Pharmacist Meeting – Clinical update

November – December 2017

P&T Updates – New Formulary Meds

- **Portrazza (necitumumab)**
  - Indication:
    - treatment of metastatic squamous non-small cell lung cancer, in combo with gemcitabine & cisplatin
  - Mechanism of action:
    - MAB that binds to EGFR (epidermal growth factor) and induces antibody dependent cellular cytotoxicity in EGFR expressing cells.
  - Clinical Data:
    - Slight survival benefit as compared to therapy with only gemcitabine & cisplatin (overall survival - 11.5 months vs 9.9 months; progression free survival – 5.7 months vs 5.5 months)
  - Clinical Pearls:
    - NCCN guidelines recently removed this therapy from recommendations due to potential toxicity, costs and limited improvement in efficacy when compared to therapy with gemcitabine & cisplatin alone
    - Despite NCCN change this therapy still may be beneficial in patients especially if they don't qualify for another targeted agent.
    - High incidence of dermatologic and infusion related reactions (> 40%) – pre-meds not required unless previous infusion reactions noted
    - **Black box warning for risk of cardiopulmonary arrest and hypo-magnesemia**
    - **Electrolytes must be checked prior to EVERY infusion and abnormalities promptly corrected to prevent cardiac events**
  - Restrictions:
    - Outpatient infusion use ONLY

P&T Updates – New Formulary Meds

- **Rydapt (midostaurin)** → *oral specialty oncology medication*
  - Indication:
    - FLT3 mutation positive AML – in combination with standard cytarabine and daunorubicin induction and cystarabine consolidation
  - Mechanism of action:
    - Multi-kinase inhibitor that has shown ability to inhibit FLT3 receptor signaling which in turn inhibits cell proliferation and induces apoptosis expressing this particular mutation.
  - Clinical Data:
    - Significant survival benefit in Rydapt treated patients (overall survival – 74.7 months vs 26 months for placebo)
  - Clinical Pearls:
    - Highly effective adjunct therapy for patients with FLT3 positive AML
    - Dosing begins on day# 8 of induction therapy (inpatient) and continues through day #21 of each induction cycle (also on days 8-21 of each consolidation cycle)
    - Initial therapy will be started as inpatient but patient MUST have drug prior to discharge to complete initial induction cycle
    - Typically TNONC pre-arranges shipment of Rydapt prior to admission of initial induction therapy via their own specialty pharmacy and this usually arrives prior to this being needed on day#8
  - Restrictions:
    - Since therapy doesn't begin until day #8 it is recommended to coordinate shipment via specialty pharmacy channels as a patient specific prescription due to the high cost and to ensure continuity of care when discharged. **In the event that this is unable to be coordinated prior to day #8 it may be ordered by inpatient pharmacy to prevent a delay in therapy initiation.**

Meds *NOT* added to formulary

- **Bevyxxa (betrixaban)**
  - Indication:
    - VTE prophylaxis in at-risk, acutely ill, hospitalized medical patients (for 35-42 days)
  - Mechanism of action:
    - Xa inhbitior (same class of drugs as Xarelto, Eliquis, etc.)
  - Clinical pearls:
    - Primary metabolism via gut with only minimal renal clearance (< 10%)
    - **Longest effective half-life of Xa inhibitors – 19-27 hours**
    - **Therapeutic effect lasts for at least 72 hours (problematic if unplanned procedures needed during hospitalization)**
    - Only indication is for VTE prophylaxis in hospitalized "at-risk" patients
    - Definition of "at-risk" very broad in clinical trial and its unknown which patients would most benefit
    - Compared to enoxaparin once daily dose for 6-14 days vs 35-42 days of therapy for betrixaban
    - Did not meet pre-specified primary outcome (patients with elevated D-dimer)
    - **Additional analyses showed modest efficacy benefit in overall population – 5.3% vs 7%**
    - No difference in major bleeding but higher rates of non-major bleeding (2.45% vs 1.02%)

