Pharmacy & Therapeutics Committee Meeting
Private Dining Room
August 14, 2014 7:00 a.m.

Agenda Items	Individual Responsible
1. Call to Order	Richard Pesce, MD
2. Approval of February, 2014 Minutes	Richard Pesce, MD
3. Therapeutic Interchanges and Formulary Decisions	Page
A. Tanzeum® (albiglutide)	Patrick Ellis, Pharm.D……..5
B. Sivextro® (tedizolid)	……..6
C. Exparel® (liposomal bupivacaine)	Nathan Schatzman, MD……7
D. Dulera® (mometasone/formoterol inhalation)	Patrick Ellis, Pharm.D…..…..8-9
E. Zohydro® (extended release hydrocodone)	…..10
F. Entyvio® (vedolizumab)	……..11
4. MUE	
A. Kcentra® (prothrombin complex concentrate)	Patrick Ellis, Pharm.D…....12-13
5. Policy, Procedure & Protocols	
A. Surgical Prophylaxis – Antimicrobial Dosing	Mark Anderson, MD…..……...
B. Cefazolin Dose Optimization	Patrick Ellis, Pharm.D...…....14
C. Metronidazole & Ciprofloxacin Standardized Dosing	….15
6. Nutrition Support Team	
A. Pep-uP Volume Based Feeding Protocol	….....Brian Jones, RD…..……16-21
7. Adjournment	

Next Meeting will be October 9, 2014 at 7:00am in the Private Dining Room

CATHOLIC HEALTH INITIATIVES
Memorial Health Care System

PHARMACY AND THERAPEUTICS COMMITTEE

DATE: June 12, 2014 CALLED TO ORDER: 7:00 A.M.
LOCATION: Private Dining Room ADJOURNED: 7:35 A.M.

Members Present:			**Members Absent**:		**Guests**:
Richard Pesce, M.D.	Karen Babb, Pharm.D.	Brian Jones, RD, LDN	Allen Atchley, M.D.	Don Jones, RPh	Rachel Kile, Pharm D Resident
Mark Anderson, M.D.	Vickie Burger, Lab	Nan Payne, RN	Nathan Chamberlain, M.D.	Keith Lockwitz, RN	Sarah Smith, Pharm D Resident
Samuel Currin, M.D.	Michelle Denham, RN	Melissa Roden, RN	Kevin Lewis, M.D.	Deb Moore, RN	
David Dodson, M.D.	Patrick Ellis, Pharm.D.	Hannah Walker, RN	William Oellerich, M.D.	Beverly Slate, Supply Chain	
Nathan Schatzman, M.D.	Rodney Elliott, CPT	Danine Watson, RN	Michael Stipanov, M.D.	Elvie Smith, RN	
	Patrick Hagan, Finance	Sandy Vredeveld, DPh			
	Lila Heet, Pharm.D.				

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 April 10, 2014 minutes were approved as submitted.		Complete
Therapeutic Interchanges and Formulary Decisions	The following medications were reviewed: 1. **Exparel ® (liposomal bupivacaine) –** Exparel is a liposomal injection of bupivacaine, an amide local anesthetic, indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia. CHI's clinical leadership council has made a corporate mandate to pause the expansion of use and any potential trials that would increase use until further corporate evaluation can be made.	1. Information	Complete
	2. **Ultiva® (remifentanil)** – Used as an analgesic/anesthetic agent for use during induction and maintenance of general anesthesia for surgical procedures. Dr. Schatzman explained that remifentanil could be a useful for agent as part of a total IV anesthesia regimen (TIVA) for shorter procedures in which anesthetic gases are not used or used at lower volumes and when intra-operative neurophysiological monitoring is needed (spinal surgery, carotid procedures, etc.). A cost analysis was performed and it will represent a cost increase per case as compared to Precedex® and use would need to be limited to shorter procedures (≤ 2 hrs).	2. Approved for use in cases 2 hrs or less and for cases in which remifentanil provides advantages over standard therapies. Use will be monitored and re-evaluated to ensure appropriate use.	Complete
	3. **Zontivity® (vorapaxar)** – Indicated for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction or with peripheral arterial disease. It was the recommendation of Drs. Atchley, Negus, and Thel to not approve this agent to formulary due to safety concerns (bleeding).	3. Not approved.	Complete
	4. **Anoro Ellipta® (umeclidimium/vilanterol) –** Indicated for the long-term, once-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease, including chronic bronchitis and/or emphysema. This is currently the only long acting anti-muscarinic (LAMA) – long acting bronchodilator (LABA) combination product on the market. It was recommended that until other agents are available to add this drug to formulary to provide continuity of therapy for patients utilizing this as a	4. Approved	Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	maintenance therapy for COPD. This class will be re-evaluated again once other combination products are FDA approved.		
	5. **Outpatient IV iron formulary –** Currently all IV iron products are available for outpatient use at MHCS. After a comparison of formulations of iron and considering reimbursement for each, it was recommended by CHI to remove sodium ferric gluconate and iron sucrose from outpatient formularies and only allow the use of Infed® (iron dextran) and Feraheme® (ferumoxytol) for outpatient use. Sodium ferric gluconate and iron dextran will still be on formulary for inpatient use.	5. Approved.	Complete
	6. **Namenda XR® Formulary Interchange –** The traditional immediate release formulation of Namenda (memantine) is currently the only memantine formulation on hospital formulary. A newer extended release formulation is now available but the upcoming generic availability of the immediate release formulation will offer significant savings as compared to the XR product. It was recommended to utilize a formulary interchange and to automatically convert all XR orders to a therapeutically equivalent dose of the standard product.	6. Approved	Complete
Medication Use Evaluation	• **Tranexamic Acid – Total Joint Replacement** – MUE evaluating 39 patients receiving tranexamic acid (TXA) was completed to evaluate the use of this agent in total joint replacement. The average number of blood transfusions, use of drains (blood conversation systems), and post op hemoglobin drop were all decreased for the patients that received TXA. When taking into consideration the elimination of the drain, the use of TXA resulted in an approximate savings of $62 per patient (drain cost vs. drug cost). This evaluation does demonstrate that TXA is an effective strategy to potentially decrease blood loss associated with TJR and possibly result in cost savings if post operative drains can be eliminated.	Information	Complete
Medication Safety	• **ADR Review (3rd QTR FY 14)–** No significant adverse drug reactions were reported for this evaluation period that require reporting to the FDA's MedWatch program. Overall ADR data reviewed and no significant trends or safety concerns were noted for this evaluation period. • **Anti-XA assay (LMWH) –** Patrick reviewed information related to the trialed use of utilizing the Anti-XA assay for evaluating treatment dose enoxaparin safety in patients > 70 years of age. The majority of patients in which anti-XA was used to evaluate enoxaparin dosing revealed elevated anti-XA assays which has raised questions regarding the usefulness of routine monitoring in this patient population. Although some studies have reported that high anti-XA levels were associated with an increased bleeding risk, several other studies have failed to show a relationship between anti-XA levels and bleeding. Due to the conflicting data on the usefulness of routine LMWH dose monitoring as well as the number of elevated levels it was recommended to revert back to the previous policy for anti-XA monitoring of treatment dose enoxaparin (patient	Information.	Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
	weight > 190 kg, CrCl < 20 ml/min). Patrick discussed this with Dr. Stipanov and he was in agreement.		
Policy, Procedure & Protocols	• **Fentanyl IVP –** IVP fentanyl is currently restricted to the following areas (ED, OR/procedural areas, PACU, CSSU, and ICU's. Dr. Mull requested that the committee review this restriction and consider allowing fentanyl to be used as an intermittent pain medication on the patient care areas outside of those listed above. The committee reviewed comparative safety and potency data and felt that the current restrictions should be maintained due to the potential for serious adverse events related to inaccurate dosing and/or insufficient monitoring.	Not approved	Complete
Nutrition Support Team	• **Vital High Protein –** Vital HP is a very high protein, hydrolyzed, peptide-based enteral formula for use with critically ill patients. This is unique formulation that would be useful with patients who are obese and/or on high amounts of propofol as it is the highest protein per calorie formula available from the hospital's contracted vendor. It was recommended to implement the use of this product as an enteral source of complete nutrition for patients who require a very high protein elemental enteral feedings.	Approved	Complete
Other Business	• Memorial has been asked by CHI to reduce drug supply expense by 1.3 million. The hospital is looking at all opportunities for savings. • Melissa communicated that the P & T Committee will continue to be a vital component to managing our drug budget now and in the future.	Information	Complete

There being no further business, the meeting was adjourned at 7:50 A.M. The next P&T meeting is August 14, 2014.

