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Bally's Las Vegas

Educational Program Lectures

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Understanding The Drug Formulary Decision-Making Process In Pharmacy

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Learning Objectives

- Discuss the pharmacy formulary decision making process.
- Identify contributions Pharmacy Buyers can make when considering addition of medications to formulary.
- Describe the cost/benefit analysis of medication use.

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Audience Participation

- What strategies are currently incorporated at your institution related to medication formulary decision making?

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What is a Formulary?

- "A formulary is a continually updated list of available medications and related information, representing the clinical judgment, resulting from a review of the clinical evidence, of physicians, pharmacists, and other clinicians in the diagnosis, prophylaxis, or treatment of disease and promotion of health."

Ciccarello C, et al. *Am J Health Syst Pharm*. 2021 May 6;78(10):907-918.

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Governance Process

- The Pharmacy & Therapeutics (P&T) committee oversees formulary and medication management
  - Multidisciplinary team
  - Establishes formal appointments
  - Evaluates potential conflicts of interest
  - Considers all areas of the health-system
  - Distributes education pertaining to decisions made

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Formulary Considerations

- FDA-approved prescribing information
- Clinical trial and comparative evaluation
- Clinical guideline updates
- Pharmacoeconomic considerations
- Medication use evaluations
- Impact on workflow
- Medication availability
- Restrictions

Ciccarello C, et al. *Am J Health Syst Pharm*. 2021 May 6;78(10):907-918.

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Discrepancies in Formulary Decision Making

- Evaluated 24 P&T meetings at 3 different sites
- Discussions were assigned to 7 categories
  - Evidence of need
  - Efficacy/indications
  - Safety
  - Misuse potential
  - Cost issues
  - Committee decision-making issues
  - Operational and implementation considerations
- Inconsistent time spent on each category

Schiff GD, et al. *Am J Health Syst Pharm*. 2019 Apr 8;76(8):537-542.

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New Medication Evaluation

- Innovation vs. “me-too” drug
  - Are there other medications within this class?
  - Does it have a unique mechanism of action?
- Clinical efficacy
- Adverse effects and drug-drug interactions
- Dosing and monitoring
- Cost
- Workflow impact

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Example of New Medication Evaluation

	Linezolid	Tedizolid
Therapeutic class	Oxazolidinone	Oxazolidinone
Spectrum of activity	MRSA, VISA, VRSA VRE	MRSA, VISA, VRSA VRE
Clinical pearls	Serotonin syndrome (DDI); thrombocytopenia; peripheral neuropathy; optic neuritis	Less MAO inhibition; less cumulative toxicity = less hematologic reactions
Dosing	600mg IV/PO q12h	200mg IV/PO daily
Price (per vial) **Price (per tablet)**	$22.33 $4.73	$345.06 $433.19
Price (daily IV) **Price (daily PO)**	$44.66 $9.46	$345.06 $433.19
Formulary consideration	Yes	No

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Example of New Medication Evaluation

	Vancomycin	Daptomycin	Dalbavancin	Oritavancin
Therapeutic class	Glycopeptide	Lipopeptide	Lipoglycopeptide	Lipoglycopeptide
Spectrum of activity	MRSA	MRSA VRE	MRSA, VISA VanB	MRSA, VISA, VRSA VanA, VanB
Clinical pearls	Nephrotoxicity; "red man" syndrome	CPK elevation; sequestered by lung surfactant	Renal dosage adjustment; 30 min infusion	aPTT interaction; 3 hr infusion
Dosing	15mg/kg IV q12h	4mg/kg IV daily	1500mg IV x1	1200mg IV x1
Price (per vial)	$3.02 (1000mg)	$445.49 (500mg)	$1316.25 (500mg)	$915.40 (400mg)
Price (daily)	$6.04	$445.49	$3948.75	$2746.20
Formulary consideration	---	Yes, restricted	No, outpatient	No, outpatient

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Example of New Medication Evaluation

	Colistimethate sodium	Ceftazidime/avibactam
Therapeutic class	Polymyxin	Cephalosporin
Spectrum of activity	Pseudomonas sp. Acinetobacter sp. ESBL, CRE	Pseudomonas sp. ESBL CRE
Clinical pearls	Very bactericidal activity; nephrotoxicity; neurotoxicity; considered a last-line agent	2-hour infusion
Dosing	2.5-5mg/kg/day IV in divided doses	2.5g IV q8h
Price (per vial)	$10.22 (150mg)	$333.74
Price (daily)	$20.44-$30.66	$1001.22
Formulary consideration	---	Yes, restricted

