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هيئة الدواء المصرية

National Guidelines for Preauthorization of Restricted Antimicrobials in Hospitals

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NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

National Antimicrobial Rational Use Committee

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Egyptian Drug Authority
Central Administration of Pharmaceutical Care
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NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

Antimicrobial Preauthorization Policy

INTRODUCTION

Hospital formularies include a variety of anti-infective agents that are ideally selected based on the needs of the facility. A number of these agents require some sort or extent of restriction or specific guidance for use to avoid the emergence of resistance. Antimicrobial restriction is restricted dispensing of targeted antimicrobial agent(s) on the hospital's formulary, according to approved criteria. Implementing antimicrobial restriction is one of the antimicrobial stewardship interventions for improving the prescribing practices. Antimicrobials preauthorization (expert approval prior to prescription) is considered one of the restrictive interventions (limitations to prescribing targeted antibiotics). Other restrictive interventions include: compulsory order forms for targeted agents, automatic stop orders (e.g. after a single dose of surgical prophylaxis), selective susceptibility reporting from the laboratory (report susceptible first-line narrow spectrum antibiotics to regular wards).

In terms of the rationale for restricting individual antimicrobial agents, recommendations are made based on patient safety, disease state complexity, risk of antimicrobial resistance, best practice prescribing and public health interests. Pharmacoeconomic considerations may also be taken into account, however expenditure should rarely be the sole factor involved in a recommendation for antimicrobial restriction.

Carbapenems are considered as an example of class of the antibiotics which needed to be restricted at many healthcare facilities. As per the national database of Egypt and the antimicrobial consumption data, carbapenem antibiotics are among the most antibiotics irrationally used and this leads to emergence of carbapenem resistance. Carbapenems are a class of beta-lactam antibiotics that are active against many aerobic and anaerobic gram-positive and gram-negative organisms.

The emergence of Carbapenem-resistance has become a serious public worldwide health threat. This type of antimicrobial resistance is spreading at an alarming rate, resulting in major outbreaks and treatment failure of community-acquired and nosocomial infections caused by the clinically relevant carbapenem-resistant Enterobacteriaceae.

List of Carbapenems available in Egypt:

- Ertapenem
- Imipenem / Cilastatin
- Meropenem

NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

National Office for Handling and Reduction of Medication Errors (NO HARME)/EDA received 24522 reports related to antimicrobial use from 86 hospitals of different sectors all over the different cities of Egypt during the period from March 2020 to July 2021, the reports were analyzed and given the following results regarding Carbapenems:

- Carbapenems are among the most common antimicrobial classes to be associated with Drug Therapy Problems (DTPs).

- The most common Carbapenems DTP/ME (medication error) are inappropriate dose/interval (66% of Carbapenems DTPs/MEs) and Carbapenems prescribing with no valid indication.

PURPOSE OF THE GUIDANCE

- Ensures the prudent use of antimicrobials (help control use of antimicrobials).
- Reduces rates of emerging resistance.
- Avoids overuse or misuse of broad spectrum antibiotics (e.g., use of broad-spectrum agents where narrower spectrum agents are more appropriate).
- Reserves antimicrobials for treatment of multi-drug-resistant organisms.
- Improves the quality of antimicrobial prescribing.
- Delivers a range of positive outcomes across many areas of patient care.
- Decreases risk for serious adverse effects and the medication errors.
- Pharmacoeconomic considerations (reduce medicine costs for hospitals over time).

POLICY STATEMENT

- Each hospital's antimicrobial prescribing guidelines must include a list that stipulates which antimicrobials are preauthorized (approval of authorized person/a specialist is required).
- Preauthorization policy is typically developed by the hospital antimicrobial stewardship program or antimicrobial subcommittee/team, and should be periodically reviewed and updated.
- Preauthorization prescribing form should be completed by the prescriber and approved by the antimicrobial stewardship team member (authorized person).

NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

PROCEDURES FOR ANTIMICROBIAL PREAUTHORIZATION POLICY

1- Head of pharmacy assigns a team of clinical pharmacists and supply chain pharmacists to prepare the list of available antimicrobials and the antimicrobials suggested to be preauthorized (antimicrobial preauthorization list) N.B., The criteria of antimicrobials needed to be preauthorized and the antimicrobial preauthorization list which mentioned in this document can be used as a guidance.

2- Head of pharmacy presents a list of hospital available antimicrobials and the suggested antimicrobial preauthorization list in the relevant committee meeting e.g., antimicrobial stewardship committee / rational antimicrobial use committee / drug and therapeutics committee.

