

## BC Provincial Antimicrobial Clinical Expert Committee (PACE)

### *Antimicrobial Prioritization Scheme*

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## Introduction

Antimicrobial use is a key driver of antimicrobial resistance. Containing the spread of antimicrobial resistance is an important focus of antimicrobial stewardship programs (ASPs). While avoiding antimicrobial use when it isn't indicated is ideal, many infections warrant antimicrobial use. A common concept is to prioritize antimicrobials along a hierarchy, ranging from agents that are preferred for routine use, with others that should be reserved only for the most resistant organisms. An explicit prioritization scheme can in turn inform a broad range of ASP activities including prospective audit and feedback, formulary control, education, guideline/policy development, and reporting. Several organizations have developed prioritization schemes, which will now be detailed.

## Summary of Existing Antimicrobial Prioritization Schemes

### WHO AWaRe

The World Health Organization (WHO) Access, Watch, and Reserve (AWaRe) classification is the most widely used framework. It was initially developed in 2017, with the most recent update in 2021. This tool was developed to monitor antimicrobial consumption, define targets, and monitor effects of stewardship policies.

Access antimicrobials have activity against a wide range of commonly encountered susceptible pathogens while showing lower resistant potential than antibiotics in other groups. Many Access antimicrobials are recommended as first or second choice empiric treatment options.

Watch antimicrobials have higher resistant potential and include many of the highest priority agents that are considered critically important for human medicine, or are antimicrobials at relatively high risk of selection of bacterial resistance. Watch antimicrobials should be prioritized as key targets of stewardship programs and monitoring. Selected Watch antimicrobials are recommended as first or second choice empiric treatment options for a limited number of specific infectious syndromes.

Reserve antimicrobials should be reserved for treatment of confirmed or suspected infectious due to multi-drug-resistant organisms. Reserve antimicrobials should be treated as "last resort" options. Use of Reserve antimicrobials should be tailored to highly specific patients or settings, when all alternatives have failed or are not suitable. These medicines should be protected and prioritized by ASPs to preserve their effectiveness.

Of note, the WHO has set a target of at least 60% of total antibiotic consumption at the country-level being Access group antibiotics. No specific target exists for the hospital-level setting.

The WHO AWaRe scheme is one that must be as generic as possible to account for the wide range of healthcare systems amongst member states. However, specific local microbial prevalence, antimicrobial

resistance rates, and treatment guidelines require further optimization. Two examples are the UK Modified AWaRe scheme, and Australian Commission on Safety and Quality in Health Care Priority Antibacterial List.

#### UK Modified AWaRe

Public Health England has published their process in modifying the WHO AWaRe index for the specifics of healthcare in England. A total of 37 antimicrobials had their index determined or modified during this process. These changes were made using an expert elicitation process. Changes were made to:

1. align with national guidance
2. align with policies to reduce *C. difficile* infection
3. account for the presence of emerging or established antimicrobial resistance
4. preserve certain antibiotics for multidrug-resistant infections
5. align with national policy to reduce piperacillin-tazobactam and carbapenem usage

The England AWaRe index has been used to set targets for Access group prescribing in hospital settings of  $\geq 55\%$  of total antibiotic consumption. A further target for 10% reduction in Reserve and Watch antibiotics has also been set.

#### Australian Priority Antibacterial List

Australia has an analogous Priority Antibacterial List developed by the Australian Commission on Safety and Quality in Health Care. This schema uses two overarching categories: Access and Review. Review is further classified into two subgroups based on indications and resistance potential: Curb and Contain. Criteria considered during classification included:

1. National treatment guidelines (Therapeutic Guidelines: Antibiotic), including first-line treatment for common infections in the general population
2. Expert opinion on risks of antimicrobial resistance to human health or healthcare-associated infections (HAI)
3. Expert opinion on need to reserve agents for infections resistant to all other antimicrobials

Notably, agents recommended as first-line for allergy were not considered first-line for common infections. This approach was taken to promote improvement in optimal practice around allergy de-labelling.