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Existing Medication Evaluation

- Same information evaluated as a new medication
- Generic availability / formulation change
- Utilization
- Therapeutic class reviews
- Medication use evaluations
- Clinical literature or guideline updates

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Generic Name	Omeprazole	Lansoprazole	Esomeprazole	Pantoprazole	Rabeprazole	Dexlansoprazole
Brand Name	Prilosec, Zegerid	Prevacid, Prevacid SoluTab	Nexium	Protonix	Aciphex	Dexilant
Dosage Forms and Strengths Available	10mg, 20mg, 40mg DR caps; 2.5mg, 10mg/pkt DR susp; 20mg, 40mg caps; 20mg ODT; 20mg, 40mg/pkt susp,	15mg, 30mg DR caps; 15mg, 30mg ODT;	20mg, 40mg DR caps; 2.5mg, 5mg, 10mg, 20mg, 40mg/pkt DR susp, 20mg, 40mg powder for inj	20mg, 40mg DR caps; 40mg/pkt susp; 40mg IV	5mg, 10mg DR caps (sprinkle); 20mg DR tabs	30mg, 60mg DR caps
Indications	X = FDA-approved indication * = non-FDA-approved indication - = no indication					
Duodenal Ulcer	X	X	X	-	X	-
Peptic Ulcer Disease (Eradication of H. pylori)	X	X	X	*	X	-
Gastric Ulcer	X	X	X	-	*	-
Erosive Esophagitis	X	X	X	X	X	X
Symptomatic Gastroesophageal Reflux Disease GERD	X	X	X	X	X	X
Zollinger-Ellison Syndrome (hypersecretory)	X	X	X	X	X	-
Upper GI Bleed Risk Reduction in Critically ill	*	*	*	*	-	-
NSAID-associated gastric ulcer	*	X	X	*	-	-
Heartburn (OTC labeling)	X	X	X	-	-	X
Other Potential Off-Label Uses	Gastritis	Gastritis	Gastritis	Gastritis	Gastritis	Gastritis
Dosing Frequency Range	Daily - BID	Daily - q8h	Daily - BID	Daily - BID	Daily - BID	Daily - BID
FDA Approved (Y/N)	Y	Y	Y	Y	Y	Y
Available in UD barcode (Y/N)	Y	Y	Y	Y	-	-
Generic Availability (Y/N)	Y	Y	Y	Y	Y	N
HealthTrust Contract (Y/N)	Y	Y	Y	Y	Y	N
Cost/Lowest UD ($)	Cap: $0.13- $0.20 Pckt:: $22.94 to $133.00	Cap: $0.62 ODT $8.34	Cap: $5.18 Pckt: $8.34	Cap: $0.12-$0.14 Pckt: $12.54	N/A	N/A
Cost/Bulk ($)	Cap: $0.04-$0.11	Cap: $0.17-$0.19	Cap: $0.26- $0.31 Inj: $2.54	Tab: $0.05-$0.09 Inj: $2.54	Tab: $0.31	$8.71
Avg Cost/Day ($)	Cap: <$1 Packet: $22.94 to $133.00	Cap: <$1 ODT: $8.34	Cap: <$1; Inject: <$5 Packet: $8.34	Tab: <$1 Inj: < $3.00 Packet: $13.17	<$1	<$18

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Clinical Literature Evaluation

- Goal: to optimize appropriate medication use and improve quality of patient care

- Literature strength of evidence ranges
- FDA-approved prescribing information
- Therapeutic class reviews
- Pharmaceutical company medication dossiers should be used with caution

