Name of Policy:	**Protected Antimicrobials**
Policy Number:	3364-133-106
Department:	Pharmacy: Antimicrobial subcommittee of P&T
Approving Officer:	Senior Hospital Administrator
Responsible Agent:	Director of Pharmacy
Scope:	University of Toledo Medical Center

Effective Date: 7/26/2022
Initial Effective Date: 12/1/2015

_____ New policy proposal	_____Minor/technical revision of existing policy
___X___ Major revision of existing policy	_____Reaffirmation of existing policy

(A) Policy Statement

Certain antimicrobials at The University of Toledo Medical Center (UTMC) are designated as protected in their use, either by (1) medical service, (2) prescribing criteria or (3) non-formulary status.

Antimicrobials protected by medical service require infectious diseases (ID) approval. Orders for these agents must be approved by an ID attending physician or their designee.

Antimicrobials protected by prescribing criteria are restricted to use for specific indications. Orders for use of these agents beyond 72 hours without meeting hospital-approved criteria must be approved by an ID attending physician or their designee.

Antimicrobials protected by non-formulary status also require ID approval. Orders for these agents must be approved by an ID attending physician or their designee.

ID approval will be defined as documentation of the specific ID attending physician or ID fellow approving the protected antimicrobial. This documentation will occur at order entry and will be facilitated by the computerized order entry system.

(B) Purpose of Policy

The mission of the UTMC Antimicrobial Stewardship Program (ASP) is to optimize antimicrobial therapy in all patients by providing rational, safe, effective, and cost-efficient antimicrobial use and to minimize antibiotic resistance through promoting judicious use of antimicrobials. This policy supports these aims by ensuring the appropriate involvement of ID specialists in patient care and outlines a clear procedure for obtainment of ID approval.

(C) Procedure

Protected Antimicrobials (restricted based on medical service)

1. New orders for protected antimicrobials require the approval of an ID attending physician or their designee.
2. During order entry, the ordering physician will indicate the specific ID attending physician or designee approving the protected antimicrobial.
3. If the order for the protected antimicrobial is placed prior to ID approval, the order will be tied to an infectious diseases consultation in the computerized order entry system.
    a. Pharmacy will send 24 hours of antimicrobial to allow time for approval and to avoid delays in therapy.
    b. Following ID approval, the physician will order the remainder of therapy according to step 2.
4. The pharmacy department will review all orders for restricted antimicrobials to ensure that ID approval is obtained.
    a. During regular business hours, this will be carried out with the aid of the antimicrobial stewardship pharmacist or their designee.
    b. During all other hours of operation, this will be carried out by the pharmacist processing the order.
5. If ID approval is not obtained and the primary service wishes to continue a restricted antimicrobial, it will be the responsibility of the ID attending physician to intervene with the primary team staff physician. Orders not in compliance with the restricted antimicrobial policy after ID staff physician intervention will be submitted to patient safety net (PSN) and reviewed for potential additional action including notification of medical unit director, department chair, and chief medical officer.

Criteria-Protected Antimicrobials (restricted based on prescribing criteria)

1. New orders for criteria-protected antimicrobials will be processed according to standard procedures **and have a 72 hour stop date**.
2. The pharmacy department will review all orders for criteria-protected antimicrobials to ensure that hospital-approved criteria are met or ID approval is obtained.
    a. These functions will primarily be carried out with the aid of the antimicrobial stewardship pharmacist during normal business hours.
3. Upon initial review, if hospital-approved criteria are not met, the pharmacist will discuss with the primary team the reasons for not meeting criteria and potential alternatives.
4. After 48 hours of use, if the hospital-approved criteria are still not met, the pharmacist will inform the primary team that use beyond 72 hours must be approved by an ID attending physician or their designee via ID consultation*.
5. The ID attending physician or their designee will then be responsible to document their recommendation regarding the criteria-protected antimicrobial in the medical record.
    a. Following ID approval, the physician will order the remainder of therapy according to step 2 under “Protected Antimicrobials”.
6. After discussion with the ID attending, if the primary service wishes to continue a criteria-protected antimicrobial that was not approved, the case will be submitted to PSN as described above.

*If ID consultation is not initiated by the primary team, the antimicrobial stewardship pharmacist will initiate the ID Consultation.