Access antimicrobials are recommended as first-line treatment for common infections with low antimicrobial resistance (AMR) or healthcare-associated infection (HAI) potential. Antimicrobials not recommended as first-line treatment for common infections, but with low resistance potential, were also included.

Review antimicrobials as a broad category contained all remaining antimicrobials that have high AMR or HAI potential. The Curb subgroup includes antimicrobials recommended as first-line treatment for common infections despite high AMR or HAI potential. It also includes antimicrobials that are not first-line treatment, but with moderate AMR or HAI potential. The Contain subgroup includes antimicrobials that are not recommended as first-line agents for common infections and with high AMR or HAI potential. Antimicrobials important in treatment of multidrug-resistant infections or “last resort” were typically classified as Contain. The Australian classification scheme is summarized in **Table 1**.

**Table 1.** Australian Priority Antimicrobial List Classification Scheme

Criteria		First-line treatment for common infections	
		Yes	No
Final Risk Review	Low	Access	Access
	Medum	Review: Curb	Review: Curb
	High	Review: Curb	Review: Contain

CDC SAAR Aggregation

A different approach has been taken in the United States. Many organizations report antimicrobial use to the National Healthcare Safety Network (NHSN), a tracking system operated by the Centers for Diseases Control and Prevention (CDC).

Antimicrobial usage data has been used by the CDC to generate a Standardized Antimicrobial Administration Ratio (SAAR). The SAAR is the ratio of observed antimicrobial use to predicted antimicrobial use. The predictive model takes into account the large data set of the NHSN for a variety of patient care locations (e.g., medical ward, surgical ward, medical-surgical critical care, etc.). The SAAR can be used as a high-value target or high-level indicator for ASPs. A high SAAR that achieves statistical significance may indicate antimicrobial over-use; a low SAAR that achieves statistical significance may indicate antimicrobial under-use. However, a statistically significant difference in SAAR does not necessarily mean further investigation will identify a problem; similarly, a SAAR that does not meet statistical significance may still indicate inappropriate antimicrobial use requiring further investigation.

The SAAR categorizes antimicrobials into several categories based on input to the CDC from external adult, pediatric, and neonatal infectious diseases physicians and pharmacists. The guiding principle was to categorize individual antibiotics into mutually exclusive sets of agents according to the most common clinical uses of each agent, to provide comprehensive groupings that were actionable for stewardship efforts.

For example, SAAR categories in adults include:

- All antibacterial agents
- Broad spectrum antibacterial agents predominantly used for hospital-onset infections
- Broad spectrum antibacterial agents predominantly used for community-acquired infections
- Antibacterial agents predominantly used for resistant Gram-positive infections (e.g., MRSA)
- Narrow spectrum beta-lactam agents
- Antibacterial agents posing the highest risk for *C. difficile* infection
- Antifungal agents predominantly used for invasive candidiasis
- Antibacterial agents predominantly used for extensively antibiotic resistant bacteria

**Purpose of an Antimicrobial Prioritization Scheme**

An explicit antimicrobial prioritization scheme serves several purposes, including surveillance, clinical care, prospective audit and feedback, quality improvement, clinical guidelines, and formulary decision making.

### Antimicrobial Use Surveillance

An antimicrobial prioritization scheme can improve surveillance of antimicrobial use. A proportional increase over time in lower risk antimicrobials (e.g., Access or Narrow-spectrum beta-lactams) may represent improved adherence to guidelines and more narrow-spectrum directed therapy. This contrasts with longitudinal shifts within categories (e.g., shifting from ciprofloxacin to ceftriaxone) where an elevated risk of HAI or AMR remains.

### Clinical Care

An antimicrobial prioritization scheme can guide clinical care to use more narrow-spectrum antimicrobials wherever feasible. Where multiple options for directed therapy exist, an agent with lowest risk of HAI and AMR can be prioritized. Similarly, selective microbiologic reporting by labs can be influenced by an accepted antimicrobial prioritization scheme.

### Prospective Audit and Feedback

An antimicrobial prioritization scheme can support ASPs that engage in prospective audit and feedback. Antimicrobials with a higher HAI or AMR risk would likely be higher priorities for daily review by ASPs. An established de-escalation hierarchy can support clinical recommendations by ASPs.