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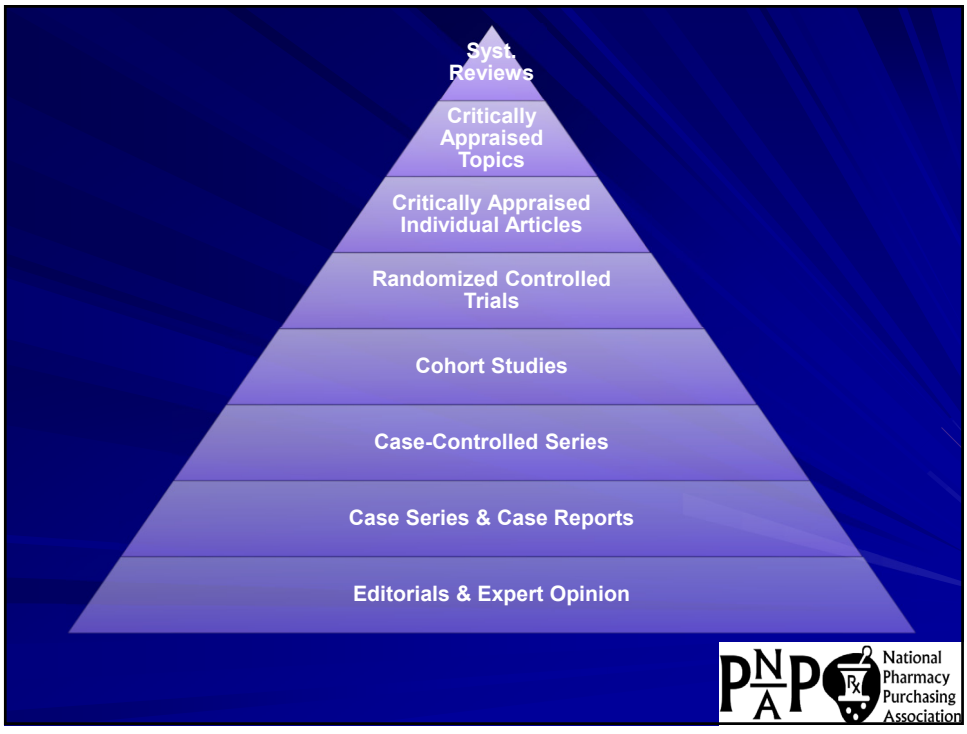

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	Omeprazole	Lansoprazole	Esomeprazole	Pantoprazole	Rabeprazole	Dexlansoprazole
Pregnancy Risk Category	C	B	C	C	C	B
Lactation (Y/N)	Use with caution					
Severe drug-drug interactions	Concomitant use of PPIs with thienopyridines (e.g., clopidogrel) could be justified in patients without strong affinity to cytochrome CYP2C19 and with high risk of bleeding (e.g., patients with prior upper gastrointestinal bleeding, H. pylori infection, advanced age, steroid treatment, and nonsteroidal anti-inflammatory drug use). Concomitant administration of PPIs and high dose methotrexate may elevate / prolong serum methotrexate concentrations and increase the risk of methotrexate toxicity.					
Black box warnings/ Key CI, warnings, precautions	No black box warnings to date. Acute interstitial nephritis has been observed in patients taking PPIs. The risk of bone fracture may be increased in patients who take PPIs at high dose and/or long-term therapy. Long-term therapy may contribute to malabsorption or cyanocobalamin deficiency. PPI therapy may be associated with an increased risk of C difficile associated diarrhea.					
Most Common Adverse Events	Adults 65 years and older are more vulnerable to hip fractures, cardiac events, iron deficiency, C. difficile infection, pneumonia					
Potential for Errors: Sentinel events/ ISMP Alerts/LASA	"ISMP's List of Confused Drug Names" omeprazole - fomepizole; protamine - Protonix; Protonix – Lotronex; Aciphex – Aricept; Nexium – Nexavar; Pristiq – Prilosec; Prilosec – Prozac					
Pediatric Dosing (Y/N with age range)	Y 2-16 yrs	Y 1-11yrs; 12-17 yrs	Y 1 mo to < 1 yr; 1-17yrs;	Y 5-16 yrs	Y 1-11 yrs ≥12 yrs	N
Geriatric Dosing (Y/N)	Y	Y	Y	Y	Y	N
Dose Adjust in Renal Dysfunction (Y/N)	N	N	N	N	N	N
Dose Adjust in Hepatic Dysfunction (Y/N)	N	N	Y	N	N	Y
Time to Peak	0.5 – 3.5 hrs	1.7 hrs	1-1.5 hrs	2.5 hrs	Tab: 2-5 hrs Cap: 1-6.5 hrs	Peak 1: 1-2 hrs Peak 2: 4-5 hrs
Half Life	0.5 – 1 hr	1.5 +/- 1 hr	1.5-2 hrs	1 hr; 3.5-10 hrs w/ CYP2C19 deficiency	1-2 hrs	1-2 hrs

