CEDARS-SINAI MEDICAL CENTER

PHARMACY AND THERAPEUTICS COMMITTEE APPROVALS, APRIL 2016

Agenda Item	P&T Committee Decision
Drugs for Formulary Consideration	**Naltrexone Extended Release Injectable (Vivitrol®)** – not added to formulary given the lack of data for preventing hospital readmissions if the initial dose is administered during an acute inpatient hospitalization Indications: prevention of relapse to opioid dependence following detoxification and for treatment of alcohol dependence in patients who are able to abstain from alcohol Usual dose: 380mg intramuscularly every 4 weeks Drug – Drug Interactions: patients may not experience benefits from opioid-containing medications such as cough, cold, antidiarrheal and opioid medications Precautions: patients may be more susceptible to opioid overdose at the end of dosing interval, after missing a dose, or after discontinuing treatment. Patients should be aware of the potential for injection site reactions, precipitation of opioid withdrawal, hepatotoxicity, depression and suicidality. Monitoring: injection site reactions, hepatotoxicity, depression, and suicidal thinking **Sugammadex (Bridion®)** – restricted usage to OR setting in patients with deep/profound blockade where neostigmine or edrophonium is ineffective, for immediate (emergency ONLY) reversal of rocuronium (not vecuronium) (ie the patient cannot be intubated or ventilated) or succinylcholine is contraindicated. Indications: reversal of shallow or profound neuromuscular blockade induced by rocuronium bromide and vecuronium bromide in adults undergoing surgery Usual dose: moderate block: 2mg/kg as a single dose; deep block: 4mg/kg as a single dose Drug – Drug Interactions: efficacy of hormonal contraceptives may be reduced for up to 7 days, toremifene should not be given same day as surgery as it has a high binding affinity for sugammadex and displacement of vecuronium or rocuronium from the complex with suggamadex could occur. Precautions: anaphylaxis, hypersenstitivity, bradycardia, coagulopathy, bleeding, renal impairment Monitoring: monitor for adequate ventilation and maintenance of a patent airway, monitor renal function and coagulation parameters in patients with preexisting coagulopathies, administered concomitant anticoagulants, administered thromboprophylaxis drugs other than UFH or LMWH, or administered thromboprophylaxis drugs with a sugammadex dose of 16 mg/kg. Observe for anaphylaxis after administration and hemodynamic changes during and after administration. **Additional Items** – Rivastigmine oral solution (Exelon®) – no longer available- removed from formulary – Auranofin (Ridaura®) – remove from formulary – Statin Automatic Substitutions- pitavastatin added to the list
Antimicrobial Stewardship  Pre-Op Abx Quick Reference FY16 03.1	**Pyrimethamine (Daraprim®) Restrictions** Pyrimethamine (Daraprim®) is an antiparasitic agent that is indicated for the treatment of toxoplasmosis and for treatment and prophylaxis of malaria. As of June 2015, pyrimethamine is no longer available in retail pharmacies in the United States and is only available through the Walgreens specialty pharmacy program. Based on a review of available literature and guidelines, it was approved to use TMP-SMX as the first-line agent for treatment of Toxoplasma gondii and restricting pyrimethamine to patients unable to take either TMP-SMX due to sulfonamide allergy (and unable to undergo sulfa desensitization) or other contraindication. **Prescriber Educational letter** The Antimicrobial Stewardship Committee (ASC) has drafted an educational letter as part of the Quality Council and CMS requirement to ensure prescriber compliance with institutional guidelines. **Pre-Operative Antibiotic(s) Quick Reference FY15-16** A quick reference chart was compiled from the comprehensive antibiotic surgical prophylaxis guidelines. **Daptomycin CPK Monitoring** Pharmacists may order CPK level for patients on daptomycin ≥7 days and weekly thereafter if a level is not available. If the pharmacist believes more frequent CPK monitoring is warranted, a call to the prescriber is necessary. **Antimicrobial Renal Dose Adjustment in Adults – Pharmacist Protocol** http://sharepoint/clinical/PharmacyKnowRepo/clinop/Clinical%20Library/Infectious%20Diseases/Antimicrobial%20Renal%20Dose%20Adjustment%20Protocol%20in%20Adults.pdf Please refer to the document for details on the following revisions: – Cefepime- documented *Pseudomonas* infections (other than UTI) was added to the dosing recommendations – Cefotetan- removed from formulary – Cefoxitin- renal dose adjustments recommendations added – Fluconazole- HD recommendations were clarified