Respectfully submitted,

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

Approved by,

Richard Pesce, M.D. Chairman

FORMULARY REVIEW

GENERIC NAME: ALBIGLUTIDE

PROPRIETARY NAME: *Tanzeum* (GlaxoSmithKline)

INDICATIONS: Albiglutide is approved by the Food and Drug Administration (FDA) as an adjunct therapy to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Albiglutide is not recommended as a first-line therapy for patients inadequately controlled on diet and exercise, is not for the treatment of type 1 diabetes mellitus nor diabetic ketoacidosis, has not been studied in patients with a history of pancreatitis, is not for patients with preexisting severe GI disease, and has not been studied in combination with prandial insulin.

CLINICAL PHARMACOLOGY: Albiglutide is a glucagonlike peptide 1 (GLP-1) receptor agonist. In addition, albiglutide augments glucose-dependent insulin secretion and slows gastric emptying. The net results of these effects are a reduction in fasting glucose and postprandial glucose. Albiglutide is the third medication of this class to be FDA approved. Previously approved GLP-1 agonists are as follows: Byetta® (exenatide) & Victoza® (liraglutide).

PHARMACOKINETICS: Following subcutaneous administration, the median time to peak plasma concentration is 2 to 5 days and the mean half-life is 5 to 8 days. Steady-state exposure occurs following 4 to 5 weeks of once-weekly administration. Changes in pharmacokinetics were observed in patients with mild or moderate renal impairment, while systemic exposure was increased by 30% to 40% in patients with severe renal impairment.

ADVERSE REACTIONS: The most commonly reported adverse reactions with albiglutide therapy versus placebo include upper respiratory tract infection (14.2% vs 13%, respectively), diarrhea (13.1% vs 10.5%, respectively), nausea (11.1% vs 9.6%, respectively), and injection-site reaction (10.5% vs 2.1%, respectively). Nausea and vomiting decreased in frequency over time following repeated weekly administrations. Acute pancreatitis has also been reported in association with albiglutide and occurred at a higher rate than patients receiving placebo (0.3% vs. 0%).

BLACK BOX WARNING: Tyhroid C-cell tumors and medullary thyroid carcinoma (MCT) have been observed in rodent studies with GLP-1 receptor agonists at clinically relevant exposures although it is unknown if this translates to human risk. Albiglutide is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2.

DRUG INTERACTIONS: Albiglutide delays gastric emptying which may impact absorption of concomitantly administered oral medications.

DOSING: Albiglutide 30 mg is given once weekly as a subcutaneous injection. If response is inadequate, the dosage may be increased to 50 mg once weekly. It can be given at any time of day, without regard to meals, and should be given at a different injection site each time. If the patient is already receiving an insulin secretagogue (eg, sulfonylurea) or insulin, the dose of these medications should be decreased when albiglutide therapy is initiated in order to reduce the risk of hypoglycemia. No adjustment in dose is required for patients with mild, moderate, or severe renal impairment; however, if the patient complains of severe GI adverse reactions, renal function should be evaluated.

PRODUCT AVAILABILITY & COST: The Biologics License Application was submitted to the FDA in January 2013 and approved in April 2014. Albiglutide is available as a lyophilized powder in a single-dose pen in strengths of 30 and 50 mg, available in a carton containing 1 or 4 pens. The powder must be reconstituted with the diluent in the pen prior to administration. The drug must be stored in the refrigerator (36°F to 46°F [2°C to 8°C]) prior to dispensing.
COST: $307.44 per month of therapy (once weekly injections)

DRUG SAFETY/RISK EVALUATION AND MITIGATION STRATEGY (REMS): A REMS is required for albiglutide, exenatide extended-release, and liraglutide injections. The REMS focuses on a communication plan, requiring that a letter to health care professionals and a highlighted information sheet be provided to prescribers regarding the possible risk of acute pancreatitis and medullary thyroid carcinoma.

CONCLUSION: Currently all of the other GLP-1 agonists are treated as non-formulary medications and these medications are not supplied for patients admitted to the hospital. If the prescriber feels that continuing this medication during the hospitalization is clinically indicated then the patients are instructed to bring their home supply to be administered during their inpatient hospital stay. It is recommended to designate albiglutide non-formulary status along with the other commercially available GLP-1 agonists.

FORMULARY REVIEW

GENERIC NAME: TEDIZOLID PHOSPHATE

PROPRIETARY NAME: *Sivextro*® (Cubist)

INDICATIONS: Tedizolid is an oxazolidinone class antibacterial drug indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria. Tedizolid is the second medication in this class to be FDA approved with the first of these agents being Zyvox® (linezolid).

CLINICAL PHARMACOLOGY: Tedizolid phosphate is a novel, next-generation oxazolidinone prodrug. Tedizolid phosphate is rapidly converted in vivo to tedizolid. Tedizolid inhibits the synthesis of bacterial proteins by interacting with the 23S ribosomal subunit, resulting in inhibition of protein synthesis. Tedizolid has been shown to have activity against clinically relevant gram-positive aerobic and anaerobic bacteria, such as Staphylococcus species, Streptococcus species, Enterococcus species, and *Haemophilus influenzae*; it has also shown activity against strains resistant to vancomycin, daptomycin, and linezolid. In comparison with linezolid, tedizolid has been shown to have 4- to 16-fold greater in vitro activity against methicillin-sensitive and methicillin-resistant S. aureus, streptococci, and enterococci. Tedizolid has nearly equivalent oral and intravenous (IV) bioavailability; therefore, the dosing is the same for both the oral and IV formulations.

PHARMACOKINETICS: Tedizolid phosphate is a prodrug that is rapidly converted to tedizolid by hydrolysis of the phosphate group by phosphatases. The area under the curve (AUC) for tedizolid in the blood is similar following IV and oral administration. Severe renal impairment does not change the pharmacokinetics of tedizolid; therefore, it is not necessary to adjust this drug in patients with reduced renal function.

ADVERSE REACTIONS: The most common adverse reactions reported with tedizolid phosphate therapy in patients with acute bacterial skin and skin structure infections included nausea (8.5%), headache (6.3%), diarrhea (4.5%), abscess (4.2%), abscess limb (3.6%), vomiting (2.7%), cellulitis (2.4%), and dizziness (2.4%).

In the phase III direct comparison studies with linezolid the safety profile of tedizolid appeared to be similar to that of linezolid.