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Medication Use Evaluations

- Internal quality evaluation of medications
- Used to measure outcome of medications
  - Adverse effects
  - Patient outcomes
  - Clinical efficacy
  - Appropriateness of use
  - Adherence to policies
  - Cost analysis

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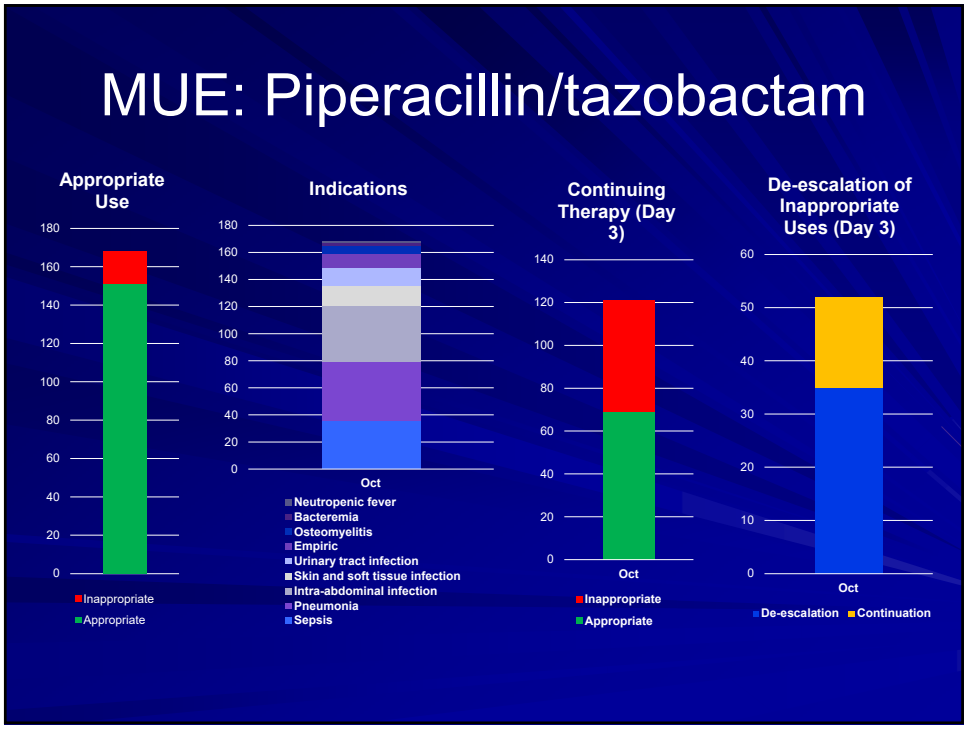
MUE: Piperacillin/tazobactam
Appropriate Use
180
160
140
120
100
80
60
40
20
0
Inappropriate
Appropriate
Indications
180
160
140
120
100
80
60
40
20
0
Oct
Neutropenic fever
Bacteremia
Osteomyelitis
Empiric
Urinary tract infection
Skin and soft tissue infection
Intra-abdominal infection
Pneumonia
Sepsis
Continuing Therapy (Day 3)
140
120
100
80
60
40
20
0
Oct
Inappropriate
Appropriate
De-escalation of Inappropriate Uses (Day 3)
60
50
40
30
20
10
0
Oct
De-escalation
Continuation