Other Updates

Atrial Fibrillation Protocol: Vitamin C, Vitamin E, and Fish Oil

The Society of Thoracic Surgeons (STS) has published a goal rate of ≤15.9% for new onset atrial fibrillation post CABG. A 2013 publication demonstrated a significant reduction in incidence of new onset atrial fibrillation in post on-pump cardiac surgery patients who were administered an antioxidant regimen consisting of n-3 polyunsaturated fatty acids (2 g/day), vitamin C (1 g/day) and vitamin E (400 units/day). Based on this study, the Quality Council has made reduction in post-CABG atrial fibrillation a priority. A test of change in elective isolated CABG patients from April-July 2016 involves:

7-days preoperatively and continued through discharge, patients will take/be administered:

1. N-3 polyunsaturated fatty acids – 3 capsules (1.8gm daily of 1:2 EPA:DHA ratio) daily. These capsules are only available from the company Pure Encapsulations due to the particular EPA:DHA ratio and will only be dispensed when ordered from the cardiac post-op order set. If fish oil is ordered outside of the order set, the usual Naturemade fish oil product will be dispensed.
2. Vitamin C 1gm daily
3. Vitamin E capsule 400 units daily

CS-Link Changes

Albuterol Neb, Ipratropium Neb, Duoneb®

- 5 day autostop or 30 doses
- Duoneb® will be added to order sets with both albuterol and ipratropium
- Frequencies will be changed to QID from Q4 hours in order sets

Acetylcysteine inhalation in order sets

- Frequencies will be changed to QID from Q4 hours

Glycopyrrolate Injection outside of Comfort Care Order Set

- Due to the 700% price increase of the glycopyrrolate generic product, changes were previously made to the Comfort Care order set to include lower initial doses and alternatives. The glycopyrrolate order in CS-Link will now be defaulted to 0.2mg and a panel will be included with alternatives for secretions.

Look-Alike & Sound-Alike Annual Review

An evaluation of Midas events from 2015 for potential look alike-sound alike medications was performed. The Institute of Safe Medication Practice has not published an updated list of LASA potential medications since the last review in 2015. It was determined that there would be no new recommendations for 2016 and that the list would remain as in 2015 with the following medications included:

Cephalosporins (ceFAZolin, ceFEPime, cefoTAXime, cefoTEtan, cefUROXime	HYDROmorphone/morphine inj
HydrALAZINE/HydrOXYzine/HydroCHLOROthiazide/haloperidol	Carvedilol and captopril
HYDROcodone/oxyCODONE	levOCARNitine/levETIRAcetam/levofloxacin
oxyCONTIN/oxyCODONE	DOPamine/DOBUTamine
LABEtalol inj/METOprolol inj	valGANciclovir/valACYclovir
Lantus and Lispro	Pradaxa and Plavix

Vincristine IVPB Preparation

National and international organizations have reported deaths due to inadvertent intrathecal administration when vincristine is prepared in a syringe. Currently, CSMC allows for the preparation of vincristine in syringes and administration as a slow IV push in an effort to prevent extravasation. Based on a 2016-2017 Best Practice recommendation from ISMP, leading cancer centers have converted to IV bags and IVPB infusions for vincristine. With input from THO, SOCCI, inpatient adult and pediatric nursing as well as pediatric oncology providers, the following recommendations were made:

1. Prepare vincristine in 25-50ml IVPB to be infused through the pump over 15mins via central line
2. Prepare vincristine in a 25ml IVPB to be infused by gravity over at least 5mins via peripheral line
   - Nurse to remain at bedside during peripheral infusion to assess venous patency by checking for blood return every 1-2 minutes