3- The responsible committee members discuss the suggested antimicrobial preauthorization list, approve it and assign an authorized person/s (e.g., clinical pharmacist who is a member of the antimicrobial stewardship team (AMS clinical pharmacist)) to approve the use of preauthorized antimicrobials.

4- The antimicrobial preauthorization list and the policy should be available to all healthcare providers.

5- The antimicrobial preauthorization list must be reviewed on a regular basis, in light of the hospital's antimicrobial usage data and rates of antimicrobial resistance.

6- An authorized person will be available promptly through a clearly defined pathway 24 hours/seven days a week OR the antimicrobials can be dispensed during weekends, holidays and nightshifts till the authorization next day (N.B., any antimicrobial agent proven to be prescribed and dispensed inappropriately should be stopped).

7- If a physician is considering prescribing one or more preauthorized antimicrobial agents, he/she should contact the authorized person on-call.

8- The prescriber should complete a preauthorization prescribing form with clinical details to justify use of the preauthorized antimicrobial agents, including the following information:

   a. Patient identification(s), patient`s demographics (gender, age, weight and height of the patient).
   b. Diagnosis, indication and site of infection.
   c. Clinical indication for antimicrobial therapy.
   d. Drug allergies.
   e. Microbiology culture results, if available.
   f. Renal and hepatic function.
   g. Patient's clinical notes.
   h. Prescriber`s signature.

NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

PROCEDURES FOR ANTIMICROBIAL PREAUTHORIZATION POLICY , cont.,

9- Authorized person will respond to the prescriber in a timely manner, and on the basis of the above information, may:

a. Recommend the use of the restricted agent(s)
b. Recommend an alternative therapeutic option
c. Recommend further investigations or clinical follow-up

10- The authorized person should complete a preauthorization prescribing form:

a. Specify whether approve or not.
b. Rationale if not approved.
c. Comments and recommendations.
d. Signature and date.

11- Dispensing pharmacist should confirm approval before dispensing preauthorized antimicrobials, sign and date the preauthorization prescribing form upon dispensing.

12- Preauthorization approval should be updated every 7 days to assess whether the preauthorized antimicrobial agent should be continued or stopped or replaced by other antimicrobials (depending on the culture results and patient response), dispensing pharmacist should confirm that the approval gets updated by the authorized person before dispensing.

13- ASP team should train healthcare professionals about the policy, distributing educational materials; auditing and giving feedback to ensure applying the policy (to determine if preauthorization policy is followed).

PERFORMANCE METRICS (KPIS)

The following KPIs can be used to assess the performance and impact of the antimicrobial preauthorization policy:

- Consumption of preauthorized antimicrobials e.g., carbapenems.
- Compliance with preauthorization policy.
- Resistance to the preauthorized antimicrobials.

NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

THE CRITERIA OF ANTIMICROBIALS NEEDED TO BE PREAUTHORIZED

A number of agents require restrictions or specific guidance for use because of one or more of the following:

- Potential to promote resistance e.g., some antibiotics in watch category of AWaRe. (Annex I)
- Need to reserve for treatment of multi-drug-resistant organisms e.g., Reserve category of AWaRe. (Annex I)
- Potential for/documented overuse or misuse (e.g., use of broad-spectrum agents where narrower spectrum agents are more appropriate).
- Pharmacoeconomic considerations.
- Threaten the patient safety.

GUIDE FOR ANTIMICROBIAL PREAUTHORIZATION LIST

The following antimicrobial classes, or specific agents, should be considered for inclusion in preauthorization lists, following local agreement from the responsible Committee (N.B., The agents in this table fulfil the criteria of antimicrobials needed to be preauthorized):

Antimicrobial	Rational for preauthorization
Colistin IV Tigecycline Aztreonam Ceftaroline fosamil Ceftazidime and Avibactam Ceftolozone and Tazobactam Tedizolid Antivirals: Ganciclovir, Valganciclovir Antifungals: Micafungin, Anidulafungin, Caspofungin, Voriconazole & Amphotericin B	• Used in the management of complex, resistant or emerging infectious diseases • Rarely indicated as a first line agent
Carbapenems (e.g., meropenem, imipenem, ertapenem)	• Broad-spectrum agent; linked with emergence of multi-resistant Gram negative organisms
Azithromycin	• It is one of the most frequently used antibiotic substances (according to WHO GLASS report for the Egyptian antimicrobial consumption data).
Fluoroquinolones (e.g ciprofloxacin, ofloxacin, levofloxacin)	• linked with emergence of multi-resistant
Teicoplanin Linezolid	• Rarely indicated as a first line agent
Aminoglycosides (e.g. gentamicin)	• High toxicity • It is one of the most frequently used antibiotic substances (according to WHO GLASS report for the Egyptian antimicrobial consumption data).