### Quality Improvement

An antimicrobial prioritization scheme, in conjunction with antimicrobial use surveillance, could lead to further investigation for potentially inappropriate antimicrobial prescribing. This could then provide the basis for a targeted quality improvement project. An antimicrobial prioritization scheme can assist the design of the quality improvement project and aid in its the assessment.

### Clinical Guidelines

An antimicrobial prioritization scheme can help inform clinical guideline development to use agents with lower HAI or AMR risk wherever feasible. Where multiple effective options for therapy exist, agents with lower HAI or AMR risk can be prioritized.

### Formulary Decision Making

An antimicrobial prioritization scheme can influence formulary decision making. Agents with lower HAI or AMR risk can be readily accessed by clinicians. Agents with higher HAI or AMR risk can have restrictions placed on their use to support appropriate and cautioned use.

## **Developing an Antimicrobial Prioritization Scheme for British Columbia**

Explicitly enumerating the principles used in development of an antimicrobial prioritization scheme is important to ensure they reflect good clinical care and support broad acceptance from clinicians. Several principles need to be carefully weighed and balanced, such as:

- Is an antimicrobial first line agent for a common infection
- What is the AMR risk for the antimicrobial agent: what AMR does the agent select for and how potent is the selective pressure
- What is the HAI risk for the antimicrobial agent: what is the burden of selected AMR organisms in HAI and what alternative treatment options exist
- What is the *C. difficile* infection risk for the antimicrobial agent
- What is the toxicity profile of the antimicrobial agent
- What is the cost of the antimicrobial agent in relation to comparator agents

WHO AWaRe scheme is widely recognized and provides a good starting point. Adaptation for the British Columbia context to ensure it is optimized and relevant for our locale is an expected part of the implementation process, similar to that done by Public Health England for the England AWaRe. Many agents in the WHO AWaRe are not marketed for use in Canada, nor are they often imported for use through the Health Canada Special Access Program.

British Columbia AWaRe antimicrobial categorization modifications from WHO AWaRe are shown in **Table 2**. The complete British Columbia AWaRe antimicrobial classification is shown in **Table 3**.

**Table 2.** British Columbia AWaRe antimicrobial categorization modifications from WHO AWaRe.

Antimicrobial	WHO AWaRe	B.C. AWaRE	Rationale
Amikacin	Access	Reserve	Reserve for resistant Gram-negative infections. Elevated toxicity profile. Difficulty with obtaining levels.
Amoxicillin-clavulanate	Access	Watch	Broad-spectrum agent with AMR risk for gram-positive, gram-negative, and anaerobic organisms.
Clindamycin	Access	Watch	Associated with increased risk of <i>C. difficile</i> . Elevated resistance.
Ertapenem	Watch	Reserve	Reserve for resistant Gram-negative infections. Selection for carbapenem resistant organisms is a major HAI concern.
Gentamicin	Access	Watch	Toxicity
Imipenem-cilastatin	Watch	Reserve	Reserve for resistant Gram-negative infections. Selection for carbapenem resistant organisms is a major HAI concern.
Meropenem	Watch	Reserve	Reserve for resistant Gram-negative infections. Selection for carbapenem resistant organisms is a major HAI concern.
Chloramphenicol	Access	Reserve	Toxicity

