

**Protected Systemic Antimicrobials**

**Purpose:** To promote judicious use of antimicrobials. As part of best practices and in alignment with regulations, the following protected antimicrobial agents are restricted, based on scientific literature, for reasons related to preservation for multi-drug resistant organisms, nuanced spectrum and/or dosing, safety concerns, and availability of alternative agents and/or limited cost-benefit. Formulary status and restrictions are reviewed at a minimum of every 3 years and are supported by system and local Antimicrobial Stewardship (ASP) Subcommittees, P&T Committees and Sharp HealthCare. If there is a drug whose formulary status you'd wish to be re-evaluated (e.g. removal, addition, restrictions, etc), please contact your local ASP representative. Use of all protected antimicrobials, including those requiring pre-authorization, ID Review, and non-formulary status are monitored & tracked.

**DEFINITIONS**

**ID Restricted:** Requires pre-authorization or "ID approval" (prior to ordering) by way of a formal ID consult OR verbal approval from an approving member of the Antimicrobial Stewardship Program (ASP) – ID physician and/or ASP-trained pharmacist.

- **Business hours 8am-5pm daily:** Please obtain ID approval prior to ordering. Drug will not be verified nor dispensed by pharmacy unless ID approval is obtained. Please include the name of the approving ID physician or ASP member in the "Order Comments" when ordering.
- **Off business hours:** Pharmacy will dispense ~24 hours of drug until ID approval can be obtained the next day during business hours. It is the responsibility of the ordering physician to obtain ID approval during business hours in order for drug therapy to continue.

**ID Review:** Does not require pre-authorization. Drugs under this category will be reviewed by a designated member of the ASP team at the earliest availability, ideally within 24-72 hours if feasible. Use will be evaluated based on P&T approved criteria for use. If use of the antimicrobial agent does not meet the P&T approved criteria, the attending and/or prescribing physician will be alerted by the ASP team, who will recommend that ID consultation be obtained within 24 hours if therapy is to be continued. Agents in this category may be upgraded to ID restricted as needed based on drug shortages, entity workflow, etc.

**Non-formulary\*:** Reviewed and deemed "non-formulary, excluded" at Sharp HealthCare. Drug is not available. Please consider alternative agents.

**Non-formulary, pending review\*:** Default status for new drug moieties not yet reviewed for formulary. Drug may not be readily available. Please consider alternative agents.

➔ If any non-formulary drug is required, please follow the appropriate channels for approval as outlined in Policy & Procedure 43030 and obtain ID approval.

*\*Non-formulary agents are typically NOT STOCKED by the pharmacy and may not be readily available. Best attempts will be made to obtain the requested drug, if available and appropriate approvals are granted. Please inquire with pharmacy prior to ordering in Cerner\**

**ID Restricted Agents: Pre-Authorization required** by way of a formal ID consult or approval from designated ASP members

GENERIC NAME	BRAND NAME	STATUS	RATIONALE
ANTIBIOTICS			
Bezlotoxumab	Zinplava®	ID Restricted	Formulary for outpatient use only with ID approval for high risk patients. NON-formulary for in-patient use
Ceftaroline	Teflaro®	ID Restricted	Alternatives available for CAP / ABSSSI
Ceftazidime-avibactam	AvyCaz®	ID Restricted	Fast-tracked through FDA. Preserve for MDRO GNRs resistant to all other antibiotics (e.g. CRE)
Ceftolozane-tazobactam	Zerbaxa®	ID Restricted	Preserve for MDRO Pseudomonas resistant to all other antibiotics
Cefiderocol	Fetroja®	ID Restricted	Preserve for MDRO GNRs as last line agent when resistant to all other antibiotics
Colistin / Colistimethate	Colistin®	ID Restricted	Toxicity. Preserve for MDRO GNRs resistant to all other antibiotics (e.g. CRE)
Dalbavancin	Dalvance®	INpatient: Non-formulary OUTpatient INFUSION: Insurance Pre-authorization needed	Limited safety data available. Alternatives available for SSTI. Outpatient use for compliance/convenience
Daptomycin	Cubicin®	ID Restricted Vanco intolerance (including AKI to Vanco): ID Review	Preserve for MDRO GPs.

