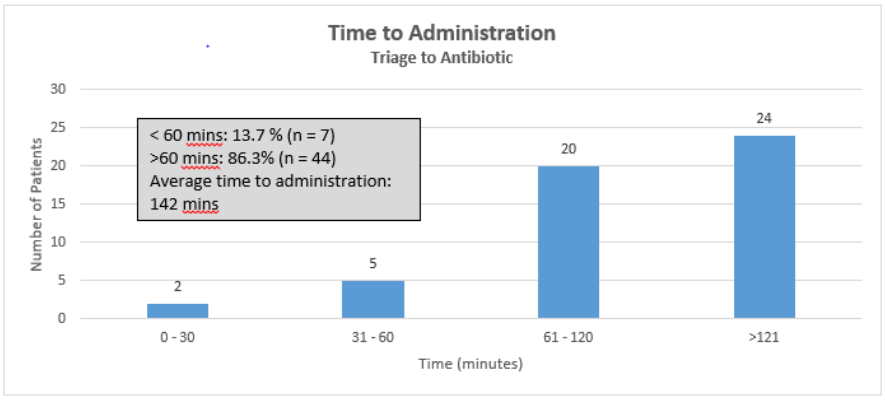
- Empiric Antibiotic Treatment Reduces Mortality in Severe Sepsis and Septic Shock From the First Hour: Results From a Guideline-Based Performance Improvement Program
  Source: Ferrer R, Martin-Loeches I, Phillips G, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. Crit Care Med. 2014;42(8):1749-55.
  - Mortality increases linearly with each hour delay in antibiotic administration.
    - Due to antibiotic only or is this a "surrogate marker" for overall quality of care?
  - Treat sepsis more like an acute MI or stroke instead of treating it as a less severe condition.

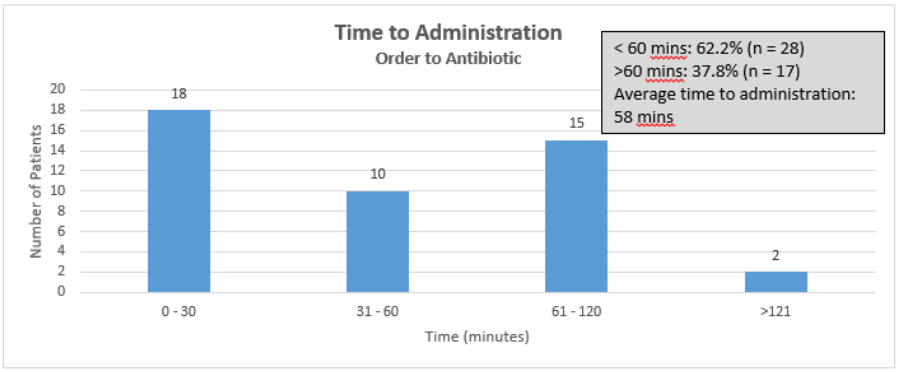
Data Collection

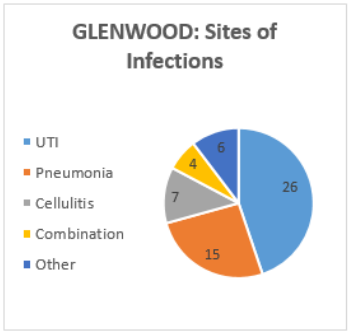
Data was evaluated from a random sampling of patients with sepsis-related DRG codes (DRG codes 870, 871, and 872) from January 2014 through December 2014. Patients were included in the analysis if a sepsis-related DRG code was present and the patient met SIRS criteria upon presentation to the ED. The presence of severe sepsis (SIRS + organ dysfunction) was not specifically evaluated as inclusion criteria for this evaluation and any patient with at least 2 positive SIRS criteria upon ED admission was included. The patient's triage time, time of first antibiotic order, and time of antibiotic administration were collected to assess the time to initial empiric antibiotic administration. Additionally, the suspected site of infection and initial antibiotic choice were examined to further evaluate the appropriateness of initial antibiotic selection. Patients with incomplete data such as missing documented antibiotic administration time were excluded from the data collection.