Estimated Creatinine Clearance in Patients <60 Inches Tall

The Cockcroft & Gault (CG) formula for eCrCl is the standard of care for assessing renal function and is the value provided in CS-Link. This formula uses ideal body weight (IBW) and has been validated in patients with a height of 60 inches (5 feet) or more raising the question of how to assess eCrCl in patients who are less than 60 inches tall. There are currently no guidelines addressing which weight should be used {ideal (IBW), lean (LBW) or actual (ABW)} in the CG formula for patients less than 60 inches tall. Based on available references and CS-Link capabilities, the following will be incorporated into CS-Link:

For patients <60” (5’) tall, the weight value equal to the lesser of LBW base weight (below) and ABW should be used to calculate eCrCl using the CG formula:

- Males – 50kg
- Females – 45.5kg

2016 Boxed Warning (BBW) Updates 04 16	**Dofetilide REMS & Boxed Warnings Update** The FDA updated the REMS process for dofetilide and discontinued the following requirements: 1. Only certified prescriber may order Tikosyn® 2. A 7-day supply is provided at time of discharge 3. The medication guide is reviewed with patient during hospitalization Based on this, the following process changes were approved: 1. Remove CS-Link order question: "Are you certified by the manufacturer to prescribe Tikosyn? Y/N" 2. Remove requirements for pharmacist to: a. Verify prescriber certification status prior to dispensing Tikosyn® b. Provide a 7-day supply at time of discharge after initiation/re-initiation of therapy or dose adjustments c. Review the medication guide with patient while the patient is admitted i. Outpatient pharmacists will continue to review the medication guide with the patient 3. Continue to follow manufacturer-recommended strategies to ensure patient safety a. Administer to patients on PCU status only for initiation, re-initiation, and dose adjustments b. Ascertain significant drug-drug interactions or other contraindications c. Electrolyte replenishment prior to and during treatment d. Dose adjustment based on patient renal function Please see the attached document for details on the Boxed Warnings Update. **Saline Flush Protocol for Pediatrics & Neonates** A saline flush protocol will be built into CS-Link for pediatrics/neonates. **PCA Pediatric Order Optimization** Previously, when titration instructions were free texted, conflicts with the ordered dose can occur. The order instruction verbiage will be updated to clarify when to titrate vs. give a bolus PCA dose.
Updated Policies, Procedures & Guidelines	The following policies, guidelines, and order sets were updated; please refer to the Policy & Procedure Manager (PPM) and Pharmacy Intranet for the most updated documents: **IV guidelines** http://web.csmc.edu/clinical/clinical-departments/pharmacy/iv-guidelines.aspx – Vincristine (Oncovin) IV Guideline **Policies & procedures** – Oral Contrast Orders & Administration for Gastrointestinal and/or Pelvic CT Radiography Studies Standardized Procedure Policy: Imaging Department- Change age cut off for pediatrics is <14 years of age. http://cshsppmweb/dotNet/documents/?docid=36057&mode=view – Annual Influenza Vaccination Program for Healthcare Providers: Epidemiology/Infection Prevention http://cshsppmweb/dotNet/documents/?docid=28460&mode=view – Liver Transplant Hepatitis C Management Guideline Procedure: Comprehensive Transplant Center http://cshsppmweb/dotNet/documents/?docid=10080&mode=view – Medication Administration and Documentation (MM.06.01.01) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=32012&mode=view – Medication Ordering and Order Types (MM.04.01.01.f) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=37451&mode=view – Performance Improvement Plan (MM.08.01.01) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=38073&mode=view – Self-Administration of Medications (MM.06.01.03) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=16619&mode=view – Medication Administration: Transdermal Fentanyl for Analgesia (MM.06.01.01.d) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=11635&mode=view – Multi-Dose Vials (MM.03.01.01.i) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=32013&mode=view – Order Management (MM.04.01.01) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=30380&mode=view – Do Not Use Abbreviations (Prohibited Abbreviations/Dangerous Abbreviations) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=39165&mode=view – Adverse Drug Reaction and Medication Error Reporting and Documentation of (MM.07.01.03) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=39197&mode=view – Physician Orders: Transcription and Acknowledgement Policy Clinical Administrative http://cshsppmweb/dotNet/documents/?docid=27850&mode=view – Non - Exempt Performance Appraisals Procedure: Pharmacy http://cshsppmweb/dotNet/documents/?docid=38537&mode=view – Review of Publications and Presentations by the Pharmacy Staff Procedure: Pharmacy http://cshsppmweb/dotNet/documents/?docid=38535&mode=view – Travel - Education Procedure: Pharmacy http://cshsppmweb/dotNet/documents/?docid=38538&mode=view – Staff Expectations Procedure: Pharmacy http://cshsppmweb/dotNet/documents/?docid=38544&mode=view – Pharmacist Rotation Coverage for Night Pharmacist Procedure: Pharmacy