Abbreviations: MDRO=multi-drug resistant organisms, ESBL=extended spectrum beta-lactamase, CRE=carbapenemase producing enterobacteriaecae, GNRs=gram negative rods, GPs=gram positive organisms, VRE=vancomycin resistant enterococcus, CAP=community acquired pneumonia, SSTI=skin and soft tissue infection, RSV=respiratory syncytial virus, DDI=drug-drug interactions

Eravacycline	Xerava®	ID Restricted	Preserve for MDR Acinetobacter. Alternatives available for other organisms and cIAI
Imipenem-cilastatin	Primaxin®	ID Restricted	Preserve for Acinetobacter and MDRO GNRs where enhanced Enterococcal coverage is also desired. Other carbapenems available.
Imipenem-cilastatin-relebactam	Recarbrio®	ID Restricted	Preserve for MDRO GNRs resistant to all other antibiotics (e.g. CRE or MDR PSA)
Meropenem-Vaborbactam	Vabomere®	ID Restricted	Preserve for MDRO GNRs resistant to all other antibiotics (e.g. CRE)
Minocycline IV	Minocin®	ID Restricted	Preserve for combination treatment of MDRO Acinetobacter
Moxifloxacin IV and PO	Avelox®	ID Restricted	For mycobacterial infections only with no other alternatives
Polymyxin B	---	ID Restricted	Toxicity. Preserve for MDRO GNRs resistant to all other antibiotics (e.g. CRE)
Quinine sulfate	Qualaquin®	ID Restricted	Toxicity. Preserve for treatment of drug-resistant malaria
Streptomycin	---	ID Restricted	Preserved for MDRO Mycobacterium, enterococcus resistant to gentamicin synergy
Sulbactam-durlobactam	Xacduro®	ID Restricted	Reserved for patients with carbapenem-resistant A. baumannii calcoaceticus (CRAB) infections, including HAP/VAP or bacteremia and/or who are unable to tolerate alternative first line agents
<b>ANTIFUNGALS</b>			
Amphotericin B (conventional, liposomal formulation)	Amphotericin B deoxycholate, Ambisome® (liposomal)	ID Restricted	Toxicity. Preserve for severe fungal infections
Isavuconazole	Cresemba®	ID Restricted	Invasive aspergillosis and mucormycosis that failed or could not tolerate first line therapies
<b>ANTIVIRALS</b>			
Maribavir	Livtency®	ID Restricted	Refractory/resistant CMV treatment in post-transplant patients
Peramivir	Rapivab®	Initial 5 day course: Restricted to ID or ICU Subsequent or >5 days use: ID Restricted	Limited evidence of efficacy.
<b>MISCELLANEOUS</b>			

**ID Review Agents:** Pre-authorization NOT required. Requires review by designated ASP members

GENERIC NAME	BRAND NAME	STATUS	RATIONALE
<b>ANTIBIOTICS</b>			
Amikacin	Amikin®	ID Review	Preserve for MDRO GNRs resistant to gentamicin and tobramycin.
Ertapenem	Invanz®	ID Review	Preserve for MDRO GNRs (e.g. ESBL)

Abbreviations: MDRO=multi-drug resistant organisms, ESBL=extended spectrum beta-lactamase, CRE=carbapenemase producing enterobacteriaeae, GNRs=gram negative rods, GPs=gram positive organisms, VRE=vancomycin resistant enterococcus, CAP=community acquired pneumonia, SSTI=skin and soft tissue infection, RSV=respiratory syncytial virus, DDI=drug-drug interactions

Fidaxomicin	Difficid®	ID Review	Preserve for patients with or at high risk of recurrent <i>Clostridium difficile</i>
Fosfomycin	Monurol®	ID Review only for >1 dose/hospitalization	Preserve for MDR URINARY pathogens (e.g. ESBL, VRE)
Linezolid	Zyvox®	ID Review	Preserve for MDROs GPs.
Meropenem	Merrem®	ID Review	Preserve for MDRO GNRs (e.g. ESBL)
Tedizolid	Sivextro®	ID Review	Preserve for MDROs GPs, nuanced penetration
<b>ANTIFUNGALS</b>			
Micafungin	Mycamine®	Heme/Onc Px: No restrictions Tx: ID Review	Preserve for treatment of invasive candidiasis
Itraconazole	Sporanox®	ID Review	Nuanced indication/dosing/monitoring, DDIs.
Posaconazole PO	Noxafil®	Heme/Onc Px: No restrictions Tx: ID Review IV: Non-formulary, pending review	Nuanced dosing/monitoring, DDIs.
Voriconazole	Vfend®	Heme/Onc Px: No restrictions Tx: ID Review	Nuanced dosing/monitoring, DDIs.
<b>ANTIVIRALS</b>			
Cidofovir	Vistide®	ID Review	Toxicity. Indicated for treatment of resistant viruses
Foscarnet	Foscavir®	ID Review	Toxicity. Indicated for treatment of resistant viruses
Ganciclovir IV	Cytovene®	ID Review	Toxicity
<b>MISCELLANEOUS</b>			