Meds *NOT* added to formulary

- **Northera (droxidopa)** → *oral specialty **cardiology** medication*
  - Indication:
    - Orthostatic hypotension or dizziness in patients with neurogenic orthostatic hypotension (Parkinson's disease, pure autonomic failure, etc.)
  - Mechanism of action:
    - Norepinephrine pro-drug with resulting increase in BP by inducing peripheral and venous vasoconstriction
  - Clinical pearls:
    - Cost per month of therapy – minimum of $2500 per month
    - Clinical studies show minimal to no benefit beyond two weeks of treatment.
    - Droxidopa is now included in ACC/AHA syncope treatment guideline – see next slide
    - Same strength of recommendation as midodrine and fludrocortisone
    - Very difficult to determine patient cost-share/affordability and benefits coordination while admitted
  - Cardiology recommendation:
    - **Very limited role for inpatient initiation and not needed to be added to formulary & stocked by pharmacy. Non-formulary use may be considered for patients with primary autonomic failure (Shy Drager syndrome, primary autonomic failure) on a case by case basis after consultation with neurology, EP, or cardiology providers on a case by case basis.**
  - If ordered – contact Patrick and Marissa to begin benefits evaluation process

Syncope guidelines (ACC/AHA)

IIa	**B-R**	**Midodrine can be beneficial in patients with syncope due to neurogenic OH (458-467).**
See Online Data Supplements 33 and 34.		Midodrine improves symptoms of OH in patients with neurogenic OH (458-467). There is a dose-dependent effect, usually corresponding to an increase in standing blood pressure (459,460,462,463,466,467). Its use may be limited by supine hypertension, and other common side effects include scalp tingling, piloerection, and urinary retention (459,460,463,467).
IIa	**B-R**	**Droxidopa can be beneficial in patients with syncope due to neurogenic OH (380,468-471).**
See Online Data Supplements 33 and 34.		Droxidopa improves symptoms of neurogenic OH due to Parkinson disease, pure autonomic failure, and multiple system atrophy (380,468,470,471). Droxidopa might reduce falls, according to small studies (472). Use of carbidopa in patients with Parkinson disease may decrease the effectiveness of droxidopa (380). Use and titration of droxidopa may be limited by supine hypertension (380,469), headache, dizziness, and nausea (468,470-472).
IIa	**C-LD**	**Fludrocortisone can be beneficial in patients with syncope due to neurogenic OH (473-476).**
See Online Data Supplements 33 and 34.		Fludrocortisone increases plasma volume, with a resultant improvement in symptoms of OH (473,477,478). When taken regularly, fludrocortisone may prevent OH, at least in astronauts after space flight (476). Supine hypertension may be a limiting factor. When supine hypertension is present, other medications should be used before fludrocortisone. Other side effects commonly seen include

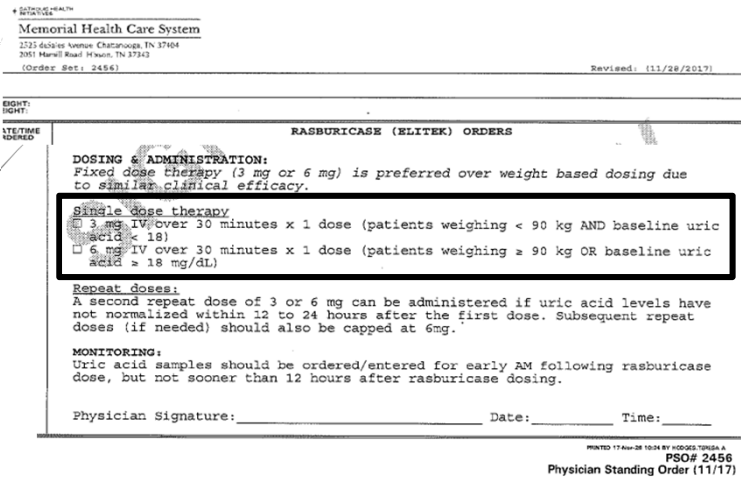
Formulary Interchange Updates

- **GLP-1 agonist combination insulin products**
  - The below conversion can be found on Form Web