	http://cshsppmweb/dotNet/documents/?docid=38534&mode=view – Pharmacist Working Greater than 80 Hours Per Pay Period - Applies to Exempt Pharmacists Procedure: Pharmacy http://cshsppmweb/dotNet/documents/?docid=38542&mode=view – Staffing Plan Procedure: Pharmacy http://cshsppmweb/dotNet/documents/?docid=38218&mode=view – Physician Request for Pharmacist Dosing Services (MM.04.01.01.b) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=19417&mode=view – Pharmacy Services Quality Assurance Program (QAPI) Procedure: Pharmacy http://cshsppmweb/dotNet/documents/?docid=38248&mode=view – Telephones Procedure: Pharmacy – delete – Therapeutic Interchange (MM.02.01.01.b) Procedure: Medication Management – delete – Certification and Recertification of Pharmacists: Pharmacokinetics and Dosing Protocols Procedure: Pharmacy – delete – Reference Sources Procedure: Pharmacy – delete – Chemotherapy Administration –Competency/ Skills Checklist http://cshsppmweb/dotNet/documents/?docid=37144&mode=view – Management of High-Alert Medications (MM.01.01.03) Procedure: Medication Management http://cshsppmweb/dotNet/documents/?docid=38737&mode=view – Chemotherapy Administration, Safe Handling Precautions, Accidental Spill Clean-up and Medical Surveillance of Employees Policy: Clinical Manual/General Clinical http://cshsppmweb/dotNet/documents/?docid=37084&mode=view – Post Kidney Transplant Treatment of Infections Guideline Procedure: Comprehensive Transplant Center http://cshsppmweb/dotNet/documents/?docid=13837&mode=view – Kidney Transplant Treatment of Acute Rejection Guideline http://cshsppmweb/dotNet/documents/?docid=25594&mode=view – Lung, Heart-Lung Post Transplant Infectious Prophylaxis Guideline Procedure: Comprehensive Transplant Center

Requests for full monographs or questions regarding this listing may be addressed to the Drug Information Center at **(310) 423-3784**

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PRE-OPERATIVE ANTIBIOTIC(S) QUICK REFERENCE FY15-16

PROCEDURE	No β-Lactam Allergy Concern	History of Severe β-Lactam Allergy Concern
Cardiac Hernia repair Neurosurgery/Craniotomy Ortho Plastic (clean with risk factors) Spine Thoracic Vascular	Cefazolin 2 gm# IVP x 1	Vancomycin 15 mg/kg IVPB x 1, per dosing chart**
Head and Neck	**Clean Procedures:** Cefuroxime 1.5 gm IVP x 1	Clindamycin 900 mg IVPB x 1
	Clean-Contaminated procedures: Cefuroxime 1.5 gm IVP x 1 **PLUS** Metronidazole 500 mg IVPB x 1	
Biliary Tract Procedures Caesarean Section and Hysterectomy Gastroduondenal Resection	Cefazolin 2 gm# IVP x 1	Clindamycin 900 mg IVPB x 1 **PLUS** Gentamicin 1.5 mg/kg IVPB x 1, pharmacy may adjust per protocol
Appendectomy Colorectal Elective Bowel Resection GU with Bowel Extenteration Lower Limb Amputation	Cefoxitin 2 gm IVP x 1	Gentamicin 1.5 mg/kg IVPB x 1, pharmacy may adjust per protocol **PLUS either** Clindamycin 900 mg IVPB x 1 **OR** Metronidazole 500 mg IVPB x 1
Radical Prostatectomy Transurethral Resection of Prostate	Cefazolin 2 gm# IVP x 1	Gentamicin 1.5 mg/kg IVPB x 1, pharmacy may adjust per protocol