COMPARATIVE EFFICACY: The efficacy and safety of tedizolid was assessed in a randomized non-inferiority trial utilizing a 6 day oral tedizolid therapy for treatement of ABSSSI versus 10 days of oral linezolid therapy. Compared with linezolid, tedizolid was statistically non-inferior in terms of early clinical response (i.e., within 48-72 hrs of initiation of therapy; 85.2% vs. 82.6%) and sustained clinical response at the end of treatment (87% vs. 88%). The only published literature to date is related to the treatment of ABSSSI and only tissue penetration studies have been conducted for treatment of lung infections although phase III studies are currently ongoing.

DRUG INTERACTIONS: Tedizolid is a weak, reversible MAO inhibitor as has been demonstrated during in vitro research. It appears based on the available literature that tedizolid is a weaker MAO inhibitor than linezolid and may not have the same potential for interaction with serotenergic agents, however this remains to be proven in a larger population of patients with various risk factors or longer durations of therapy. Patients on serotenergic agents were excluded from the published phase III trials.

DOSING & COST COMPARISON: 200 mg ONCE daily x 6 days (ABSSSI treatment)

Tedizolid	Linezolid
Tablet & IV cost per day of therapy → $235/day	Tablet cost per day of therapy → $238/day IV cost per day of therapy → $261/day

CONCLUSION: Tedizolid is now the second oxazolidinone on the market that can be used orally or IV for the treatment of gram-positive bacterial skin and skin structure infections and has demonstrated non-inferiority to linezolid in the published phase III studies. The apparent reduced risk of drug interactions with seratonergic agents provides promise for use in patients concomitantly taking these types of medications although the lack of human data proving this in practice still makes the use of tedizolid along with SSRI's and other agents problematic at this time. The majority of linezolid use at MHCS is for the treatment of pulmonary infections and currently there is no data available demonstrating non-inferiority or superiority over linezolid for this indication. At this time due to only a marginally better price as compared to linezolid and lack of respiratory data it is recommended to not approve tedizolid at this time and automatically substitute all tedizolid orders for a therapeutically equivalent dose of linezolid as indicated below. This decision may be re-evaluated if further pricing adjustments are made by either company and/or additional data becomes available (use with seratonergic agents, respiratory data, etc.).

Tedizolid 200 mg Daily → Linezolid 600 mg BID

FORMULARY REVIEW

GENERIC NAME: Bupivacaine Liposomal

PROPRIETARY NAME: Exparel (Pacira)

Requested for use by Dr. Brzezienski for use in breast surgery

INDICATIONS: Exparel is a liposome injection of bupivicaine, an amide local anesthetic, indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia.

CLINICAL PHARMACOLOGY: Local anesthetics block the generation and the conduction of nerve impulses presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers.

PHARMACOKINETICS: Local infiltration of EXPAREL results in significant systemic plasma levels of bupivacaine which can persist for 96 hours. The rate of systemic absorption of bupivacaine is dependent upon the total dose of drug administered, the route of administration, and the vascularity of the administration site. Systemic plasma levels of bupivacaine following administration are not correlated with local efficacy. For the FDA approved indications the difference in pain intensity when compared to placebo occurred only during the first 24 hours following study drug administration. Between 24 and 72 hours after study drug administration, there was minimal to no difference between liposomal bupivacaine and placebo on mean pain intensity.

ADVERSE REACTIONS: Nausea, Constipation, and Vomiting were reported in greater than or equal to 10% of the patients.

DRUG INTERACTIONS: Do not admix with lidocaine or other non-bupivacaine-based local anestheics.

DOSING: Is intended for single-dose administration only. The recommended dose is based on the surgical site and the volume required to cover that area:

Surgery	Dose of EXPAREL	Volume of EXPAREL
Bunionectomy	106 mg	8 mL
Hemorrhoidectomy	266 mg	20 mL

CONTRAINDICATIONS: Do not use in obstetrical paracervical block anesthesia.

WARNINGS AND PRECAUTIONS: Monitoring of cardiovascular and neurological status, as well as vital signs should be performed during and after injection. It is metabolized by the liver, so use with caution in patients with hepatic disease. It is substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function.

Bupivacaine liposome injectable suspension must NOT be mixed with or come in direct contact with non-bupivacaine-based local anesthetics, including lidocaine. These products may cause an immediate release of bupivacaine from the liposomes. Bupivacaine hydrochloride products if injected immediately before bupivacaine liposome injectable suspension may alter the pharmacokinetic and/or physicochemical properties of the drugs if the dose of bupivacaine hydrochloride solution exceeds 50% of the bupivacaine liposome injectable suspension (Exparel) dose.

MAMMAPLASTY STUDY RESULTS: To date only one clinical trial has been published outlining the use of Exparel for patients undergoing breast surgery. The trial was a double-blind, randomized trial in which patients were randomized to receive either a single dose of Exparel 300 mg or bupivacaine 200 mg into each implant pocket at the conclusion of surgery. The study was terminated early due to "administrative reasons" and was thus underpowered to detect statistically significant differences in treatment groups. Assessments of cumulative pain score and opioid usage trended in favor of Exparel, however neither reached a *P* value of less than .05. Numerically lower pain intensity scores were observed for Exparel at 8 hrs and 12 hrs, however the scores were not significantly different at the other timed assessments. Overall, due to the early termination of this trial it is difficult to draw accurate comparisons between treatments.

COST: $285/20 ml

FORMULARY REVIEW

GENERIC NAME: Mometasone Furoate and Formoterol Fumarate Inhalataion Aerosol

PROPRIETARY NAME: *Dulera (Merck)*

SIMILAR DRUGS: Fluticasone Propionate and Salmeterol (Advair® HFA, Advair® Diskus), Fluticasone Furoate and Vilanterol (Breo® Ellipta), Budesonide and Formoterol Fumarate (Symbicort®)

INDICATIONS: Mometasone/formoterol inhalation aerosol is indicated for the treatment of asthma in patients 12 years of age and older. It is not indicated for the relief of acute bronchospasm.

CLINICAL PHARMACOLOGY: Mometasone is a synthetic corticosteroid with potent anti-inflammatory activity. Formoterol is a selective long-acting beta-2 adrenergic receptor agonist that acts as a bronchodilator in the lungs.

PHARMACOKINETICS: Mometasone peak concentration (C_{max}) was reached within 0.5 to 4 hours following mometasone/formoterol inhaler use. Formoterol C_{max} was reached within 0.2 to 2 hours. The effective half-life for mometasone furoate following inhalation is 25 hours. The terminal half-life of formoterol is 9 to 11 hours.

CLINICAL EFFICACY: Mometasone/formoterol inhalation aerosol was studied in 2 placebo-and active-controlled trials and a 52-week safety trial enrolling a total of 1,913 patients 12 years of age and older with asthma. The 12-week, randomized, double-blind study enrolled 728 patients 12 to 84 years of age with persistent asthma uncontrolled on high-dose inhaled corticosteroids. The primary end point was the mean change in FEV_1 from baseline to week 12. Increases from baseline were greater in both mometasone/formoterol groups compared with the mometasone group. Clinically judged deterioration in asthma or reduction in lung function occurred in 12% of patients treated with either mometasone/formoterol dose and 18% of patients treated with mometasone alone.