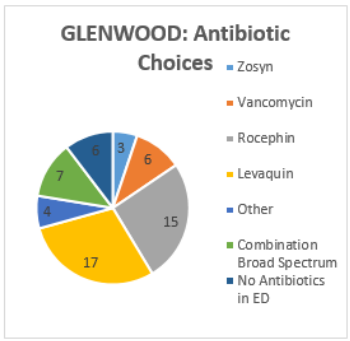
- Time period: January 2014 – December 2014
- Patients:
  - Glenwood – 58
    - Average LOS: 5.6 days
      - Range: 1 – 16
    - Average age: 67
      - Range: 20 – 94
    - Average BMI: 29.4
      - Range 17.8 – 59.3
  - Hixson – 30
    - Average LOS: 6.5 days
      - Range: 2 – 28
    - Average age: 68
      - Range: 25 – 98
    - Average BMI: 29.9
      - Range 18.4 – 89.5

Glenwood

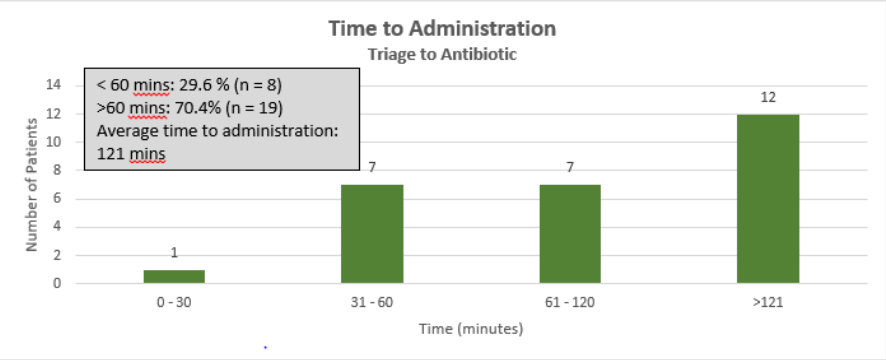

Time to Administration
Triage to Antibiotic
< 60 mins: 13.7 % (n = 7)
>60 mins: 86.3% (n = 44)
Average time to administration: 142 mins
Number of Patients
Time (minutes)
0 - 30
31 - 60
61 - 120
>121
2
5
20
24

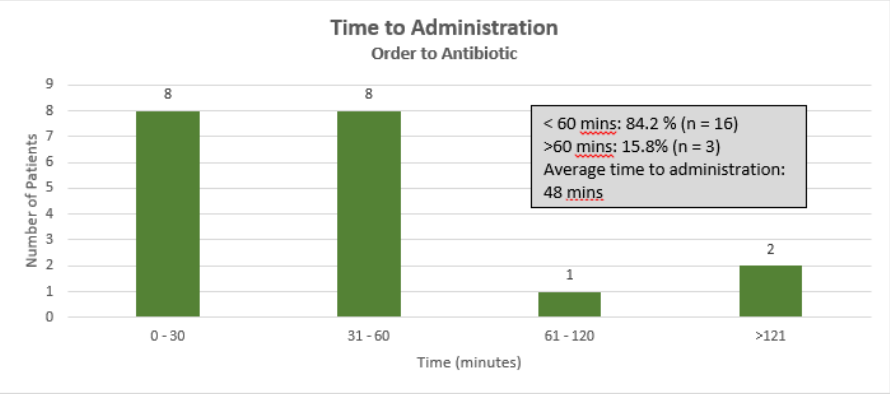

Time to Administration
Order to Antibiotic
< 60 mins: 62.2% (n = 28)
>60 mins: 37.8% (n = 17)
Average time to administration: 58 mins
Number of Patients
Time (minutes)
0 - 30
31 - 60
61 - 120
>121
18
10
15
2

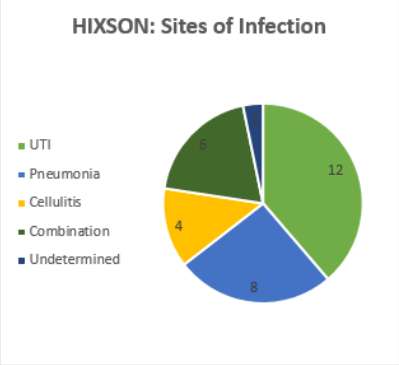

GLENWOOD: Sites of Infections
UTI
Pneumonia
Cellulitis
Combination
Other
26
15
7
4
6