Ordered	Provided
Soliqua® (insulin glargine/lixisenatide) daily injection (*each Soliqua® unit contains 1 unit of insulin glargine*)	**Insulin detemir (Levemir®)** • Convert Soliqua® unit per unit to levemir units, divide evenly into two doses and give twice daily • Start 24hrs after patient received last home dose of Soliqua®
Xultophy® (insulin degludec/liraglutide) daily injection (*each Xultophy® unit contains 1 unit of insulin degludec*)	**Insulin detemir (Levemir®)** • Convert Xultophy® unit per unit to levemir units, divide evenly into two doses and give twice daily • Start 24hrs after patient received last home dose of Xultophy®

Elitek (rasburicase) order set

- New order set to assist with appropriate dosing when ordered by non-oncology provider OR when ordered as non-fixed dose (weight based dosing)



Memorial Health Care System
2525 deSales Avenue Chattanooga, TN 37404
2051 Harrell Road Hixson, TN 37343
(Order Set: 2456) Revised: (11/28/2017)

RASBURICASE (ELITEK) ORDERS

DOSING & ADMINISTRATION:
Fixed dose therapy (3 mg or 6 mg) is preferred over weight based dosing due to similar clinical efficacy.

Single dose therapy
☐ 3 mg IV over 30 minutes x 1 dose (patients weighing < 90 kg AND baseline uric acid < 18)
☐ 6 mg IV over 30 minutes x 1 dose (patients weighing ≥ 90 kg OR baseline uric acid ≥ 18 mg/dL)

Repeat doses:
A second repeat dose of 3 or 6 mg can be administered if uric acid levels have not normalized within 12 to 24 hours after the first dose. Subsequent repeat doses (if needed) should also be capped at 6mg.

MONITORING:
Uric acid samples should be ordered/entered for early AM following rasburicase dose, but not sooner than 12 hours after rasburicase dosing.

Physician Signature:_____ Date:_____ Time:_____

PSO# 2456
Physician Standing Order (11/17)

"Fixed" doses of 3 or 6 mg preferred – clinical data has shown this to be as effective as weight based dosing

Anaphylaxis & Acute Drug Hypersensitivity Policy/Protocol

- **Existing anaphylaxis standing orders modified**
  - Incorporates treatment options for mild and moderate reactions to expedite care for patients experiencing acute medication related reactions
  - Allows nurse to treat the patient instead of waiting on the physician to call back with specific orders
  - Orders must be validated/signed by the provider ASAP after treatment is given
  - Treatments based on objective clinical findings as detailed on the orders
- **Most applicable to infusion center but can be used in any inpatient location**
  - Education to non-infusion staff to happen in the next few weeks
- **See handout for details**

High Alert Medications – *modification to existing policy*

- Adding required eMAR documentation for any drug with a known hypersensitivity reaction to minimize the risk of pump programming errors and patient safety risk if infused too rapidly

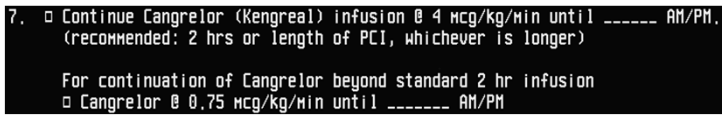
Hazardous antineoplastic medications	Refer to Policy MM-05404 Cytotoxic Drug Management & Administration.
Non-hazardous biologic medications with known risk of acute hypersensitivity or infusion related reactions	Documentation of 2nd nurse verification is required with every dose administration to verify the drug, concentration, and settings on the infusion pump against the eMAR or provider order.