The 26-week, randomized, double-blind study enrolled 781 patients 12 to 76 years of age with persistent asthma not well controlled on medium-dose inhaled corticosteroids. Patients received 2 inhalations twice daily of mometasone 100 mcg/formoterol 5 mcg (n = 191), mometasone furoate 100 mcg metered-dose inhaler (n = 192), formoterol 5 mcg metered-dose inhaler (n = 202), or placebo (n = 196). Co-primary end points were FEV_1 change from baseline and clinically judged deterioration in asthma or reduction in lung function. Mean FEV_1 was increased to a greater extent with mometasone/formoterol than with mometasone alone or placebo (both $P < 0.001$) at weeks 12 and 26. A decrease in FEV_1 was observed in 9% of patients treated with mometasone/formoterol, 10%of patients treated with mometasone alone, 15% of patients treated with formoterol alone, and 21% of patients treated with placebo. Clinically judged deterioration in asthma or reduction in lung function occurred in 30% of patients treated with mometasone/formoterol, 34% of patients treated with mometasone alone, 54% of patients treated with formoterol alone, and 56% of patients treated with placebo.

CONTRAINDICATIONS: Mometasone/formoterol inhalation aerosol is contraindicated as primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures.

WARNINGS & PRECAUTIONS: Labeling for all LABAs includes a black box warning regarding the increased risk of asthma-related death. A study comparing salmeterol with placebo in patients with asthma revealed an increase in asthma-related deaths in the salmeterol treatment group; this adverse effect is considered a class effect for the LABAs.

ADVERSE REACTIONS: The most common adverse reactions reported with mometasone/formoterol inhalation aerosol therapy included nasopharyngitis, sinusitis, and headache.

DOSING & COST: The recommended dosage of mometasone/formoterol inhalation aerosol is 2 oral inhalations twice daily (morning and evening). The starting dose of mometasone 100 mcg/formoterol 5 mcg and mometasone 200 mcg/formoterol 5 mcg is based on prior asthma therapy. Patients previously treated with a medium dose of inhaled corticosteroid should receive mometasone 100 mcg/formoterol 5 mcg twice daily, with a maximum daily dosage of mometasone 400 mcg/formoterol 20 mcg (4 inhalations). Those previously treated with high-dose inhaled corticosteroids should receive mometasone 200 mcg/formoterol 5 mcg, with a maximum daily dosage of mometasone 800 mcg/formoterol 20 mcg (4 inhalations). If an adequate response is not observed after 2 weeks at the lower dose, the dose may be increased to the higher strength.

Cost Comparison

Drug	Strength	Price per Day
Dulera®	100/5 mcg	$4.94
Dulera®	200/5 mcg	$4.94
Symbicort®	160/4.5 mcg	$7.54

Potential annual cost savings ~ $5,000 annually

RECOMMENDATION:
A new respiratory agreement is expected to be signed by our group purchasing organization in October that will designate the Merck products as the preferred contracted respiratory medications (Dulera, Asmanex, and Proventil HFA). However, we have an opportunity to go ahead and capture the Dulera savings in advance of the upcoming contract change by signing a temporary letter of participation with Merck if Dulera is added to the hospital formulary at this time.

1. Remove Symbicort® from formulary
2. Add Dulera® to formulary
3. Approve Dulera® for use in the Common Canister program
4. Approve the following update to the existing Therapeutic Interchange:

Inhaled Corticosteroid/Beta-agonist Combination	
ORDERED	**SUBSTITUTION**
Fluticasone-salmeterol (Advair Diskus®) 100 mcg-50 mcg, 1 puff BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Fluticasone-salmeterol (Advair Diskus®) 250 mcg-50 mcg, 1 puff BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Fluticasone-salmeterol (Advair Diskus®) 100 mcg-50 mcg, 1 puff BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Fluticasone-salmeterol (Advair HFA®) 45 mcg-21 mcg, 2 puff BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Fluticasone-salmeterol (Advair HFA®) 115 mcg-21 mcg, 2 puff BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Fluticasone-salmeterol (Advair HFA®) 230 mcg-21 mcg, 2 puff BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Budesonide-formoterol (Symbicort®) 80 mcg-4.5 mcg, 2 puffs BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Budesonide-formoterol (Symbicort®) 160 mcg-4.5 mcg, 2 puffs BID	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID
Fluticasone-vilanterol (Breo Ellipta®) 100 mcg-25 mcg, 1 puff DAILY	Mometasone-formoterol (Dulera®) 200 mcg-5 mcg, 2 puffs BID

Alternatively, it would be acceptable for a patient to bring in their own supply of their inhaled combination corticosteroid/LABA should they desire to continue on it while in the hospital.

FORMULARY REVIEW

GENERIC NAME: HYDROCODONE EXTENDED-RELEASE CAPSULES (C-II)

PROPRIETARY NAME: *Zohydro ER* (Zogenix)

INDICATIONS: Hydrocodone extended-release (ER) capsules are Food and Drug Administration (FDA)–approved for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

CLINICAL PHARMACOLOGY: Hydrocodone ER capsules contain a combination of ER beads (80%) and immediate-release beads (20%). This system combines 2 types of drug-containing beads. The first type of bead formulation has no rate-controlling polymers, and the second uses a series of polymers that control the rate of drug diffusion from the product as it passes through the GI tract.

PHARMACOKINETICS: Compared to immediate release formulations of hydrocodone, the overall exposure from hydrocodone extended release is similar but maximum concentrations are lower. Time to maximum concentration is 5 hours. Steady-state concentrations are achieved on or before day 7 of scheduled dosing. Food has no significant effect on the extent of absorption.

ADVERSE REACTIONS: The most commonly seen adverse reactions in clinical trials include constipation, nausea, vomiting, abdominal pain, headache, dizziness, dry mouth, somnolence, back pain, pruritus, peripheral edema, upper respiratory tract infection, muscle spasms, urinary tract infections, and tremor.

BLACK BOX WARNINGS: This medication has the following black box warnings associated with its use: (1) Risk of addiction, abuse and misuse, (2) Risk of life threatening or fatal respiratory depression may occur upon initiation or following a dose increase, (3) Risk of fatal overdose following accidental consumption – particularly in children, (4) Risk of neonatal opioid withdrawal if taken during pregnancy, (5) Risk of fatal plasma hydrocodone levels if taken with alcohol or products containing alcohol.

DRUG INTERACTIONS: Hydrocodone is metabolized by cytochrome P450 (CYP-450) 3A4. Drugs that inhibit the CYP3A4 enzyme (eg, ketoconazole) may cause an increase in systemic exposure to hydrocodone and an unsafe increase in plasma levels of hydrocodone. Use caution when coadministering hydrocodone with inhibitors of CYP3A4, and monitor patients for signs and symptoms of toxicity, including respiratory depression and sedation. Alcohol consumption can result in significantly increased absorption and peak hydrocodone concentrations.

DOSING: Hydrocodone ER should be initiated in non-opioid tolerant patients at 10 mg every 12 hours. The capsules should be swallowed whole and must not be chewed, crushed, or dissolved. Titration should be performed every 3 to 7 days in increments of 10 mg every 12 hours. Single doses of hydrocodone ER greater than 40 mg per dose or a total daily dose greater than 80 mg should only be used in patients in whom tolerance to an opioid of comparable potency is established. Close monitoring should be performed when administering hydrocodone ER to patients with hepatic impairment. Comparative efficacy: Hydrocodone 10 mg = Oxycodone 10 mg.

PRODUCT AVAILABILITY & COST: Hydrocodone ER capsules were approved by the FDA on October 25, 2013 despite a previous recommendation by the FDA's analgesic advisory panel that the drug should not be approved due to safety and the drug's risk/benefit profile.
Cost - $5.57 – 6.81 per dose (depending on dosage size)

CONCLUSION: Zohydro ER is the first hydrocodone-only product and is classified as Drug Enforcement Agency Schedule II. The FDA approval for this medication has sparked much controversy due to the lack of an abuse deterrent formulation for this product and its potential for abuse. This product likely has little potential for use in the inpatient setting for the purpose of starting patients on this therapy, however we will likely encounter patients who receive this therapy as a home medication.