#Weight ≥ 120 kg, use cefazolin 3 gm

CS Antimicrobial Stewardship Committee (Updated 2.4.16)

KEY PRINCIPLES

- If more than one surgery is planned, use recommended antibiotic prophylactic regimen for each surgery.
- If on active treatment prior to surgery, appropriate pre-op dose is still recommended within 60 minutes before incision (120 minutes for vancomycin).
- Severe beta-lactam allergy (and consideration of cephalosporin alternatives) includes: anaphylaxis, angio - or laryngeal edema, or urticaria
- Timing of first post-operative dose should be based on the timing of the last antibiotic dose given (pre-operative/pre-incisional or intra-operative dose)
- Antimicrobial infusion should be completed prior to first incision
- Re-dosing is indicated when the surgery exceeds two half-lives of the drug or there is excessive blood loss (i.e. > 1500 mL).

**VANCOMYCIN DOSE BASED ON TOTAL BODY WEIGHT AND INFUSION DURATION

	VANCOMYCIN	
Patient weight	**Dose**	**Infusion duration**
≤ 40 kg	500 mg	60 minutes
41 – 55 kg	750 mg	60 minutes
56 – 75 kg	1000 mg	90 minutes
76 – 90 kg	1250 mg	90 minutes
91 – 110 kg	1500 mg	120 minutes
> 110 kg	2000 mg	180 minutes

GENTAMICIN DOSING RECOMMENDATIONS BY PATIENT WEIGHT (INFUSE DOSE OVER 30 MINUTES)

- ☐ ≤ 40 kg (90 lbs) = 60 mg
- ☐ 41 – 50 kg (91 – 110 lbs) = 80 mg
- ☐ 51 – 60 kg (111 – 130 lbs) = 90 mg
- ☐ 61 – 70 kg (131 – 150 lbs) = 110 mg
- ☐ 71 – 80 kg (151 – 176 lbs) = 120 mg
- ☐ 81 – 90 kg (177 – 198 lbs) = 140 mg
- ☐ 91 – 100 kg (199 – 220 lbs) = 150 mg
- ☐ > 100 kg (> 220 lbs) – contact pharmacy; use adjusted body weight [AdjBW = IBW + 0.4(TBW-IBW)]

Antibiotic	Infusion Time	Re-dose if case delayed > 60 min from end of infusion		Intra-op re-dosing%	
		Patient wt < 80 kg	**Patient wt ≥ 80 kg**	**Frequency**	**Dose**
Cefazolin (Ancef®) 1st Generation	IV push (3-5 min)	1 gm	repeat pre-op dose	4 hours	1 gm
Cefuroxime (Zinacef®, Kefurox®) 2nd Generation	IV push (3-5 min)	750 mg	repeat pre-op dose	4 hours	750 mg
Cefoxitin (Mefoxin®) 2nd Generation	IV push (3-5 min)	1 gm	repeat pre-op dose	2 hours	1 gm
Clindamycin	30 min	600 mg	repeat pre-op dose	6 hours	600 mg
Metronidazole	60 min	250 mg	repeat pre-op dose	NA	NA
Gentamicin^	30 min	Repeat pre-op dose only when delay > 120 min		6 hours	consult pharmacist
Vancomycin^	See Vancomycin dose table above	Repeat pre-op dose only when delay > 120 min (see below)		NA	NA

^Contact the pharmacist for any dosing related questions

%For prolonged procedures, re-dose at frequency listed x 3 doses, then at usual dosing interval: Q8H for cefazolin, cefuroxime, and clindamvcin: Q6H for cefoxitin

Vancomycin^ For delays > 120 min from end of infusion	**Delay < 8 hours:** 500 mg or 7 mg/kg (whichever is lower)
	Delay ≥ 8 hours: CrCi ≥ 30 mL/min: 1 g or 15 mg/kg (whichever is lower) CrCi < 30 mL/min: 500 mg or 7 mg/kg (whichever is lower)