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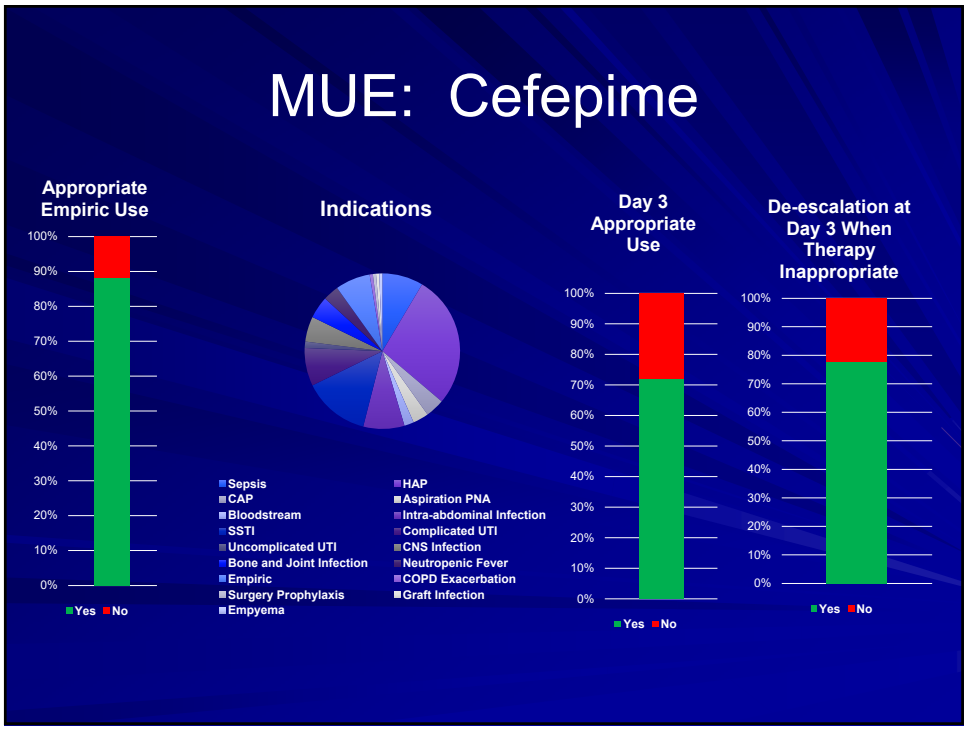
MUE: Cefepime
Appropriate Empiric Use
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yes
No
Indications
Sepsis
CAP
Bloodstream
SSTI
Uncomplicated UTI
Bone and Joint Infection
Empiric
Surgery Prophylaxis
Empyema
HAP
Aspiration PNA
Intra-abdominal Infection
Complicated UTI
CNS Infection
Neutropenic Fever
COPD Exacerbation
Graft Infection
Day 3 Appropriate Use
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yes
No
De-escalation at Day 3 When Therapy Inappropriate
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yes
No

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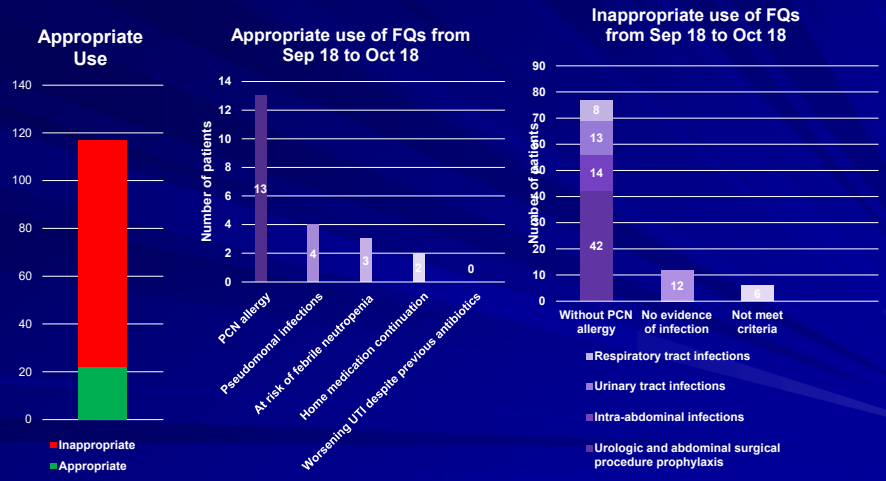
MUE: Fluoroquinolones



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Clinical Practice Guidelines

Clinical Definition	Recommended treatment options
Initial episode, non-severe	• VAN 125 mg PO QID for 10 days • FDX 200 mg PO BID for 10 days • If above are unavailable: MTR 500 mg PO TID for 10 days
Initial episode, severe	• VAN 125 mg PO QID for 10 days • FDX 200 mg PO BID for 10 days
Initial episode, fulminant	• VAN 500 mg PO/PT QID • If ileus: VAN 500 mg PR QID • If ileus: MTR 500 mg IV TID

BID: twice daily, FDX: fidaxomicin, IV: intravenous, MTR: metronidazole, PO: by mouth, PR: per rectum, PT: per feeding tube, QID: four times daily, TID: three times daily, VAN: vancomycin

- Re-evaluated metronidazole and fidaxomicin role in formulary

McDonald LC, et al. *Clin Infect Dis*. 2018;66(7):e1-e48.