FORMULARY REVIEW

GENERIC NAME: VEDDOLIZUMAB

PROPRIETARY NAME: *Entyvio*® (Takeda Pharmaceuticals)

INDICATIONS: Vedolizumab was approved by the Food and Drug Administration (FDA) as a treatment for adults with moderately to severely active Crohn's disease and ulcerative colitis to reduce signs and symptoms and to induce and maintain clinical remission in patients who have an inadequate response to conventional therapy. Treatment with vedolizumab is appropriate for patients who have failed to fully respond to TNF blockers, immunomodulators, or corticosteroid therapy or who are intolerant to or demonstrated dependence on corticosteroids.

CLINICAL PHARMACOLOGY: Vedolizumab is a humanized monoclonal antibody that binds to and blocks the interaction between integrin alpha-4-beta-7 and mucosal addressin cell adhesion molecule-1 (MAdCAM-1) in the gut which inhibits the migration of specific memory T-lymphocytes across the endotherlium into inflamed GI parenchymal tissue. MAdCAM-1 is mainly expressed on gut endothelial cells and plays a critical role in the homing of T-lymphocytes to guy lymph tissue. Blocking this action reduces the chronic inflammatory process present in both ulcerative colitis and Crohn's disease.

PHARMACOKINETICS: Vedolizumab serum concentrations and area under the curve increased linearly with dose. The serum half life is approximately 25 days at 300 mg dosage. Similar pharmacokinetics were observed in ulcerative colitis and Crohn's disease patients. Population PK analysis showed that the severity of disease state, prior treatment with TNF blocker therapy, serum albumin, co-administered immunomodulators, and co-administered amionsalicylates did not have a clinically meaningful effect on the PK of vedolizumab.

CLINICAL EFFICACY: The safety and effectiveness of Entyvio for ulcerative colitis were established in two clinical trials involving approximately 900 patients who had not responded adequately to corticosteroids, immunomodulators, or tumor necrosis factor blocker medications. Evaluations of patients included measures of stool frequency, rectal bleeding, endoscopic findings and a physician's overall assessment. Results showed that a greater percentage of participants treated with Entyvio compared to a placebo achieved and maintained clinical response, achieved and maintained clinical remission, achieved corticosteroid-free clinical remission, and as seen during endoscopy, had improved appearance of the colon.

The safety and effectiveness of Entyvio for Crohn's disease were established in three clinical trials involving approximately 1,500 patients who had not responded adequately to corticosteroids, immunomodulators, or tumor necrosis factor blocker medications. Results showed that a greater percentage of participants treated with Entyvio compared to a placebo achieved clinical response, achieved clinical remission, and achieved corticosteroid-free clinical remission.

ADVERSE REACTIONS: The most common adverse reactions associated with vedolizumab therapy are headache, nausea, exacerbation of the treated condition, abdominal pain, fatigue, and nasopharyngitis.

WARNINGS & PRECAUTIONS:

- Infusion related reactions & hypersensitivity reactions: allergic reactions including dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate have been observed.
- Infections: increased risk for developing infections with upper respiratory tract infections most commonly encountered although the risk of more serious infections does exist
- Progressive Multifocal Leukoencephalopathy: no cases have been observed with vedolizumab although another integrin receptor antagonist (Tysabri®) has been associated with PML.
- Liver injury: reports of elevations of transaminase and/or bilirubin in patients receiving vedolizumab have been observed.

DRUG INTERACTIONS: No significant drug interactions have been observed.

DOSING & COST: 300 mg IV infusion over 30 minutes at weeks 0, 2, and 6 as induction therapy. Thereafter, a maintenance regimen of 300 mg IV is given every 8 weeks.
Cost: $4819/300 mg; Estimated annual cost ~$35,000 per patient/year

CONCLUSION: Vedolizumab will be an alternative agent for patients who have either failed conventional therapies (TNF blockers, corticosteroids, etc.) or had inadequate response to these therapies. Unfortunately, per Takeda pharmaceuticals this medication will likely not be assigned a specific HCPCS "J" code to be utilized for outpatient reimbursement until January, 2016. It has generally been the hospital's practice to not add non-chemotherapy agents to formulary until a medication specific "J" code is available in order to guarantee reimbursement.

Kcentra Use Evaluation
Memorial Health Care System
August 2014

Introduction
Kcentra began being utilized at Memorial beginning in July 2013. A medication use evaluation was performed to determine the appropriateness of Kcentra use including indication and the concurrent use of IV Vitamin K.

Methods
All patients receiving Kcentra from July 2013 to August 2, 2014 were included in this evaluation (34 patients, 35 events). The patients who received Kcentra for coagulopathy, reversal of a novel anticoagulant or were not on an anticoagulant were separated from those in whom Kcentra was used for reversal of Coumadin (12 patients). Data collected: reason for admission, indication for use, time of surgery after Kcentra use, INR before and after, time between INRs, previous use of reversal agents (FFP, Novoseven, protamine, cryoprecipitate), concurrent IV Vitamin K, outcome and thromboembolism complication post use.

Results

	N = 22	Comments
Appropriate Indication	**N=18 (82 %)**	
Acute Major Bleeding	7/18	
Reversal for Urgent Surgery[1]	11/18	
INR Before Administration	**N = 22**	
< 2	1/22	INR < 2 (indication: emergent spinal fusion)
2 - <4	11/22	
4 – 6	5/22	
> 6	5/22	
Average	5.0 (1.8 – 15)	
INR After Administration	**N = 19**	3 with no post-INR due to death/transfer
< 2	17/19	
≤ 1.5	11/17	
> 2	2/19	INR >2 - 1 surgery (3.8 to 3.6), 1 bleed (2.8 to 2.6)
Average	1.6 (1.1 – 3.6)	
Previous Therapies	**N = 22**	
Ordered	12/22	
Administered	10/12	FFP not available in 2 cases
None Ordered	10/22	
Concurrent IV Vitamin K[2]	**N = 22**	
Yes	18/22	
No	4/22	
Outcome	**N = 22**	
Discharge	16/22	
Death	4/22	
Other	2/22	Transferred to Erlanger
Medicare	**N = 22**	
Yes	16/22	
No	6/22	

1. Urgent surgery – within 18 hours of arrival. 2. Concurrent IV Vitamin K – within 6 hours of Kcentra reversal

Other Observations/Data Summary

- 4 of the 22 uses of Kcentra were not for an appropriate indication.
  - 2 were for acute, minor bleeding
  - 2 were for non-urgent surgeries
- Kcentra use could have been prevented in one case. SQ Vitamin K, FFP had been used to reverse the INR. If IV Vitamin K had been used for reversal, Kcentra would not have been needed before surgery.
- Only 1 patient had a thromboembolic complication 29 days post Kcentra use. Due to secondary reason according to the note in the patient's chart.

- Kcentra was used on 7 patients who were taking a novel anticoagulant at home.
    - 5 cases were for bleeding reversal (2 intracranial hemorrhages, 1 case not indicated)
    - 1 case was for reversal prior to emergent surgery (STEMI – cath lab)
    - 1 case the patient was bleeding and an EGD was performed. Found Mallory-Weiss tear.