Anticoagulation updates

- **Factor Xa inhibitors – use of Kcentra (PCC) for bleeds**
  - For serious bleeds (intracranial hemorrhage, life threatening hemorrhage, etc.) please remember that doses up to 50 units/kg (5000 unit max) may be used
  - Please reference the laminated reversal guideline cards for more information
- **Warfarin dosing – cardiac surgery patients (valve surgery, etc.)**
  - Updated dosing scheme for initial dosing seems to be effective in decreasing elevated INRs without delay to therapeutic INR. We will continue with the below for any patient that is acute, s/p cardiac surgery needing warfarin therapy.
    - INR ≤ 1.2 → 4 mg
    - INR 1.3-1.4 → 3 mg
    - INR ≥ 1.5 → 2 mg

Anticoagulation updates – *continued*

- **Cangrelor dosing – post cardiac cath lab**
  - If a patient is unable to swallow and unable to receive oral loading dose of platelet inhibitor post intervention the second option below should be used for patients needing prolonged cangrelor infusion (after initial 2 hour infustion)
  - The 4 mcg/kg/min dose should only be used during the procedure and up to 2 hours
  - The 0.75 mcg/kg/min dose approximates a maintenance dose effect of platelet inhibition



- **Xarelto – new indication**
  - *Reduction in the risk of recurrence of DVT and/or PE in patients at continued risk for DVT and/or PE* → **10 mg ONCE daily** with or without food, and **after at least 6 months of standard anticoagulant treatment**
  - Compared to ASA, decreased incidence of recurrent VTE (1.2% vs 4.4%) with similar rates of major bleeding (0.4% vs 0.3%) and non-major bleeding (2% vs 1.8%)
  - CrCl < 30 ml/min: this dose was not studied so use should be avoided

Antibiotic Stewardship

- **Valproic Acid – Meropenem drug interaction**
  - Concomitant use will result in decreased concentrations of valproic acid
  - If ordered together please assess clinical significance of interaction
    - Seizure indication – consider alternative antimicrobial if/when possible
    - Bipolar or other indication – notify prescriber of potential interaction to determine if changes in therapy are necessary
- **Please don't disregard drug – drug interactions → this is a dangerous practice and can result in serious consequences**

Acyclovir Dosing Standardization – *renal dosing & IV to oral considerations*

Acyclovir (Zovirax®) IV dosing only *Use IBW; if TBW >20% IBW, use adjBW*			
CrCl (ml/min)	**HSV encephalitis/Herpes zoster**	**Herpes simplex infections**	**Prevention of HSV/VZV when unable to tolerate PO**
> 50	10mg/kg/dose IV q8h	5mg/kg/dose IV q8h	5mg/kg/dose IV q12
25-50 or CRRT	10mg/kg/dose IV q12h	5mg/kg/dose IV q12h	5mg/kg/dose IV q24
10-24	10mg/kg/dose IV q24h	5mg/kg/dose IV q24h	2.5mg/kg/dose IV q24h
<10 or HD	5mg/kg/dose IV q24h	2.5mg/kg/dose IV q24h	

* Please clarify indication with provider prior to selecting a dosing strategy

** When transitioning a patient from PO valacyclovir to IV acyclovir, please consider this conversion: Valacyclovir 1,000mg PO TID → Acyclovir 5mg/kg/dose IV q8h

Dosing weight: IBW, or Adj. Body Weight for patients 20% over IBW.
See ForWeb for renal dosing considerations.

Automatic repeat blood cultures – *coag (-) staph bacteremia*

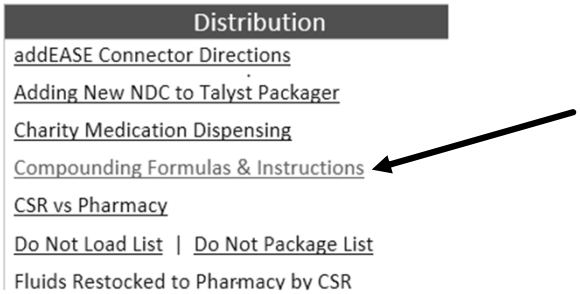
Title:
AUTOMATIC REPEAT BLOOD CULTURES FOR COAGULASE NEGATIVE *STAPHYLOCOCCUS* BACTEREMIA

PROCEDURE:

A. Indications
   a. ≥ 2 blood cultures growing CoNS and no active antibiotics received
B. Exceptions
   a. Comfort measures only or MD not planning to treat the positive culture
C. Protocol
   a. The Antimicrobial Stewardship Program (ASP) pharmacist will identify patients eligible for intervention via TheraDoc®
   b. The pharmacist will automatically order repeat set of blood cultures
   c. The pharmacist will notify primary physician of the positive blood cultures as well as the pending repeat blood cultures