**Table 3.** Summary British Columbia AWaRe antimicrobial classification.

<b>Access</b>	<b>Watch</b>	<b>Reserve</b>
Amoxicillin	Amoxicillin/clavulanic acid	Amikacin
Ampicillin	Azithromycin	Aztreonam IV^
Benzathine benzylpenicillin	Cefepime	Cefiderocol^
Penicillin G	Cefixime	Ceftaroline fosamil^
Cefadroxil*	Cefotaxime	Ceftazidime/avibactam^
Cephalexin	Cefoxitin	Ceftobiprole medocaril*
Cefazolin	Cefprozil	Ceftolozane/tazobactam*
Cloxacillin	Ceftazidime	Chloramphenicol
Doxycycline	Ceftriaxone	Colistin
Metronidazole	Cefuroxime	Dalbavancin*
Nitrofurantoin	Ciprofloxacin	Daptomycin
Penicillin V	Clarithromycin	Ertapenem
Sulfamethoxazole/trimethoprim	Clindamycin	Eravacycline^
Tetracycline	Erythromycin	Fidaxomicin*
Trimethoprim	Fosfomycin (oral)	Fosfomycin (IV)*
	Gentamicin	Imipenem/cilastatin
	Levofloxacin	Imipenem/cilastatin/relebactam^
	Minocycline (oral)	Linezolid
	Moxifloxacin	Meropenem
	Neomycin	Meropenem/vaborbactam^
	Norfloxacin*	Minocycline (IV)^
	Piperacillin/tazobactam	Omadacycline^
	Rifabutin	Oritavancin^
	Rifampin	Plazomicin^
	Rifaximin	Tedizolid*
	Streptomycin	Telavancin*
	Tobramycin	Tigecycline
	Vancomycin (IV)	
	Vancomycin (oral)	

\* Health Canada approved agents not on BCHA Formulary (including Formulary excluded)

^ Agents without Health Canada approval, but potentially available through Health Canada Special Access Program

## References:

Australian Commission on Safety and Quality in Health Care. Priority Antibacterial List for Antimicrobial Resistance Containment. 2020 April. <https://www.safetyandquality.gov.au/publications-and-resources/resource-library/priority-antibacterial-list-antimicrobial-resistance-containment>

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World Health Organization. 2021 AWaRe classification. 2021 September. <https://www.who.int/publications/i/item/2021-aware-classification>

## APPENDICES

### WHO AWaRe Classification (2021)

Access	Watch	Reserve
Amikacin	Arbekacin	Aztreonam
Amoxicillin	Aspoxicillin	Carumonam
Amoxicillin/clavulanic-acid	Azithromycin	Cefiderocol
Ampicillin	Azlocillin	Ceftaroline-fosamil
Ampicillin/sulbactam	Bekanamycin	Ceftazidime/avibactam
Azidocillin	Biapenem	Ceftobiprole-medocaril
Bacampicillin	Carbenicillin	Ceftolozane/tazobactam
Benzathine-benzylpenicillin	Carindacillin	Colistin_IV
Benzylpenicillin	Cefaclor	Colistin_oral
Brodinoprim	Cefamandole	Dalbavancin
Cefacetile	Cefbuperazone	Dalfopristin/quinupristin
Cefadroxil	Cefcapene-pivoxil	Daptomycin
Cefalexin	Cefdinir	Eravacycline
Cefaloridine	Cefditoren-pivoxil	Faropenem
Cefalotin	Cefepime	Fosfomycin_IV
Cefapirin	Cefetamet-pivoxil	Iclaprim
Cefatrizine	Cefixime	Imipenem/cilastatin/relebactam
Cefazedone	Cefmenoxime	Lefamulin
Cefazolin	Cefmetazole	Linezolid
Cefradine	Cefminox	Meropenem/vaborbactam
Cefroxadine	Cefodizime	Minocycline_IV
Ceftezole	Cefonicid	Omadacycline
Chloramphenicol	Cefoperazone	Oritavancin
Clindamycin	Ceforanide	Plazomicin
Clometocillin	Cefoselis	Polymyxin-B_IV
Cloxacillin	Cefotaxime	Polymyxin-B_oral
Dicloxacillin	Cefotetan	Tedizolid
Doxycycline	Cefotiam	Telavancin
Epicillin	Cefoxitin	Tigecycline
Flucloxacillin	Cefozopran	
Furazidin	Cefpiramide	
Gentamicin	Cefpirome	
Hetacillin	Cefpodoxime-proxetil	
Mecillinam	Cefprozil	
Metampicillin	Cefsulodin	
Meticillin	Ceftazidime	
Metronidazole_IV	Cefteram-pivoxil	
Metronidazole_oral	Ceftibuten	
Nafcillin	Ceftizoxime	
Nifurtoinol	Ceftriaxone	
Nitrofurantoin	Cefuroxime	
Ornidazole_IV	Chlortetracycline	
Ornidazole_oral	Cinoxacin	
Oxacillin	Ciprofloxacin	
Penamecillin	Clarithromycin	
Phenoxymethylpenicillin	Clofoctol	
Pivampicillin	Clomocycline	
Pivmecillinam	Delafloxacin	