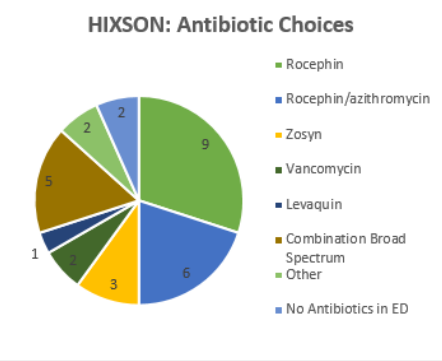

GLENWOOD: Antibiotic Choices
Zosyn
Vancomycin
Rocephin
Levaquin
Other
Combination Broad Spectrum
No Antibiotics in ED
3
6
15
17
4
7
6

Hixson


Time to Administration
Triage to Antibiotic
< 60 mins: 29.6 % (n = 8)
>60 mins: 70.4% (n = 19)
Average time to administration: 121 mins
Number of Patients
0 - 30
31 - 60
61 - 120
>121
Time (minutes)


Time to Administration
Order to Antibiotic
< 60 mins: 84.2 % (n = 16)
>60 mins: 15.8% (n = 3)
Average time to administration: 48 mins
Number of Patients
0 - 30
31 - 60
61 - 120
>121
Time (minutes)


HIXSON: Sites of Infection
UTI
Pneumonia
Cellulitis
Combination
Undetermined


HIXSON: Antibiotic Choices
Rocephin
Rocephin/azithromycin
Zosyn
Vancomycin
Levaquin
Combination Broad Spectrum
Other
No Antibiotics in ED

Discussion:

Time to initial antibiotic administration:

Time to initiation of effective antimicrobial therapy has been shown to improve sepsis related mortality and LOS. The most recent *Surviving Sepsis Campaign* guidelines also include a recommendation that IV antibiotic therapy should be started within the first hour of recognition of severe sepsis after initial cultures have been obtained. The sampling of data collected from patients in this review reveal that some opportunities for shortening the time to initial antibiotic administration do exist at both campuses. Overall (including both facilities), 78% of all patients received their first dose of any antibiotic greater than 60 minutes following their initial triage time. Additionally, once the initial antibiotic is ordered by the ED physician, 31% of patients were administered the first dose of antibiotic greater than 60 minutes following the initial order being written. The longer time period between the triage time and the initial antibiotic administration likely represents a delay in the initial infectious diagnosis being identified following triage and will likely be harder to improve unless routine initial screening can be performed to expedite the identification of patients with SIRS criteria suggesting a diagnosis of sepsis. In contrast, the delay in the time to administration following the physician order may be an area that can be targeted for process improvement and better coordination of care to ensure that the nurse is aware that an antibiotic has been ordered for a patient with suspected sepsis.

Initial antibiotic choice

The evaluation demonstrated a wide variability in initial antibiotic prescribing based on the suspected site of infection. Urinary tract infection and pneumonia were the two most commonly encountered sites of infection. However, within these two disease states there was significant variation in the choice of initial antibiotic. In many situations the initial empiric antibiotic was appropriate based on the patient's suspected source of infection, however some patients were prescribed therapies that may not have been optimal based on local resistance patterns, etc. (Example: levofloxacin utilized for patients presenting with uro-sepsis) Per the most recent sepsis guidelines "initial empirical anti-infective therapy should include one or more drugs that have activity against the likely pathogens and the choice of drugs should be guided by the susceptibility patterns of microorganisms in the community and in the hospital." Based on the data included in this review a standardized reference and/or protocol highlighting optimal initial antibiotics per disease should likely be developed and utilized to best ensure appropriateness of initial antimicrobial treatment for patients with sepsis.