Compounding Rolodex

- The compounding Rolodex has now been retired and replaced with an online Form Web reference – see screenshots below



Compounding Formulas & Instructions
CHI Memorial Hospital Pharmacy Department
Last Updated: November 2017

Product	Ingredients	Preparation Instructions	Expirati
Epinephrine/cocaine gel (Dr. Minton in ER may use)	Epinephrine 1 mg/ml – 0.8 ml Cocaine 10% - 1.8 ml Methylcellulose 0.15 gm	1. Mix 0.8 ml of epinephrine 1 mg/ml with 1.8 ml cocaine 10%. 2. Mix in 0.15 gm methylcellulose.	Unknow before u
Amphotericin B for	Amphotericin B 50 mg vial	1. Add amphotericin B 50 mg to D5W 500 ml.	14 days

Pre-op Holding of Medications - *reminder*

- **Heart Surgery Pre-op orders:** This order set should accompany the anesthesia orders but it may not always due to the timing of the anesthesia orders being completed and signed by anesthesia staff. The ACE/ARB hold parameter is already outlined on our reference document and the anticoagulants are typically addressed by surgery staff but it's always good to double check that this was not also missed by the surgeon/provider.

- **Pre-PCI/arteriogram orders:** Anesthesia is not involved with these procedures and thus this order will not apply to these cases. The majority of these procedures are for outpatients and the hold parameters will not apply since they are showing up the day of procedure and these instructions are relayed to the patient by CHI staff. However, for patients that are inpatients and then have this procedure please screen for any meds that may need to be deactivated as outlined on the orders. This will be a small minority of these patients.

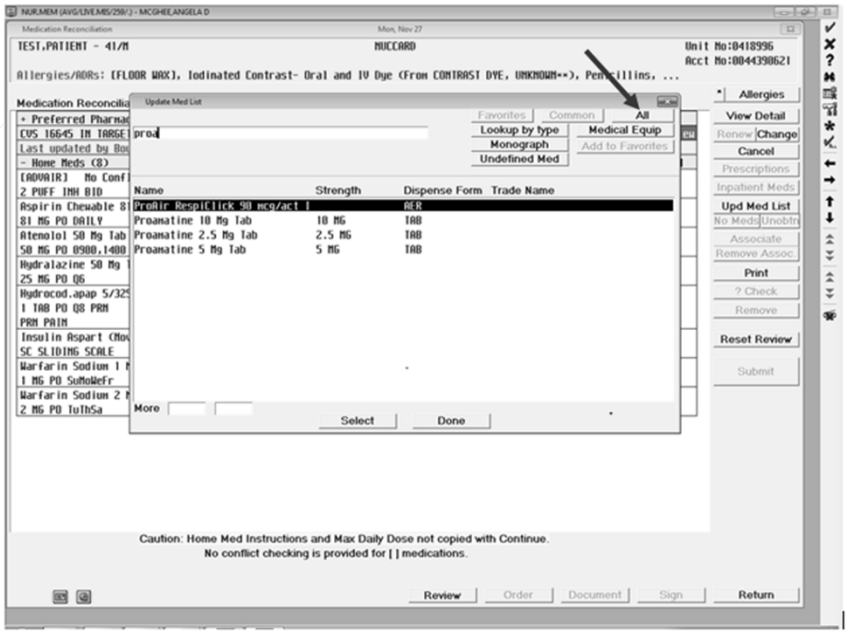
Pharmacokinetics

- **Shift to Shift communication of levels**
  - Please communicate all pending drug levels to 2nd and 3rd shifts
  - 2nd and 3rd shifts to re-run PK consult list to confirm any levels pending
    - 2nd shift kinetics pharmacist: run PK consult list at 5:30
    - 3rd shift pharmacist: run PK consult list again at 9:30
- **Loading doses – we will soon be modifying our methodology for calculating Vancomycin loading doses based on recent MUE results**
  - Update expected in late December or early January