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Pharmacoeconomic Considerations

- Cost-minimization analysis
  - For medications therapeutically equivalent
- Cost-benefit analysis
  - For medications not therapeutically equivalent
- Cost-effectiveness analysis
  - Amount spent to achieve an outcome
- Cost-utility analysis
  - Amount spent to improve quality-adjusted life years

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Ready to Use Products

- Minimizes risk of medication errors
- Improves workflow efficiency
  - Increase ease of access
  - Decrease pharmacy demand
- Allow for better inventory control tracking
  - Decrease medication waste
- Enhance stability data
- Potentially more costly

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Hepler CD, et al. *Am J Hosp Pharm*. 1990;47:533-43.
ASHP. *Am J Health Syst Pharm*. 2013:70:448-552.

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Audience Participation

- Which strategy do you think is most important to consider in relation to medication formulary decision making?
- What ready-to-use products do you wish was available that is currently not available?

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Minimizing Formulary

- Therapeutic interchange
- Criteria for use
- Restricted medications
  - By medical specialty
  - Limited to specific patient units
  - Require escalation by pharmacy or medical director
- Non-formulary classification

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Therapeutic Interchange

CATEGORY	NON-FORM AGENT					FORMULARY AGENT				
	GENERIC	BRAND	DOSE	ROUTE	FREQ	GENERIC	BRAND	DOSE	ROUTE	FREQ
HMG-COA REDUCTASE INHIBITOR	FLUVASTATIN	LESCOL	80 MG	PO	DAILY	ATORVASTATIN	LIPITOR	10 MG	PO	DAILY
			20 MG	PO	DAILY			10 MG	PO	DAILY
			40 MG	PO	DAILY	PRAVASTATIN	PRAVACHOL	20 MG	PO	DAILY
	MEVACOR	LOVASTATIN	10 MG	PO	DAILY			10 MG	PO	DAILY
			40 MG	PO	DAILY	ATORVASTATIN	LIPITOR	10 MG	PO	DAILY
			20 MG	PO	DAILY	PRAVASTATIN	PRAVACHOL	20 MG	PO	DAILY
			80 MG	PO	DAILY	ATORVASTATIN	LIPITOR	20 MG	PO	DAILY
	PITAVASTATIN	LIVALO	2 MG	PO	DAILY			10 MG	PO	DAILY
			1 MG	PO	DAILY	PRAVASTATIN	PRAVACHOL	20 MG	PO	DAILY
			4 MG	PO	DAILY			20 MG	PO	DAILY
	ROSUVASTATIN	CRESTOR	5 MG	PO	DAILY	ATORVASTATIN	LIPITOR	10 MG	PO	DAILY
			10 MG	PO	DAILY			20 MG	PO	DAILY
			20 MG	PO	DAILY			40 MG	PO	DAILY
			40 MG	PO	DAILY			80 MG	PO	DAILY
	SIMVASTATIN	ZOCOR	5 MG	PO	DAILY	PRAVASTATIN	PRAVACHOL	10 MG	PO	DAILY
			10 MG	PO	DAILY			20 MG	PO	DAILY
			20 MG	PO	DAILY	ATORVASTATIN	LIPITOR	10 MG	PO	DAILY
			40 MG	PO	DAILY			20 MG	PO	DAILY
			80 MG	PO	DAILY			40 MG	PO	DAILY