Exparel (liposomal bupivacaine)

Preliminary data – orthopedics

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Surgeon	Procedur	Group	Data	Nar.Block	NO BLOCK	Grand Total
HARTLEY	TKA	Control	Average Pain 1st 24 hrs		5.5	5.5
			Average Pain 2nd 24 hrs		4.0	4.0
			Average Pain 3rd 24 hrs		4.2	4.2
			Average Pain at 48 hrs		4.7	4.7
			Average Pain at 72 hrs		5.0	5.0
			Average Total Morphine Eqv (mg)		274.6	274.6
			Count of Procedure		22	22
			Average of Length of stay (midnights)		2.3	2.3
			Average of Length of stay (hours)		57.4	57.4
			Average Morphine Eqv per Hour (mg/hr)		4.8	4.8
		Exparel	Average Pain 1st 24 hrs	4.4	4.9	4.7
			Average Pain 2nd 24 hrs	3.8	3.8	3.8
			Average Pain 3rd 24 hrs	4.1	3.5	3.7
			Average Pain at 48 hrs	4.1	4.3	4.2
			Average Pain at 72 hrs	4.4	4.3	4.3
			Average Total Morphine Eqv (mg)	189.8	180.8	185.5
			Count of Procedure	37	34	71
			Average of Length of stay (midnights)	2.1	2.3	2.2
			Average of Length of stay (hours)	53.8	58.7	56.2
			Average Morphine Eqv per Hour (mg/hr)	3.7	3.1	3.4
		Naropin Cocktail	Average Pain 1st 24 hrs	3.8		3.9
			Average Pain 2nd 24 hrs	4.1		4.1
			Average Pain 3rd 24 hrs	6.5		6.5
			Average Pain at 48 hrs	3.9		4.0
			Average Pain at 72 hrs	5.1		5.1
			Average Total Morphine Eqv (mg)	154.1		156.7
			Count of Procedure	20		21
			Average of Length of stay (midnights)	2.0		2.0
			Average of Length of stay (hours)	51.0		51.0
			Average Morphine Eqv per Hour (mg/hr)	3.2		3.2

Surgeon	Procedur	Group	Data	Exp.Block	Nar.Block	Grand Total
BALLARD	TKA	Exparel	Average Pain 1st 24 hrs	4.2	3.4	4.1
			Average Pain 2nd 24 hrs	3.7	3.2	3.7
			Average Pain 3rd 24 hrs	3.6	3.3	3.5
			Average Pain at 48 hrs	3.9	3.2	3.8
			Average Pain at 72 hrs	3.9	3.2	3.7
			Average Total Morphine Eqv (mg)	158.7	148.9	157.0
			Count of Procedure	19	4	23
			Average of Length of stay (midnights)	2.3	2.3	2.3
			Average of Length of stay (hours)	55.9	57.8	56.3
			Average Morphine Eqv per Hour (mg/hr)	3.0	2.7	3.0

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Memo

Date: February 11, 2015

To: National and Market Pharmacy Leaders; National Heart and Orthopedic Care Service Line Leaders; Physician and Nursing Executive Councils

Cc: Market Presidents; SVPs of Operations; Clinical Supply Chain Leaders, Physician Executive Council, Pharmacy Directors, Cardiovascular and Orthopedic and Spine Service Line Leaders

From: CHI Clinical Leadership Council and National Pharmacy Services Leadership

RE: Update regarding use of Exparel® and Ofirmev®

On November 17, 2014, The Clinical Leadership Council (CLC) approved an extension of the pause through February, 2015 to allow further data analysis and a more holistic approach in understanding use of the agents within CHI markets. Use of these agents related to clinical outcomes such as length of stay, complications, extubation times, readmissions and pain management needed to be evaluated.

Over past few months, the Orthopedic and Spine Service Line, in partnership with Pharmacy, Clinical and Operational Excellence and the Analytics Center of Excellence teams, conducted an extensive data review and gathered surgeon input. Based on discussions and data findings, there is no clear quantitative evidence of superior therapeutic value of Exparel®. Though there may be benefit for total knee replacement surgery, the considerable variation between hospitals and surgeons for length of stay, readmissions and complications made any correlation difficult to determine. Adopting a standard care pathway for total knees is clearly our greatest opportunity for overall improvement of clinical outcomes and total cost of care. To move this work forward, the CLC approved the following:

1. Prohibit use of **Exparel®** in all procedures except for total knee, bunion and hemorrhoid surgeries. Use of Exparel® is prohibited for all other orthopedic procedures, including hip replacement, and all non-orthopedic procedures not listed above.

2. The Orthopedics and Spine Service Line further agreed:
   - To develop a care pathway for primary arthroplasty procedures (DRG 470) across all markets, and provide oversight for the use of Exparel with accountability metrics developed in partnership with the Center of Operational and Performance Excellence teams, and
   - Adopt a market pharmacy distribution methodology for compliance.