Procaine-benzylpenicillin	Demeclocycline	
Propicillin	Dibekacin	
Secnidazole	Dirithromycin	
Spectinomycin	Doripenem	
Sulbactam	Enoxacin	
Sulfadiazine	Ertapenem	
Sulfadiazine/tetroxoprim	Erythromycin	
Sulfadiazine/trimethoprim	Fidaxomicin	
Sulfadimethoxine	Fleroxacin	
Sulfadimidine	Flomoxef	
Sulfadimidine/trimethoprim	Flumequine	
Sulfafurazole	Flurithromycin	
Sulfaisodimidine	Fosfomicin_oral	
Sulfalene	Fusidic-acid	
Sulfamazone	Garenoxacin	
Sulfamerazine	Gatifloxacin	
Sulfamerazine/trimethoprim	Gemifloxacin	
Sulfamethizole	Grepafloxacin	
Sulfamethoxazole	Imipenem/cilastatin	
Sulfamethoxazole/trimethoprim	Isepamicin	
Sulfamethoxyipyridazine	Josamycin	
Sulfametomidine	Kanamycin_IV	
Sulfametoxydiazine	Kanamycin_oral	
Sulfametrole/trimethoprim	Lascufloxacin	
Sulfamoxole	Latamoxef	
Sulfamoxole/trimethoprim	Levofloxacin	
Sulfanilamide	Levonadifloxacin	
Sulfaperin	Lincomycin	
Sulfaphenazole	Lomefloxacin	
Sulfapyridine	Loracarbef	
Sulfathiazole	Lymecycline	
Sulfathiourea	Meropenem	
Sultamicillin	Metacycline	
Talampicillin	Mezlocillin	
Tetracycline	Micronomicin	
Thiamphenicol	Midecamycin	
Tinidazole_IV	Minocycline_oral	
Tinidazole_oral	Miocamycin	
Trimethoprim	Moxifloxacin	
	Nemonoxacin	
	Neomycin_IV	
	Neomycin_oral	
	Netilmicin	
	Norfloxacin	
	Ofloxacin	
	Oleandomycin	
	Oxolinic-acid	
	Oxytetracycline	
	Panipenem	
	Pazufloxacin	
	Pefloxacin	
	Penimepicycline	
	Pheneticillin	

	Pipemidic-acid Piperacillin Piperacillin/tazobactam Piromidic-acid Pristinamycin Prulifloxacin Ribostamycin Rifabutin Rifampicin Rifamycin_IV Rifamycin_oral Rifaximin Rokitamycin Rolitetracycline Rosoxacin Roxithromycin Rufloxacin Sarecycline Sisomicin Sitafloracin Solithromycin Sparfloxacin Spiramycin Streptoducin Streptomycin_IV Streptomycin_oral Sulbenicillin Tazobactam Tebipenem Teicoplanin Telithromycin Temafloracin Temocillin Ticarcillin Tobramycin Tosufloxacin Troleandomycin Trovafloracin Vancomycin_IV Vancomycin_oral	
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## English AWaRe modifications from WHO AWaRe (2017)