For more complete information, please consult the full guidelines which can be found in CS-Link in the Web Activities tab under the folder "Medication guidelines"

2016 Boxed Warning (BBW) Updates

04/01/2016

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Summary

Medication Name & BBW Language	Recommendation
New Black Box Warning (BBW) – Formulary Agents	
Methotrexate injection • Use preservative-free formulation for intrathecal and high-dose therapy	• Compounding recipe already requires the use of preservative-free formulation when preparing intrathecal or high-dose methotrexate therapy • No changes to current practice
Gleostine® (lomustine) • Prescribe, dispense, and administer only enough capsules for one dose. Fatal toxicity occurs with overdosage of Gleostine. Both physician and pharmacist should emphasize to patient that only one dose of Gleostine is taken every 6 weeks	• Only 1 dose is prescribed and dispensed to patients at a time • No changes to current practice
Updated Black Box Warning (BBW) – Formulary Agents	
Propylthiouracil • ~~Because of the risk of fetal abnormalities associated with methimazole~~, propylthiouracil may be the treatment of choice when an antithyroid drug is indicated during or just prior to the first trimester of pregnancy.	• Propylthiouracil is used during or just prior to the first trimester of pregnancy • No changes to current practice
Clozaril®, Fazaclo®, Versacloz® (clozapine) • BBW language updated to match updated REMS requirements	• Current practice follows REMS requirements and updated BBW language • No changes to current practice
Zidovudine, lamivudine-containing products • Hepatic function should be monitored closely ***with both clinical and laboratory follow-up for at least several months in patients who discontinue lamivudine and are co-infected with HIV-1 and HBV***. • ***Discontinue*** ~~**suspend**~~ treatment if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity occur	• Hepatic function and signs of lactic acidosis are monitored in patients on zidovudine, lamivudine-containing products • No changes to current practice
Updated Black Box Warning (BBW) – Non- Formulary Agents	
Lotronex® (alosentron hydrochloride) • Removal of requirements for physician enrollment in the prescribing program and for patient to read and sign the Patient -Physician Agreement Form	• No changes in current practice
Dysport® (abobotulinum toxin A) • In unapproved uses, including spasticity in children ~~**and adults**~~, and in approved indications, cases of spread of effect have been reported at doses comparable to ~~**those used to treat cervical dystonia**~~ or ~~**at**~~ lower ~~**doses**~~ ***than the maximum recommended total dose***.	• No changes in current practice

NEW – Methotrexate Injection

Boxed Warning

For intrathecal and high-dose therapy, use the preservative-free formulation of methotrexate. Do not use the preserved formulation for intrathecal or high-dose therapy because it contains benzyl alcohol**.**

Formulary Status: Formulary

Recommendation:

No change to current practice

- Compounding recipe already requires the use of preservative-free formulation when preparing intrathecal or high-dose methotrexate therapy.

Feedback Received From: Department of Hematology & Oncology.

NEW – Gleostine® (Lomustine)

Boxed Warning

Prescribe, dispense, and administer only enough capsules for one dose. Fatal toxicity occurs with overdosage of Gleostine. Both physician and pharmacist should emphasize to patient that only one dose of Gleostine is taken every 6 weeks**.**

Formulary Status: Formulary

Recommendation:

No change to current practice

- Only 1 dose is prescribed and dispensed to patients at a time

Feedback Received From: Department of Hematology & Oncology.