Non-formulary Antimicrobials (restricted based on non-formulary status)

1. New orders for non-formulary antimicrobials will be processed according to policy 3364-133-01: Formulary System.
2. The request may only be made by an ID attending physician or their designee.
3. The order will be processed as outlined in steps 2-5 under "Protected Antimicrobials" (see above).

(D) Definitions

Protected Antimicrobials
Amphotericin B intravenous (liposomal and deoxycholate)
Bezlotoxumab (outpatient use only and may also be approved by gastroenterology (GI) attending physicians or their designee)
Cidofovir intravenous
Colistimethate sodium inhaled and intravenous
Daptomycin (additional criteria for use listed below)
Fidaxomicin (may also be approved by gastroenterology (GI) attending physicians or their designee)
Flucytosine
Foscarnet
Itraconazole
Pentamidine intravenous
Polymyxin B intravenous
Quinupristine-Dalfopristin
Rifabutin
Voriconazole IV (oral may also be approved by pulmonary attending physicians or their designee)

Daptomycin
1. Documented VRE bacteremia
    a. Linezolid is preferred for VRE infections secondary to a urinary, skin and soft tissue, or intra-abdominal source
2. Documented MRSA infection (with the exception of pneumonia) with vancomycin failure or intolerance
    a. Failure is defined as greater than 5 days of bacteremia after source control is achieved
    b. Intolerance defined as development of acute kidney injury (increase in Scr $\geq$ 0.5 mg/dL) related to vancomycin, occurring after at least 72 hours of vancomycin IV therapy AND absence of other causes of acute kidney injury
    c. Intolerance is defined as either a documented vancomycin allergy with high-risk reactions or severe adverse event
        i. Any immediate hypersensitivity reaction (anaphylaxis, hives, urticaria, angioedema, respiratory symptoms, vasculitis, DRESS syndrome)
        ii. Bone marrow suppression (neutropenia, thrombocytopenia)
        iii. Ototoxicity

Peramivir (no doses may be dispensed prior to infectious diseases approval)
1. Documented influenza positive
2. Contraindication to enteral oseltamivir administration including presence of ileus, bowel obstruction, malabsorption/short-gut or recent surgery (within 72 hours)

Criteria-Protected Antimicrobials

Aztreonam

1. Treatment of documented aerobic gram-negative bacilli infections in which β-lactams are contraindicated (e.g., documented, severe (IgE-mediated) β-lactam hypersensitivity (anaphylaxis, angioedema)
2. Recommended by ID consult service

Ciprofloxacin

1. Alternative to β-lactam therapy for empiric treatment of infections where *Pseudomonas aeruginosa* and/or other gram-negative organisms are suspected in patients with **documented, severe (IgE-mediated)** β-lactam hypersensitivity (anaphylaxis, angioedema)
2. Documented, culture and susceptibility proven gram-negative infections due to:
    a. Organisms resistant to multiple antimicrobial agents but susceptible to ciprofloxacin
    b. Susceptible organisms in patients with multiple drug allergies (e.g., β-lactams, sulfonamides)
3. Transition from intravenous to oral antimicrobial therapy in susceptible isolates when alternative therapies are not available or feasible
4. Surgical prophylaxis for select procedures in patients with severe β-lactam allergies (maximum 24-hour duration)
5. Oral prophylaxis for spontaneous bacterial peritonitis
6. Recommended by ID consult service

Linezolid

1. Treatment of documented VRE infection (other than UTI)
2. Documented MRSA or enterococcus infection that is unresponsive to vancomycin despite adequate vancomycin concentrations
3. Patient with documented hypersensitivity or toxicity to vancomycin AND documented infection with MRSA or enterococcus
4. Patient with multi-drug resistant gram-positive organism and unable to receive long term IV therapy
5. Step down oral therapy for treatment of documented gram-positive organism resistant to trimethoprim/sulfamethoxazole or doxycycline OR documented patient intolerance to trimethoprim/sulfamethoxazole or doxycycline
6. MRSA in a sputum culture or BAL in the presence of pneumonia
7. Recommended by ID consult service