Regarding the use of **Ofirmev®**, the pause remains in effect. A Cardiovascular Service Line workgroup is being convened to follow the same data analysis and physician engagement approach that the Orthopedic and Spine Service Line followed with a recommendation to the CLC. Clinical standards to decrease the significant variance that exists with key outcome metrics and an ongoing oversight process for accountability and therapeutic review will need to be defined.

For questions or comments, please contact Mike Kimbel, Administrative VP, CHI Orthopedic Care or John Cicero, interim VP, CHI Pharmacy Services.

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Adverse Drug Reaction (ADR) Summary
1st Quarter (FY15) July-December 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.

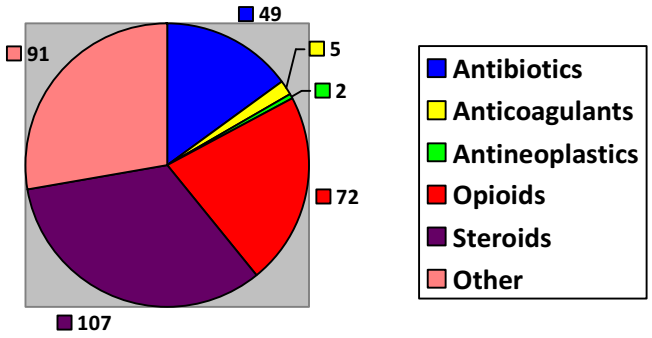
Category 3: A serious or rare ADR which has abnormal characteristics compared with published reports of the reaction (e.g. heparin induced platelet aggregation resulting in limb amputation). ADR's from this category should be reported to the manufacturer and/or the FDA (MedWatch or the Vaccine Adverse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

Inpatient: 330 (43%)
Prior to hospitalization: 769 (57%)
Total: 551

Category 1: 868
Category 2: 205
Category 3: 1

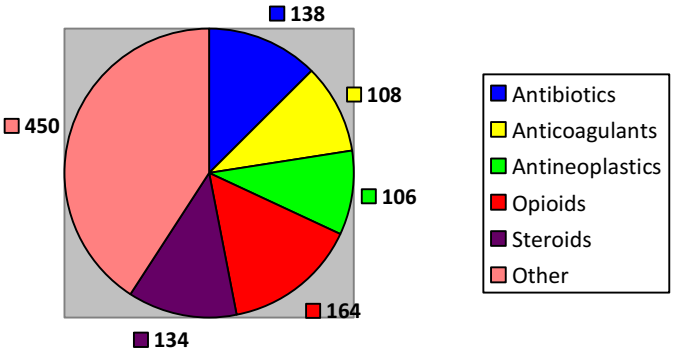
Category 3 to discuss: 86 yo male who developed conjunctivitis symptoms, then developed a desquamating, full body rash. He was followed initially by an ophthalmologist who expressed concern for Stevens-Johnson reaction, who then referred him to primary care for further evaluation. He was immediately 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 moity 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 (16) was most common---AKI. Others included rash (12), nausea (6), and diarrhea (10).
Anticoagulants: Heparin (2) and Warfarin (3) were most common---nose bleed and hematuria.
Narcotics: Reactions included AMS (34), nausea, constipation, and respiratory distress (12). One patient was transferred to a higher level of care.
Steroids: Hyperglycemia.
Other: Mostly blood pressure or arrhythmia related (20)

Total ADRs



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

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CHI MEMORIAL Policy – Procedure		
SUBJECT: Pharmacy and Therapeutics Committee **DEPARTMENT(S): Administrative**	**Policy No:** **Page 1 of 1**	
Effective Date:	**Approved:**	
This replaces: N/A	**Review dates:**	

Purpose: The primary purposes of the Pharmacy and Therapeutics Committee (P&T) are formulary management and education.

Policy: The Pharmacy and Therapeutics (P&T) Committee establishes and maintains CHI Memorial and CHI Hixson hospital formularies and assists in the formulation of policies-procedures regarding the evaluation, selection, procurement, distribution, safety procedures, and other matters relating to the use of medications. The Committee assists in the formulation of programs designed to meet the needs of the professional staffs for complete current knowledge on matters and practices related to medications.