**Approving ASP Members:**

- Any ID MD on the antimicrobial stewardship team
- Antimicrobial Stewardship Pharmacist or designee

**ID Review Agents: Criteria for Use**

<b>Agent</b>	<b>Acceptable Uses for ID Review</b>	<b>Uses for which Pre-authorization or ID Approval is Required</b>
Amikacin	MDR GNRs with documented gentamicin/tobramycin resistance	All other indications require ID approval
Ertapenem	Serious infections caused by MDR GNRs where other broad-spectrum antibiotics (Pip/tazo, cefepime, levofloxacin, ciprofloxacin) are resistant  As consolidation therapy <u>prior to discharge</u> for patients with polymicrobial infections requiring broad-spectrum therapy in which once-daily therapy is needed for the out-patient setting  Continuation of outpatient ertapenem for patients admitted on existing therapy	All other indications require ID approval
Fidaxomicin	Patients with or at high risk of recurrent CDI (a combination of following criteria: Age >65, Concomitant high risk antibiotics (clindamycin, FQs, beta-lactams), Immunocompromised (e.g. receiving chemotherapeutic or immunosuppressant agents, ANC <1500), WBC > 15, Scr 1.5x > baseline, Serum albumin ≤ 3.2)	All other indications require ID approval

Abbreviations: MDRO=multi-drug resistant organisms, ESBL=extended spectrum beta-lactamase, CRE=carbapenemase producing enterobacteriaecae, GNRs=gram negative rods, GPs=gram positive organisms, VRE=vancomycin resistant enterococcus, CAP=community acquired pneumonia, SSTI=skin and soft tissue infection, RSV=respiratory syncytial virus, DDI=drug-drug interactions

	Patients with CDI that have failed vancomycin therapy or have allergies to vancomycin therapy	
Fosfomycin >1 dose	Documented MDR GNR complicated UTI or UTI in patients intolerable to all other alternative antibiotics	1 dose acceptable for suspected or documented MDR GNR cystitis All other indications require ID approval
Linezolid	Documented (or empirically for) MRSA/MRSE in patients with documented allergy to vancomycin (excluding Red Mans Syndrome)  Documented (or empirically for) VRE infections (exception – UTIs susceptible to alternative agents such as amoxicillin, nitrofurantoin, doxycycline)  Documented vancomycin-intermediate or resistant S. aureus  Documented MRSA pneumonia with no clinical improvement on vancomycin x 2-3 days or vancomycin MIC $\geq 2$  Oral therapy alternative at discharge for patients with documented MRSA where other oral alternatives are not acceptable (allergy, resistance, etc)	All other indications require ID approval
Meropenem	Documented MDRO GNRs resistant to all other beta-lactams +/- fluoroquinolones or empirically for patients with a history of such organisms  Documented necrotizing pancreatitis or infected pancreatic pseudocysts	All other indications require ID approval
Tedizolid	Oral therapy alternative at discharge for patients with documented MRSA <u>skin and soft tissue infections</u> where other oral alternatives are not acceptable (allergy, resistance, etc)	All other indications require ID approval
Micafungin	Documented invasive non-albicans Candidiasis  Empiric treatment of candidemia, particularly in critically ill patients or patients with prior azole exposure  Prophylaxis of invasive fungal infections in high-risk transplant patients unable to tolerate oral anti-fungals	Treatment of aspergillosis All other indications require ID approval
Itraconazole	Continuation of outpatient therapy in patients on existing therapy	All other indications require ID approval
Posaconazole	Continuation of outpatient therapy in patients on existing therapy  Prophylaxis of invasive fungal infections in high-risk transplant patients	Treatment of mucormycoses All other indications require ID approval
Voriconazole	Continuation of outpatient therapy in patients on existing therapy  Prophylaxis of invasive fungal infections in high-risk transplant patients	Treatment of aspergillosis All other indications require ID approval
Cidofovir	BK cystitis  Resistant viral infections	All other indications require ID approval
Foscarnet	Resistant viral infections	All other indications require ID approval
Ganciclovir	Treatment of CMV	All other indications require ID approval

Abbreviations: MDRO=multi-drug resistant organisms, ESBL=extended spectrum beta-lactamase, CRE=carbapenemase producing enterobacteriaecae, GNRs=gram negative rods, GPs=gram positive organisms, VRE=vancomycin resistant enterococcus, CAP=community acquired pneumonia, SSTI=skin and soft tissue infection, RSV=respiratory syncytial virus, DDI=drug-drug interactions