Miscellaneous

- **Clinical interventions changes – questions??**
- **Non-formulary, specialty medications**
  - If you have a home med continuation order for a product that we do not have the specific strength built that is needed → please notify Angie, Jeff, or myself so a new entry can be built
  - Please do not use a lower dose entry due to risk of error (example: order for Gleevec 400 mg – do not key using the Gleevec 100 mg tablets). Key as "NF" entry until the appropriate strength entry can be built
- **IV Push Antibiotics**
  - Meropenem, Aztreonam, Cefepime now also administered as IVP
  - Sterile water for injection will be used for dilution of all IVP antibiotics now
  - Pyxis pop-ups will instruct nurse on the diluent volume needed & reminder to remove sterile water from Pyxis along with antibiotic vial
  - **PLEASE KEY ALL ANTIBIOTICS USING THE "SET" SO THE STERILE WATER IS ALSO PROFILED FOR THE NURSE TO REMOVE FOR DILUTION PURPOSES**

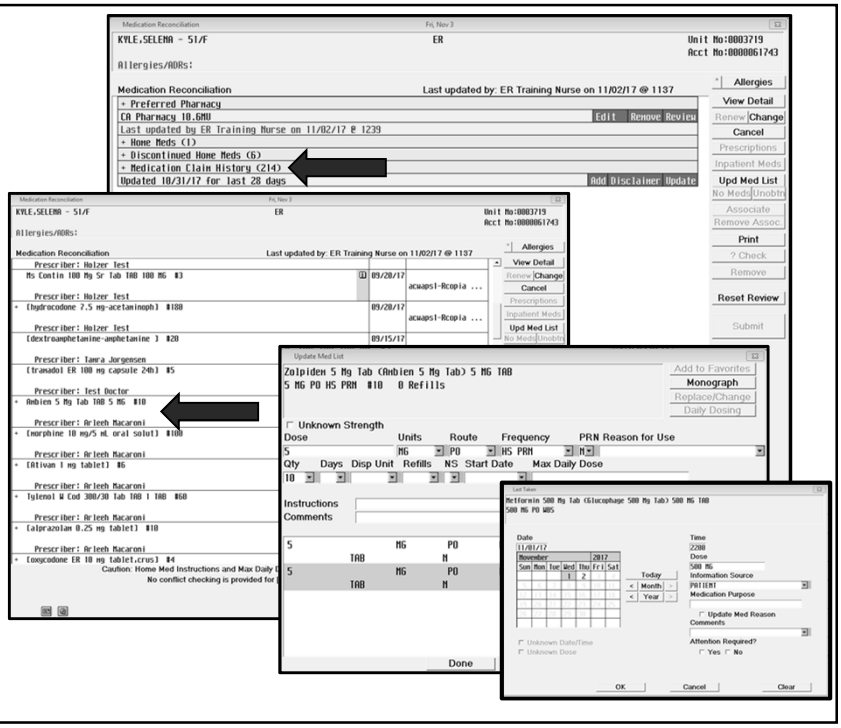
RXM Dictionary Changes, Dr. First Integration



Medication Claim History can be used to assist in accurately updating home medication list.

- Expand **Medication Claim History**
- Click on medication order to be added to home med list
- Select correct order string
- Select **Date** of last dose by clicking on calendar date
- Key **Time** of last dose
- Key **Dose**
- Select **Information Source** from drop down menu
- Click **OK**

EDM: Medication Reconciliation



ED Medication History Changes – *Increased responsibility of ED RN's*

- **Chest Pain Accreditation**
  - Now requiring that medication reconciliation occur for ALL patients seen in the ED including patients being discharged to home from ED
  - This will require med lists to be completed for ALL patients following triage
- **Pharmacy impact**
  - This means that ALL med lists will be "updated" and very few "Profile Not Reviewed" med lists will originate from the ED
  - Don't let your guard down on reviewing these lists → if something doesn't look right PLEASE verify with Dr. First, CSMD or have ED tech repeat the list
  - ED techs will repeat/verify these med histories while they are there but after staffed hours this will be a potential source of errors

Midline Catheters (PowerWand)