N.B., The above list is not exhaustive, and hospitals may choose to include other agents on preauthorization lists such as anti-fungal agents, anti-viral agents, or other antibiotics.

N.B., The national policies issued by the National Committee for the Rational Antimicrobial Use at the Egyptian Drug Authority include guiding procedures that can be tailored according to the different circumstances within each institution / entity.

Annex I: List of Antibiotics (Watch and Reserve according to WHOAWaRe list) Registered in Egyptian Drug Authority Database

Watch	Reserve
This group includes: • Antibiotic classes that have higher resistance potential. • Selected Watch group antibiotics are recommended as essential first or second choice empiric treatment options for a limited number of specific infectious syndromes.	This group includes: • Antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi- drug-resistant organisms. • Reserve group antibiotics should be treated as “last resort” options. • These antibiotics should be tailored to highly specific patients and settings, when all alternatives have failed or are not suitable.
Azithromycin	Aztreonam
Cefaclor	Ceftaroline fosamil
Cefdinir	Ceftazidime and Avibactam
Cefepime	Ceftolozane and Tazobactam
Cefixime	Colistimethate IV/Oral
Cefoperazone	Linezolid
Cefotaxime	Tedizolid
Cefoxitin	Tigecycline
Cefpodoxime	Dalbavancin
Cefprozil	Daptomycin
Ceftazidime	
Ceftriaxone	
Cefuroxime	
Ciprofloxacin	
Clarithromycin	
Cefodizime	

Cefonicid	
Cefotetan	
Cefotiam	
Cefpirome	
Ceftibuten	
Fusidic-acid	
Josamycin	
Midecamycin	
Miocamycin	
Pefloxacin	

NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

Annex II: Sample pre-authorization prescribing form

Date: ----------

Patient information & Diagnosis			
Patient name:	Medical record number:	Department:	Ward:
Age:	Weight: Height:	Sex: Male ☐ Female ☐	Allergies:
Serum Creatinine: Cr Cl/GFR: ALT: AST:		**Diagnosis:**	

Indication for antimicrobial treatment
☐ Community acquired ☐ Hospital acquired/health care associated (number of days after admission:)
Site of infection e.g., respiratory, urinary tract:

Request for pre-authorized/restricted antimicrobials				
Antimicrobial (s) requested	Dose and duration	Administration route	Interval	Reason for request

Has the patient already received antimicrobial(s)? Yes ☐ No ☐ If yes, what?				
Antimicrobial (s) prescribed	Dose and duration	Administration route	Interval	Why is the treatmentnot adequate?

Requesting physician's name/contact number: _____

Patient Response			
	Baseline (1st approval)	2nd approval	3rd approval
Clinical Parameters			
Lab Parameters			
Culture (date, specimen, pathogen sensitivity)			
Others			

Decision	
1st approval Yes No Reasons for not approving	Name/signature of approver: Date: Dispensing pharmacist:
2nd approval (after 7 days) Yes No Reasons for not approving	Name/signature of approver: Date: Dispensing pharmacist:
3rd approval (after 14 days) Yes No Reasons for not approving	Name/signature of approver: Date: Dispensing pharmacist:

Reference: WHO practical toolkit Antimicrobial Stewardship Programs in health-care facilities in low- and middle-income countries

NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

Preauthorized Antibiotic Criteria Stickers

Antibacterial Agents	
Amikacin / Gentamicin	**Azithromycin**
Treatment of serious infections due to gram-negative organisms. • bloodstream infection • bone infection • respiratory tract infection • endocarditis	• Pneumonia, community-acquired • Pelvic inflammatory disease • Uncomplicated Skin and skin structure infection
Aztreonam	**Colistin IV**
Treatment of the following infections caused by gram-negative bacilli • Urinary tract infections • lower respiratory tract infections • septicemia • skin/skin structure infections • Intra-abdominal infections • Gynecological infections	• Highly resistant gram-negative infections for which alternative therapies are not injectable appropriate
Ceftazidime and Avibactam Ceftolozone and Tazobactam	**Ceftaroline fosamil**
• Intra-abdominal infections • Pneumonia, hospital-acquired and ventilator-associated • Urinary tract infection, complicated (pyelonephritis or urinary tract infection with systemic signs/symptoms)	• Pneumonia • Skin and soft tissue infections • Bloodstream infection (pathogen-directed therapy for methicillin-resistant S. aureus)
Ciprofloxacin IV	**Ertapenem**
• Treatment of complicated urinary tract infections and pyelonephritis • complicated intra-abdominal infections (in combination with metronidazole • Surgical site infection • Peritoneal dialysis catheter-related infection	• Intra-abdominal infection, mild to moderate, community-acquired in patients • Pelvic infection • Pneumonia, community acquired • Skin and skin structure infection, complicated • Urinary tract infection, complicated