FLUOROQUINOLONE + METRONIDAZOLE	CIPROFLOXACIN + METRONIDAZOLE OR LEVOFLOXACIN + METRONIDAZOLE	ANY DOSING	IV	ANY FREQUENCY	PIPERACILLIN TAZOBACTAM	3.375G	IV	Q8H	WHEN USED FOR GI INFECTIONS (EXCEPT C DIFF) IF NO PENICILLIN ALLERGY
FLUOROQUINOLONE + METRONIDAZOLE	CIPROFLOXACIN + METRONIDAZOLE OR LEVOFLOXACIN + METRONIDAZOLE	ANY DOSING	IV	ANY FREQUENCY	CEFEPIME + METRONIDAZOLE	1 G + 500 MG	IV	Q6H + Q12H	WHEN USED FOR GI INFECTIONS (EXCEPT C DIFF) AND PENICILLIN BUT NO CEPHALOSPORIN ALLERGY

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Criteria for Use

ANALGESICS

DRUG	CRITERIA FOR USE	CAUTION & MONITORING	ACTIONS TO TAKE
Acetaminophen (Ofirmev)	1. Perioperative or in PACU post-operatively for pain or as an antipyretic 2. For pain or as an antipyretic 24 hours post-op ONLY when the patient is strictly NPO and unable to use rectal route (and an NSAID is contraindicated). 3. As an antipyretic, it may be considered for use in febrile patients who meet the all of the following 3 requirements: a) Requires antipyretic management AND b) Patient is unable to tolerate an alternative antipyretic strategy (e.g. NSAIDs), AND c) Unable to take acetaminophen by the enteral or rectal route.	▪ Currently available information does not support superiority or clinically significant differences between IV acetaminophen and other currently available treatment modalities ▪ Studies have not been able to show clinically relevant improvements in opioid related events such as LOS, ICU stay, PONV, sedation, or pruritus with the use of IV acetaminophen ▪ For moderate to severe pain management, it has not shown clinically significant opioid sparing affects and thus opioids should remain the preferred treatment option.	➢ The pharmacist verifying the order will ensure criteria for use are met. ➢ If it is not clear that the criteria for use have been met the pharmacist will contact the physician for clarification. ➢ If the physician can document that the criteria has been met, the pharmacist may verify the order.

ANTIHYPERTENSIVE/VASODILATOR/ANTIARRHYTHMICS

DRUG	CRITERIA FOR USE	CAUTION & MONITORING	ACTIONS TO TAKE
Nitroprusside (Nipride)	Recommending to discontinue and use the many alternatives are available for hypertensive emergencies	➢ Liver failure – cyanide accumulation ➢ Renal failure – thiocyanate accumulation ➢ Can draw serum cyanide and thiocynate concentrations to monitor ➢ Toxicity associated with prolonged infusions (> 72 hr) or high doses (> 3 mcg/kg/min) ➢ May result in coronary steal ➢ Increases ICP	➢ The pharmacist should recommend to discontinue and use an alternative (i.e. nicardipine, esmolol, labetalol, metoprolol etc)

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Restricted Medications

Attachment A. Antimicrobials with Restricted Criteria

Antibiotics	Criteria for Use
Ceftolozane-Tazobactam	Non-formulary criteria: 1) Pan-resistant Pseudomonas aeruginosa that is only sensitive to ceftolozane-tazobactam (may be susceptible to colistin) 2) Ensure documented susceptibility or susceptibility test ordered with microbiology laboratory
Meropenem-Vaborbactam	Non-formulary criteria 1) Positive cultures with carbapenemase-producing (i.e. ESBL or CRE; NOT Acinetobacter sp.) or other Gram-negative pathogens resistant to other treatment options (may be susceptible to colistin) 2) Preferred over ceftazidime/avibactam 3) Ensure documented susceptibility or susceptibility test ordered with microbiology laboratory
Aztreonam	Approved criteria: 1) Ig-E mediated hypersensitivity reaction to penicillin 2) Documented true allergy or intolerance to penicillins, cephalosporins and carbapenems
Intravenous doxycycline	Approved criteria: 1) Unable to use azithromycin for atypical pneumonia coverage due to QTc > 500 msec AND unable to tolerate oral antibiotics

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Buyer Impact

- Evaluate medication shortages
  - Ceftolozane/tazobactam
  - IV pantoprazole, famotidine
  - IV hydralazine
  - Bupivacaine
- Assess generics or alternatives
  - Posaconazole generic availability
  - Brovana to Perforomist conversion
  - Biosimilars

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Summary

- Many factors are considered when evaluating medications for formulary
- Multidisciplinary team should be formed to make formulary decisions
- Buyers have an important role in relation to medication formulary

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Questions?

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