	Indicated?	Previous Therapies	Concurrent IV Vit K	Outcome	Home Anticoagulant(s)
1	Yes	No	No	DC	Xarelto
2	Yes	No	Yes	Transfer	Arixtra
3	Yes	No	No	Transfer	Eliquis
4	Yes	No	Yes	DC	Xarelto
5	No	No	Yes	DC	Eliquis
6	Yes	No	No	DC	Xarelto
7	yes	No	yes	Transfer	Xarelto, Brilinta

    - Concurrent IV Vitamin K would not be needed with Kcentra in patients not on Vitamin K antagonists
    - Case without indication was a minor bleed
- Kcentra was used on 2 patients who were not on any anticoagulants
- Kcentra was used to reverse coagulopathy during or after surgery in 3 cases
    - 1 case – patient had DIC in which Kcentra is contraindicated (DIC patients excluded in clinical trial)
    - Attempts were made for reversal in all 3 cases using FFP, protamine, Novoseven or Cyroprecipitate

Conclusions

- At this current time, the two FDA indications for Kcentra are for patients on a Vitamin K antagonist who have major, acute bleeding or need urgent reversal for surgery or a procedure.
    - Kcentra must be administered with concurrent IV Vitamin K in order to sustain reversal of Coumadin. Oral and subcutaneous Vitamin K are not appropriate for concurrent use due to longer onset of action.[1,2]
- 2 main areas where Kcentra is currently not being used appropriately:
    - Patients with a GI bleed who are hemodynamically stable
    - INR reversal for placement of permacath or PEG tubes (non-emergent surgery)
- There are no defined recommendations for the use of Kcentra for reversal of novel anticoagulants or for patients with coagulopathy.
- If possible, INR should be reversed with PO or IV Vitamin K and FFP. There were several cases where these medications were not utilized appropriately before resorting to Kcentra. At the point that Kcentra was needed, it was then indicated because the previous therapies were not effective.

References:

1. Kcentra (Prothrombin Complex Concentrate) [package insert]. Kankakee, IL: CSL Behring LLC; December 2013.
2. Phytonadione, Vitamin K1. In: Clinical Pharmacology. Tampa (FL): Gold Standard. [Updated 12/4/09; accessed 08/10/14.] http://www.clinicalpharmacology-ip.com/Forms/Monograph/monograph.aspx?cpnum=487&sec=monphar&t=0

Cefazolin Dose Optimization
Weight Based Dosing Proposal

Background:
The most recent surgical prophylaxis guidelines have placed an increased emphasis on weight based prophylactic dosing of cefazolin and other antimicrobials due to obesity being linked to an increased risk for infections in these patients. However, cefazolin is often also utilized for the treatment of susceptible gram positive infections such as bacteremia and lung infections and the same importance of appropriate dosing remains an important issue. A recent review revealed that many of the patients receiving ongoing therapy with cefazolin were often obese yet were still treated with standard 1 gm Q 8 hr dosing regimens.

Proposal:
In order to optimize the therapy for patients receiving cefazolin it is recommended that all patients be reviewed for appropriate dosing by the antimicrobial stewardship pharmacists and their dosing optimized as outlined below. Surgical prophylaxis dosing of cefazolin will be optimized as previously mentioned per the most recent guidelines.

Patient weight < 80 kg: 1 gm IV Q 8 hrs
Patient weight > 80 kg: 2 gm IV Q 8 hrs

Renal impairment (CrCl < 30 ml/min): Dose will be administered every 12 hours

Hemodialysis dosing: 2 gm after every dialysis session

Standardized Dosing
Metronidazole & Ciprofloxacin

The following recommendations are submitted to the Pharmacy and Therapeutics Committee from the Antibiotic Sub-committee.

Metronidazole Dosing

Background: The dosing for metronidazole is very confusing in the literature. When the product was released the dosing was approved by the FDA per the manufacturer's package insert at giving a loading dose of 15 mg/kg (a 1 gm dose for a 70 kg person) then 7.5 mg q 6 hrs (500 mg for a 70 kg person). The maximum dose is 4 grams per 24 hours for any patient. Later, renal dosing adjustments have been recommended in several texts as 3.25 mg/kg for patients with a CrCl of < 10 ml/min or when the patient is on hemodialysis (given after HD).

Recommendation: Since metronidazole has a long half life (i.e. 6 to 14 hrs) the following dosing adjustments will be made by the Antibiotic Stewardship or Clinical Pharmacists.

- All orders for metronidazole 250-500 mg IV or PO every 6-8 hours will be automatically adjusted to 500 mg IV or PO every 8 hrs.

- If the CrCl is < 10 ml or the patient is on hemodialysis (HD) the dose will be adjusted to 500 mg every 12 hrs and if on CRRT the dose will be adjusted to 500 mg q 8 hrs.

Ciprofloxacin Dosing

Background: We occasionally have orders for Ciprofloxacin 200 mg IV or 250 mg po twice a day for patients who have decreased renal function (i.e. CrCl of < 30 ml/min).
An alternative dosing strategy is to adjust the dosing to using a once daily dosing strategy, if the CrCl is < 30 ml/min.

Recommendation: All doses for Ciprofloxacin 200 mg IV and the 250 mg PO doses ordered twice a day will automatically be adjusted by the Antibiotic Stewardship and/or the Clinical Pharmacist to either ciprofloxacin IV 400 mg daily or 500 mg PO daily if their CrCl is < 30 ml/min. Additionally, when patient's CrCl improves to > 30 ml/min the dose will automatically be adjusted to either 400 mg IV or 500 mg PO twice a day.

PEP uP volume-based feeding protocol (US PEPuP Collaborative)

Pharmacy and Therapeutics Proposal
August - 2014

Study Objectives

1. To describe nutrition practices in Intensive Care Units (ICUs) across the World.
2. To compare nutrition practices in ICUs between specific hospital and ICU site characteristics (e.g. geographic location, ICU structure, ICU size, hospital type)
3. To identify gaps between current nutrition practice and the recommendations of the Canadian Critical Care Nutrition Clinical Practice Guidelines (CPGs).
4. To monitor changes in nutrition practices in ICUs across time.

Description of Study Design

This study involves a period prevalence survey of nutrition therapies in critically ill patients in Intensive Care Units (ICU) across the World.

Data elements to be collected include hospital and ICU characteristics, patient demographics and APACHE II score. Nutrition practices such as route of nutrition, kilocalorie and protein levels prescribed and received, interruptions, supplementation, blood sugars, insulin, etc will also be collected on a daily basis on a minimum of 20 consecutive patients from ICU admission onwards, for a maximum of 12 days or until death or discharge. Data on clinical outcomes (e.g. duration of mechanical ventilation, ICU stay, hospital stay, death) will be collected up to 60 days after admission to the ICU. Most of the data collection will be done retrospectively and entered online via a secure website (www.criticalcarenutrition.com). The only direct observational data is head of the bed elevation and the collection of this data element is optional.

Assessment of Risks and Benefits

There are no risks for patients participating in the survey since no intervention is involved and data collected is part of routine care in an ICU.
The time required to complete data collection (approximately 2 hours per patient) may be burdensome to the individual collecting the data in the study. However, it is believed that these individuals will benefit personally from the experience of participating in a large International study and through local dissemination of the results of the survey.

Participating sites will benefit from a 28-page benchmarked performance report created from data collected during the study. These reports will highlight their strengths and weaknesses in comparison to other ICUs within the same geographic area and to all ICUs in the database and illuminate opportunities for improvement. Sites that distribute the questionnaire to ICU staff will also receive an additional report, which ranks barriers to optimal nutrition performance by importance, based on responses to the questionnaire in their ICU.