Procedure:

Authority – The P&T Committee members consist of the Director of Pharmacy, Pharmacy Clinical Coordinator, representatives from selected disciplines of medicine, administration, nursing, education and selected ancillary departments. The Committee reports to the Medical Executive Committee (MEC) on matters that affect all disciplines of medical staff.

Accountability – The P&T Committee will meet a minimum of four times per year (or quarterly) at a date and time convenient for the majority of its members. Ad-hoc Committee meetings occur on an agenda driven basis at a mutually convenient time and place for those attending. The Ad-hoc Committee(s) reports findings and recommendations to the P&T Committee.

Functions – The Committee functions may include, but are not limited to:

- Selects drugs for formulary and maintains by evaluating relevant clinical data and evidence-based medicine
- Completes class reviews of medications to ensure ideal, evidence-based formulary selections are in place
- Selects drugs available for stock and in Automated Dispensing Machines (ADMs) on nursing units and other applicable areas
- Establishes standards regarding the use and control of drugs, investigational drugs, etc.
- Reviews reported adverse reactions to drugs administered
- Evaluates medical records for drug use evaluations or patient therapy reviews periodically
- Investigates problems and makes recommendations related to drug use
- Plans and establishes suitable educational programs for the professional staffs on pertinent matters relating to drugs and their use
- Investigates problems involving the distribution of drugs and dissemination of drug information

Formulary Requests – Formulary requests will be requested via a Formulary Addition Request Form for drugs in which the physician would like to be considered for formulary (see Appendix A). The requestor must also submit a Disclosure Statement with the Formulary Addition Request Form (see Appendix B). The Pharmacy Department Clinical Lead (or designee) will receive and assign the request to be presented at the most appropriate P&T Committee meeting. The requestor (or designee) must be present at the assigned Committee meeting. Once assigned to a Committee agenda, a formulary evaluation will be conducted by assigned members. The evaluation shall include, but not be limited to, monograph production with a literature evaluation, a Safety and Efficacy Evaluation and an Operational/Safety addendum as necessary.

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CHI MEMORIAL
Pharmacy and Therapeutics Committee
FORMULARY ADDITION REQUEST FORM (Appendix A)

Generic/Brand Name	
Form and Strength	
Manufacturer	

1. Is this a formulary ☐ Addition or ☐ Deletion?

2. Specific pharmacologic or mechanism of action and use of drug which warrants its addition or deletion:

3. Reason(s) why this drug should be included on the Hospital Formulary (therapeutic, safety, cost savings, etc.): *Omit if Deletion*

4. Should this drug replace drug(s) currently on formulary? ☐Yes ☐No

   If yes, which drug(s)_____

5. Please list criteria for appropriate use:

6. List pertinent literature references and attach copies, if available.

Requester Information

Name	
Department	
Phone	
E-mail	

Signature _____ Date _____
(You must also complete and sign the Disclosure Statement)

Return this completed form with the completed Disclosure Statement to Patrick Ellis in the CHI Memorial Department of Pharmacy. If you have any questions, please contact Patrick Ellis at 7461 or patrick_ellis@memorial.org

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CHI Memorial
DISCLOSURE STATEMENT (Appendix B)

ALL PRESENTERS AND/OR REQUESTERS MUST SIGN THIS FORM

Having an interest or affiliation with one or more commercial organization does not prevent a requester from making a formulary request; however, the relationship(s) must be made known to the P&T Committee in advance.

Please complete Part I or Part II, as applicable.

I. **I do not have** any financial interest(s) or affiliation(s) with any commercial organizations that might affect my formulary request(s)/discussion(s).

Name (Printed) _____

Signature _____ Date _____

II. **I have** a financial interest/arrangement with one or more commercial organizations, as described below, that may be pertinent to formulary submission(s) or discussion(s).

Affiliation/Financial Interest	**Commercial Organization(s)**
Grant/Research Support	_____
Consultant	_____
Speaker's Bureau	_____
Stock Holder	_____
Other Financial Interest(s)/Affiliation(s)	_____

Name (Printed) _____

Signature _____ Date _____

Return this completed form with the completed Disclosure Statement to Patrick Ellis in the CHI Memorial Department of Pharmacy. If you have any questions, please contact Patrick Ellis at 7461 or patrick_ellis@memorial.org