• Neutropenic fever, low-risk cancer patients (empiric therapy) • Diabetic foot	N.B., not used for Pseudomonas caused infections
Imipenem	**Levofloxacin**
• Bloodstream infection (gram-negative bacteremia) • Bone and joint infections • Gynecologic infections • Intra-abdominal infection • Pneumonia • Skin and soft tissue infection, moderate to severe • Urinary tract infection (complicated and uncomplicated)	• Community-acquired pneumonia • Nosocomial pneumonia • Acute exacerbation of Chronic obstructive pulmonary disease • Urinary tract infection • Skin or skin structure infections
Linezolid	**Meropenem**
• Enterococcal infections (vancomycin-resistant) • Pneumonia • Skin and skin structure infections N.B., Linezolid is not indicated for treatment of gram-negative infections; if a concomitant gram-negative pathogen is documented or suspected, initiate specific therapy immediately.	• Intra-abdominal infection • Meningitis, bacterial • Skin and skin structure infection • Bloodstream infection (gram-negative bacteremia)
Tigecycline	**Tedizolid**
• Intra-abdominal infection • Pneumonia, community acquired • Skin and skin structure infections, complicated N.B., Not indicated for treatment of diabetic foot infections, hospital-acquired or ventilator-associated pneumonia	• Acute bacterial skin and soft tissue infections caused by susceptible isolates of gram-positive microorganisms
Teicoplanin	

• Serious infections (e.g. endocarditis, bacteraemia). • Severe sepsis or septic shock and bone/joint infections.	
Antiviral Agents	
Ganciclovir / Valganciclovir	
• Cytomegalovirus disease, prophylaxis (transplant recipients). • Cytomegalovirus retinitis (immunocompromised patients).	
Antifungal Agents	
Amphotericin B	**Liposomal Amphotericin B**
• Treatment of patients with progressive and potentially life-threatening fungal infections N.B., it should not be used to treat non-invasive forms of fungal disease such as oral thrush, vaginal candidiasis, and esophageal candidiasis in patients with normal neutrophil counts.	• Treatment of cryptococcal meningitis in patients with HIV. • Empiric treatment in febrile neutropenic patients with presumed fungal infection. • Systemic fungal infections in patients refractory to conventional amphotericin B deoxycholate therapy or when renal impairment or unacceptable toxicity precludes the use of the deoxycholate formulation. • Leishmaniasis (visceral)
Anidulafungin	**Caspofungin**
• Treatment of candidemia and other forms of Candida infections (intra-abdominal abscess and peritonitis). • Candidiasis, esophageal, refractory disease	• Aspergillosis, invasive in patients who are refractory to or intolerant of other therapies (e.g., amphotericin B, lipid formulations of amphotericin B). • Treatment of candidemia and the following Candida infections Intra-abdominal abscesses, peritonitis, and pleural space infections. • Candidiasis, esophageal • Empiric therapy for presumed fungal infections in febrile neutropenia. **Limitations of use:** ▪ Has not been studied in endocarditis, osteomyelitis, and meningitis due to Candida.

	▪ Not approved for the treatment of oropharyngeal candidiasis.
Micafungin	**Voriconazole**
• Candidemia, acute disseminated candidiasis, and Candida peritonitis and abscesses • Esophageal candidiasis • Prophylaxis against invasive fungal infections (hematopoietic cell transplant recipients)	• Treatment of fungal infections in patients intolerant of, or refractory to, other therapy

NATIONAL GUIDELINES FOR PREAUTHORIZATION OF RESTRICTED ANTIMICROBIALS IN HOSPITALS

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REFERENCES

1- National Office for Handling and Reduction of Medication Errors (NO HARME)/EDA.
2- National database for antimicrobial consumption /EDA.
3- WHO practical toolkit Antimicrobial Stewardship Programmes in health-care facilities in low- and middle-income countries
4- Public health Ontario Antimicrobial Stewardship Strategy: Formulary restriction
5- WHO AWaRe classification 2021
6- Quality Use of Antimicrobials in Healthcare- Antimicrobial Stewardship Toolkit-Clinical Excellence Commission 2017 Australia.
7- JOHNS HOPKINS Antibiotic Guidelines 2015-2016
8- Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust. Guidelines for use of teicoplanin (July 2020)
9- Lexicomp online, last seen on 21/8/2022.