Description of patient population
The study will involve collecting data on 20 adult critically-ill patients who stay in the ICU for a minimum of 3 days, because this is the population who receive nutrition therapy, and to whom the Canadian Critical Care Nutrition Clinical Practice Guidelines are directed. Patients admitted to the ICU but who are under the age of 18 years, or are not mechanically ventilated within the first 48 hours of admission will be excluded from the study to ensure only data from adult patients who were truly critically ill (i.e. had an acute life threatening condition) are captured. Twenty patients are required in order to ensure an accurate representation of usual nutrition practices.

Participation
Processes will be implemented in MICU under the supervision of Dr. Pesce, Mary Long – Nurse Manager, Melissa Rice – Nurse Educator, Brian Jones – Clinical Nutrition Manager and Lori Wilson – Clinical Dietitian.

Critical Care Nurses will be educated on the process using provided posters, protocols and pocket guides. A clinical nurse champion will be identified to assist with nursing involvement.

Products Utilized
Products previously approved by P&T will be utilized for this protocol. Beneprotein modular protein supplements along with Vital High Protein will be the primary products employed. The MD and RD can adjust the nutritional formula to another item on formulary per patient need.

*IRB, Nursing Research along with privacy compliance are concurrently reviewing PEPuP. Protocol implementation and data collection will not commence until all have given approval.

PEP UP

Increased protein and energy delivery

POCKET GUIDE

Upon admission to ICU:
physician should complete "Enteral Feeding Initiation Orders" and **select one** of the following three **feeding strategies**:

1 Volume-Based Feeds
(most patients)

Day 1 - 25 mL/hr (until end of flow sheet)
Day 2 (and subsequent days) - Rate determined by 24-hr volume goal
- Consult RD to determine goal
- If no RD available, use weight-based goals (see "Enteral Feeding Initiation Orders") until RD can assess

Calculating rate from 24-hr volume goal:

24-hr Volume goal − Volume already received today = Volume remaining for today

Volume remaining for today ÷ Hours remaining today = Rate

Rate should never exceed 150 mL/hr.
For more assistance calculating rate, consult "volume-based feeding schedule".

2 Trophic Feeds

- Feed @ 10 mL/hr
- Appropriate for patients:
  - On vasopressors (if adequately resuscitated)
  - Who are not suitable for high volume feeding (ruptured AAA, surgically placed jejunostomy, upper intestinal anastomosis, impending intubation, risk of re-feeding syndrome).

3 NPO

- Appropriate for patients with:
  - ✓ Bowel perforation
  - ✓ Bowel obstruction
  - ✓ Proximal high output fistula

The following are not automatic contraindications to EN – Individual assessment is needed:
- ✗ Recent operation
- ✗ High NG output

Interruptions due to procedures?
Consult "EN guideline for surgical procedures"
Volume-based feeds: If patient is scheduled to be NPO, adjust rate so volume goal is met before feeding is stopped

High gastric residual volumes?
Trophic feeds: Do not monitor GRVs
Volume-based feeds: Consult "Gastric Feeding Flow Chart"

Diarrhea?
Consult "Nurses' Guideline for Management of Diarrhea"

Discuss at rounds every day
1. Trophic feeds or NPO: Ability to progress to volume-based feeds
2. Daily nutritional adequacy (Volume patient received ÷ 24-hr volume goal ×100)
3. Appropriateness of enteral formula, motility agents and protein supplements

This protocol is a guideline: it does not replace clinical judgment. If uncomfortable with any aspect of the protocol, discuss it with a dietitian or physician.

Remember
Patients on volume-based or trophic feeds should also be started on:
- Metoclopramide: 10 mg IV q 6h
- Beneprotein: 2 packets (14 g) mixed in 120 mL water administered bid via NG

Questions?
Contact the PEP uP Team

MD:
RN:
RD:

A collaboration of:

Critical Care Nutrition | NestléHealthScience — NOURISHING PERSONAL HEALTH

Weight (kg)	Allergies

Addressograph

ENTERAL FEEDING INITIATION ORDERS
To Be Completed by Nursing, the Dietitian or MD and signed by an MD

TRANSCRIPTION

1. ☐ CXR to confirm initial tube placement.
   OR
   ☐ _____ tube placement confirmed _____.
   (gastric, intestinal) *(e.g. radiographically, endoscopically)*

2. ☐ **Begin Volume-Based Feeding**. (24 hour period as per flow sheet - Xam to Xam).
   a) On Day 1 of enteral feeding, start with Peptamen Bariatric@ 25 ml/hr
   b) On Day 2 of enteral feeding, dietitian to calculate 24 hr target volume based on patient's actual admission weight. If dietitian is not available use*:
      ☐ ≤ 50 kg → 1050 ml/24 hrs
      ☐ 50.1 – 65 kg → 1350 ml/24 hrs
      ☐ 65.1- 80kg → 1650 ml/24 hrs
      ☐ 80.1 – 95 kg → 1950 ml/24 hrs
      ☐ > 95.1 kg → 2400 ml/24 hrs
   c) Calculate the hourly rate of infusion using the 24 hr target volume from part (b) divided by the number of available hours for feeding today (Day 2), or use the Volume Based Feeding Schedule. Do not exceed 150 ml/hr.
   d) Consult dietitian to reassess 24 hr target volume (continue weight based 24 hr target volume calculating hourlyrate as per Volume Based Feeding Schedule until dietitian review)
   e) Monitor gastric residual volumes as per Gastric Feeding Flow Chart

OR

☐ **Begin Trophic Feeds**

- Start Peptamen Bariatric at 10 mL/h. Do not monitor gastric residual volumes. Reassess ability to transition to Volume-Based Feeding the next day. [For patients on vasopressors (regardless of dose) as long as they are adequately resuscitated OR patients not suitable for Volume Based Feeding *(e.g. ruptured AAA, upper intestinal anastomosis, surgically place jejunostomy, impending intubation or risk of refeeding syndrome)].*

OR

☐ **NPO.** Please write in reason: _____.*(For contraindications to EN only: bowel perforation, bowel obstruction, proximal high output fistula).* Note: recent OR and high NG output are not contraindications to EN.Reassess and switch to Volume-Based Feeding the next day. Do not start metoclopramide or protein supplements in patients who are NPO.

3. Unless NPO: Start metoclopramide: ☐ 10 mg IV q 6 hr, or ☐ 5 mg q6h IV if renal dysfunction. Reassess daily.
4. Unless NPO: Protein supplementBeneprotein® - 2 packets mixed in 120 ml sterile water bid via NG (consider holding in renal failure if not on dialysis or if pt. has hepatic encephalopathy).
5. Monitor nutritional adequacy daily: (volume of EN rec'd in last 24 hour period/prescribed 24 hour target volume) and report this percentage intake on daily rounds.
6. Monitor lytes and Ca, Mg, Phos q12h x 72 hours then as per ICU admission orders.
7. Flush tube with at least 10 mL sterile water q4 h during feedings, if feedings are held, after aspiration for residuals, and before and after medication and Beneprotein administration.
8. For declogging tubes, give pancrelipase 8,000 units mixed with crushed Na bicarbonate 500 mg in 25 mL warm water prn.
9. You may override Total Fluid Intake (TFI) order if needed; Do not increase IV rate to make up for held feedings because this volume will be made up later with increased rates of EN.

Signature & Designation:	Printed Name:
Date (YYYY/MM/DD)&Time (HHMM):	

*These weight based volumes are based on a 1.0 kcal/ml formula. Refer to the PEP uP: Volume Based Feeding Calculations to determine the weight-based target volume if using a 1.2 kcal/ml or 1.5 kcal/ml formula.