Levofloxacin

1. Alternative to β-lactam therapy for empiric treatment of infections where *Pseudomonas aeruginosa* and/or other gram-negative organisms are suspected in patients with **documented, severe (IgE-mediated)** β-lactam hypersensitivity (anaphylaxis, angioedema)
2. Documented, culture and susceptibility proven gram-negative infections due to:
    a. Organisms resistant to multiple antimicrobial agents but susceptible to ciprofloxacin
    b. Susceptible organisms in patients with multiple drug allergies (e.g., β-lactams, sulfonamides)
3. Transition from intravenous to oral antimicrobial therapy in susceptible isolates when alternative therapies are not available or feasible
4. *Stenotrophomonas maltophilia* infections in the following scenarios:
    a. Documented sulfa allergy
    b. Documented resistance to trimethoprim/sulfamethoxazole
5. Antibacterial prophylaxis during prolonged periods of neutropenia
6. Recommended by ID consult service

Meropenem

1. Treatment of documented infection due to extended-spectrum β-lactamase (ESBL) positive gram-negative bacilli where other antimicrobials are either inappropriate or resistant
2. Treatment of infections due to multi-drug resistant gram-negative organisms (e.g. *Eschercihia coli, Enterobacter* spp. *, Klebsiella* spp. *, Pseudomonas* spp. , etc.*),* which are resistant to at least one other β-lactam antibiotic (e.g. cefepime, piperacillin/tazobactam)
3. Treatment of documented *Acinetobacter* spp. infections which are resistant to ampicillin/sulbactam, or cefepime, or in cases of intolerance/contraindication to their use
4. Treatment of patients who have received piperacillin/tazobactam or cefepime for $\geq$ 72 hours and show worsening in their clinical status due to infection
5. Treatment of patients with documented infected necrotizing pancreatitis and prior broad-spectrum antimicrobial use (e.g., piperacillin/tazobactam, cefepime)
6. Recommended by ID Consult Service

Micafungin

1. Treatment of documented candidemia due to *Candida glabrata* or *Candida krusei*
2. Culture-proven invasive candidiasis
    a. Consider switch to azole after 3-5 days for susceptible candida species unless serious drug interactions prevent the use of an azole (e.g., amiodarone)
3. Presumptive invasive candidiasis in patients with specific risk factors (TPN use, surgery on ICU admission, multifocal candida colonization, severe sepsis)
    a. If no culture-proven, azole-resistant candida is identified, consider switch to azole after 3-5 days unless serious drug interactions prevent the use of an azole (e.g., amiodarone)
4. Treatment of invasive candidiasis in patients who are neutropenic, hemodynamically unstable, or with recent fluconazole use
5. Empiric treatment in patients with neutropenic fever who are persistently febrile despite appropriate treatment with broad-spectrum antimicrobials
6. Treatment of patients with documented invasive aspergillosis who have failed therapy with voriconazole and amphotericin B
7. Recommended by ID Consult Service

Aminoglycosides (amikacin, gentamicin, streptomycin, tobramycin)

1. Treatment of multi-drug resistant gram-negative organism which is resistant or intermediate to at least one other β-lactam antibiotic (e.g., cefepime, piperacillin/tazobactam) AND fluoroquinolones
2. Treatment of gram-positive infections requiring synergy with aminoglycosides (gentamicin and streptomycin ONLY)
3. Recommended by ID Consult Service

Note: Use of aminoglycosides is permitted for up to 72 hours for empiric double-coverage of gram-negative organisms and for grade III open-fracture prophylaxis. Beyond 72 hours, ID approval must be obtained if the above criteria are not met.

Posaconazole

1. Antifungal prophylaxis in patients with acute myeloid leukemia
2. Recommended by ID Consult Service

Non-formulary Antimicrobials
Anidulafungin
Caspofungin
Ceftaroline
Ceftazidime/avibactam
Ceftolozane/tazobactam
Dalbavancin – **NO BUY**
Delafloxacin
Doripenem
Eravacycline
Ertapenem
Fosfomycin
Imipenem/cilastatin
Isavuconazole
Meropenem/vaborbactam
Moxifloxacin
Omadacycline
Oritavancin – **NO BUY**
Plazomicin
Tedizolid – **NO BUY**
Tigecycline

The list of protected antimicrobials is maintained by the UTMC antimicrobial subcommittee of the P&T. Policy review will occur at a minimum of once per year.

<table>
<tr>
<td>Approved by:

/s/
Lindsey Eitniear Pharm D BCPS AAHIVP
Director of Pharmacy
Date

/s/
Russell Smith PharmD BCPS MBA
Senior Hospital Administrator
Date

Review/Revision Completed By:
Pharmacy</td>
<td>Review/Revision Date:
2/1/2021
5/7/2021
4/28/2022

Next Review Date: 5/1/2024</td>
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