UPDATED – Formulary Agents

Medication(s)	Black Box Warning (BBW)	Recommendations/ Feedback Received From
Propylthiouracil	• Severe liver injury and acute liver failure, in some cases fatal, have been reported in patients treated with propylthiouracil. These reports of hepatic reactions include cases requiring liver transplantation in adult and pediatric patients. • Propylthiouracil should be reserved for patients who cannot tolerate methimazole and in whom radioactive iodine therapy or surgery are not appropriate treatments for the management of hyperthyroidism. • ~~Because of the risk of fetal abnormalities associated with methimazole~~, propylthiouracil may be the treatment of choice when an antithyroid drug is indicated during or just prior to the first trimester of pregnancy.	• **Recommendation**: No change in current practice • **Feedback received from**: Department of Endocrinology
Clozaril®, Fazaclo®, Versacloz® (clozapine)	• Clozapine treatment has caused severe neutropenia, defined as an absolute neutrophil count (ANC) less than 500/µL. Severe neutropenia can lead to serious infection and death. Prior to initiating treatment with Clozaril a baseline ANC must be at least 1500/ µL for the general population; and must be at least 1000/µL for patients with documented Benign Ethnic Neutropenia (BEN). During treatment, patients must have regular ANC monitoring. Advise patients to immediately report symptoms consistent with severe neutropenia or infection (e.g., fever, weakness, lethargy, or sore throat). Because of the risk of severe neutropenia, Clozapine is available only through a restricted program under a Risk Evaluation Mitigation Strategy (REMS) called the Clozapine REMS Program	• **Recommendation**: No further changes - Clozapine REMS procedure updated to reflect changes (Dec'15 P&T) • **Feedback received from**: Department of Neurology
Zidovudine, lamivudine-containing products (Combivir®, Epzicom®, Triumeq®, Trizivir®)	• **Lamivudine** – Severe acute exacerbations of hepatitis B have been reported in patients who are co-infected with hepatitis B virus (HBV) and human immunodeficiency virus (HIV-1) and have discontinued lamivudine. Hepatic function should be monitored closely ***with both clinical and laboratory follow-up for at least several months in patients who discontinue lamivudine and are co-infected with HIV-1 and HBV***. If appropriate, initiation of anti-hepatitis B therapy may be warranted. • **Zidovudine** – ❑ has been associated with hematologic toxicity including neutropenia and severe anemia, particularly in patients with advanced Human Immunodeficiency Virus (HIV-1) disease. ❑ Prolonged use of zidovudine has been associated with symptomatic myopathy • **Lamivudine & zidovudine** - Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues and other antiretrovirals. ***Discontinue*** ~~**suspend**~~ treatment if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity occur.	• **Recommendation**: no change to current practice • **Feedback received from**: Department of Infectious Disease

UPDATED - Non-Formulary Agents

Medication(s)	Black Box Warning (BBW)	Recommendations/ Feedback Received From
Lotronex® (alosetron hydrochloride)	• Serious gastrointestinal adverse events, some fatal, have been reported with the use of LOTRONEX. These events, including ischemic colitis and serious complications of constipation, have resulted in hospitalization, blood transfusion, surgery, and death. • ~~**Only physicians who have enrolled in GlaxoSmithKline's Prescribing Program for LOTRONEX, based on their attestation of qualifications and acceptance of responsibilities, should prescribe LOTRONEX**~~ • LOTRONEX is indicated only for women with severe diarrhea-predominant IBS who have failed to respond to conventional therapy . ~~**Less than 5 percent of IBS is considered severe. Before receiving the initial prescription for LOTRONEX, the patient must read and sign the Patient-Physician Agreement**~~ • LOTRONEX should be discontinued immediately in patients who develop constipation or symptoms of ischemic colitis. ***Patients should immediately report constipation or symptoms of ischemic colitis to their prescriber***. ~~**Physicians should instruct patients to immediately report constipation or symptoms of ischemic colitis.**~~ LOTRONEX should not be resumed in patients who develop ischemic colitis. ***Patients who have constipation should immediately contact their prescriber if the constipation does not resolve after LOTRONEX is discontinued***. ~~***Physicians* should instruct patients who report constipation to immediately contact them if the constipation does not resolve after discontinuation of LOTRONEX**~~. Patients with resolved constipation should resume LOTRONEX only on the advice of their treating physician.	• **Recommendation**: No change in current practice • **Feedback Received From**: Department of Gastroenterology
Dysport® (abobotulinum toxin A)	• Post-marketing reports indicate that the effects of Dysport and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children ~~**and adults**~~, and in approved indications, cases of spread of effect have been reported at doses comparable to ~~**those used to treat cervical dystonia**~~ or ~~**at**~~ lower ~~**doses *than***~~ ***the maximum recommended total dose***.	• **Recommendation**: No change in current practice • **Feedback Received From**: Department of Neurology