Please note: These are suggested guidelines for enteral feeding based on Enhanced Protein-Energy Provision via the Enteral Route in Critically Ill Patients (PEP uP) Protocol. They are not intended as a substitute for medical advice.

Text highlighted in yellow may be re-worded to match the protocols and/or schedules already in place in your ICU.

PEPUP: Volume Based Feeding Calculations

If the dietitian has not yet assessed the patient on day 2, when volume-based feedings are ordered by a physician, use a weight-based target volume until the dietitian assesses the patient:

Weight	Peptamen® Bariatric 24-hour target volume with a 1.0 cal/mL feeding	Peptamen AF® 24-hour target volume with a 1.2 cal/mL feeding	Peptamen 1.5® or Peptamen 1.5® with Prebio™ 24-hour target volume with a 1.5 cal/mL feeding
≤50 kg	1050 mL/24 hrs	875 mL/24 hrs	700 mL/24 hrs
50.1-65 kg	1350 mL/24 hrs	1125 mL/24 hrs	900 mL/24 hrs
65.1-80 kg	1650 mL/24 hrs	1375 mL/24 hrs	1100 mL/24 hrs
80.1-95 kg	1950 mL/24 hrs	1625 mL/24 hrs	1300 mL/24 hrs
≥95.1 kg	2400 mL/24 hrs	2000 mL/24 hrs	1600 mL/24 hrs

How to use the table:

1. Calculate the feeding goal for the volume based enteral feeding for the patient for a 24 hour period (i.e 7 am to 7 am each day)
2. Read the chart below corresponding to the 24 hour feeding goal for the patient. For example, if the total volume over a 24 hour period was 1800 mL, the first column will give the hourly feeding rate for the patient (in this instance 75 ml/hr)
3. If the patient was already fed 450 mL (over a 6 hr period at the rate of 75mL/hr) and the patient is on 'hold' for 5 hours, calculate the following:

   (a) New Feeding Goal = Volume still remaining to attain the feeding goal

   = Total Goal Volume - Already fed Volume

   = 1800-450=1350mL (Round the volume, if needed, to the closest 50 mL)

   (b) Time remaining to attain goal = 24 - Time Fed - Hold Time

   = 24-6-5= 13hrs
4. Now read the chart again with the New Feeding Goal and the corresponding time remaining as follows:

   For 1350 mL, go to column 13 (the number of hours remaining to attain goal) to get the new hourly feeding rate. In this instance, the new feeding rate is 104 mL/hr*. The patient will receive 1352 mL in 13 hours.

Important Nursing Assessment

Volume based feeding should be used with caution. Nurses should always assess for feeding intolerance. Examples of intolerance include: abdominal distention, abdominal cramping, nausea & vomiting, diarrhea defined as 5 stools or 750 mL per 24 hour period, and gastric residuals greater than 300 mL**.

*Hourly rate not to exceed 150 mL/hr

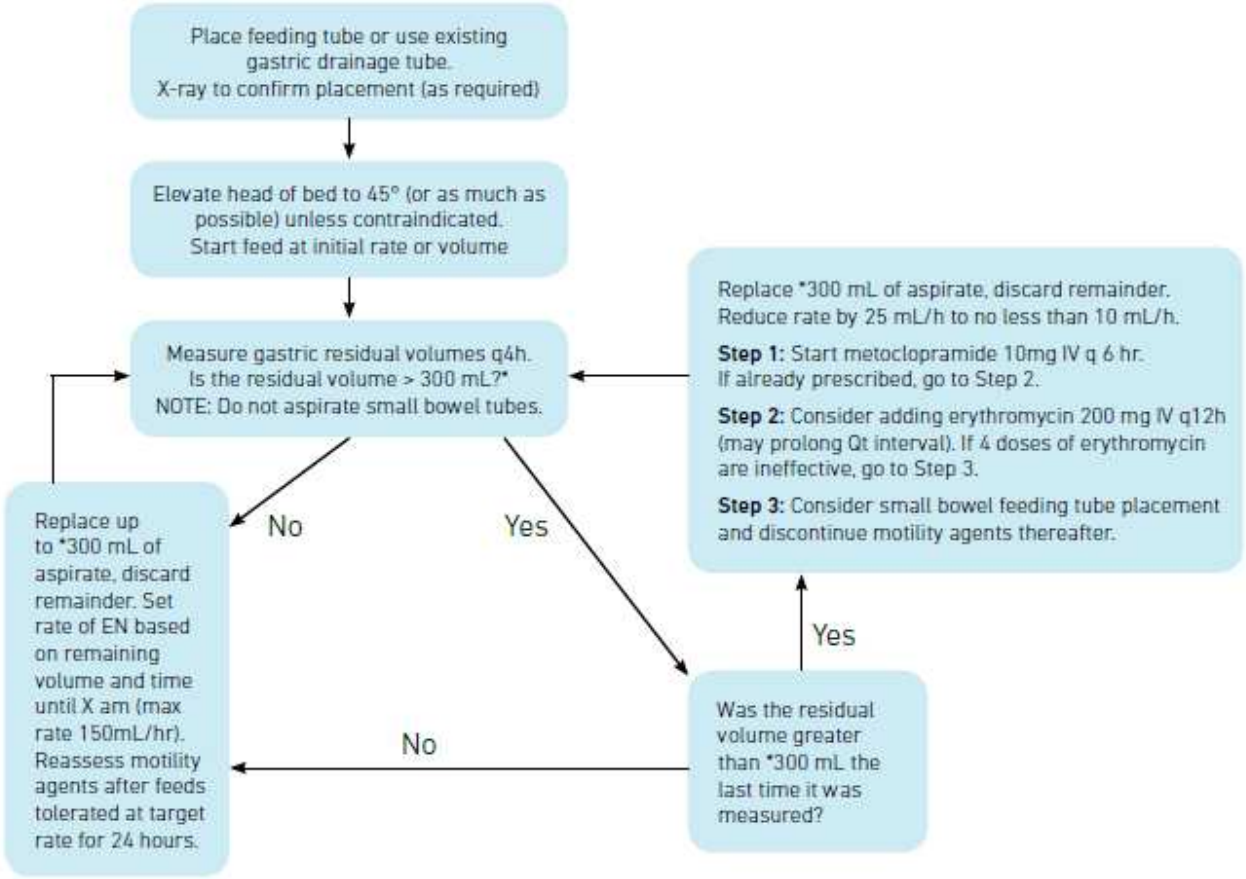
**Sites may customize the gastric residual volume threshold in keeping with their current practice and best available evidence which supports a gastric residual volume between 250 – 500 mL. Source: 2013 Canadian Clinical Practice Guidelines www.criticalcarenutrition.com, 2009 ASPEN/SCCM Guidelines

Please note: These are suggested guidelines for enteral feeding based on Enhanced Protein-Energy Provision via the Enteral Route in Critically Ill Patients (PEP uP) Protocol. They are not intended as a substitute for medical advice/their current practice and best available evidence

Please contact your ICU dietitian if you have any questions

PEPUP
Increased protein and energy delivery

GASTRIC FEEDING FLOW CHART



*Sites may customize the gastric residual volume threshold in keeping with their current practice and best available evidence which supports a gastric residual volume between 250 – 500 mL. Source: 2012 Canadian Clinical Practice Guidelines www.criticalcarenutrition.com, 2009 ASPEN/SCCM Guidelines.

Please note: These are suggested guidelines for enteral feeding based on Enhanced Protein-Energy Provision via the Enteral Route in Critically Ill Patients (PEP uP)Protocol. They are not intended as a substitute for medical advice.

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