ATC name	ATC code	AWaRe WHO	AWaRe England	Rationale for movement
Amikacin	J01GB06	Access	Watch	antibiotic used for resistant Gram-negative infections
Amoxicillin and enzyme inhibitor	J01CR02	Access	Watch	to avoid overuse as resistance increasing and associated with increased risk of <i>C. difficile</i> infections
Ampicillin combinations	J01CA51	Other	Access	similar category as amoxicillin; rare use
Cefaclor	J01DC04	Other	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefadroxil	J01DB05	Other	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefalexin	J01DB01	Access	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefamandole	J01DC03	Other	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefazolin	J01DB04	Access	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefoxitin	J01DC01	Other	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefprozil	J01DC10	Other	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefradine	J01DB09	Other	Watch	associated with increased risk of <i>C. difficile</i> infections
Cefuroxime	J01DC02	Other	Watch	associated with increased risk of <i>C. difficile</i> infections
Ceftazidime and enzyme inhibitor	J01DD52	Watch	Reserve	novel combination reserved for treatment failures
Chloramphenicol	J01BA01	Access	Watch	second-line antibiotic, use in penicillin allergy
Clindamycin	J01FF01	Access	Watch	associated with increased risk of <i>C. difficile</i> infections
Dalbavancin	J01XA04	Watch	Reserve	novel antibiotic reserved for treatment failures and OPAT
Doripenem	J01DH04	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Ertapenem	J01DH03	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Fosfomycin (oral)	J01XX01	Other	Access	narrow spectrum, recommended for uncomplicated UTI
Fusidic acid	J01XC01	Other	Access	narrow spectrum
Imipenem	J01DH51	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Lymecycline	J01AA04	Other	Watch	used for acne, alternative non-antimicrobial drugs available
Meropenem	J01DH02	Watch	Reserve	reserved to conserve use for resistant Gram-negative infections
Minocycline	J01AA08	Other	Watch	used for acne, alternative non-antimicrobial drugs available
Neomycin	J01GB05	Other	Access	not routinely used in England, monitor carefully for change in use
Oxytetracycline	J01AA06	Other	Watch	used for acne, alternative non-antimicrobial drugs available
Piperacillin	J01CA12	Other	Watch	avoid overuse as resistance increasing
Pivmecillinam	J01CA08	Other	Access	narrow spectrum, recommended for uncomplicated UTI
Pristinamycin	J01FG01	Other	Watch	not routinely used in England, monitor carefully for change in use
Quinupristin	J01FG02	Other	Watch	not routinely used in England, monitor carefully for change in use
Telavancin	J01XA03	Watch	Reserve	not routinely used in England, monitor carefully for change in use
Temocillin	J01CA17	Other	Watch	antibiotic used for resistant Gram-negative infections
Tetracycline	J01AA07	Other	Access	narrow spectrum, recommended in treatment guidelines
Ticarcillin	J01CA13	Other	Watch	not routinely used in England, monitor carefully for change in use
Tobramycin	J01GB01	Other	Watch	antibiotic used for resistant Gram-negative infections
Tetracycline combinations	J01AA20	Other	Watch	used for acne, alternative non-antimicrobial drugs available

### Australian Access/Curb/Contain Classification

Access	Review	
	Curb	Contain
amoxicillin	amoxicillin–clavulanic acid	amikacin
ampicillin	azithromycin	aztreonam
benzathine benzylpenicillin	cefaclor	cefepime
benzylpenicillin	cefalexin	ceftaroline
chloramphenicol	cefalothin	ceftazidime
dicloxacillin	cefazolin	ceftazidime–avibactam
doxycycline	cefotaxime	ceftolozane–tazobactam
flucloxacillin	cefoxitin	colistin
gentamicin	ceftriaxone	daptomycin
metronidazole	cefuroxime	doripenem
minocycline	clarithromycin	ertapenem
nitrofurantoin	ciprofloxacin	fosfomicin
phenoxymethylpenicillin	clindamycin	imipenem–cilastatin
procaine benzylpenicillin	erythromycin	linezolid
streptomycin	fidaxomicin	meropenem
sulfamethoxazole– trimethoprim	lincomycin	moxifloxacin
tetracycline	norfloxacin	pivmecillinam
tinidazole	piperacillin–tazobactam	polymixin B
tobramycin	rifampicin	pristinamycin
trimethoprim	rifaximin	tigecycline
	roxithromycin	
	sodium fusidate	
	spiramycin	
	teicoplanin	
	vancomycin	

### CDC NHSN SAAR Categories

Note: Adult categories are shown below. Pediatric and Neonatal categories are also available with some differences.

All antibacterial agents

Broad spectrum antibacterial agents predominantly used for hospital-onset infections

- Amikacin (IV only)
- Aztreonam (IV only)
- Cefepime
- Ceftazidime
- Doripenem
- Gentamicin (IV only)
- Imipenem/cilastatin
- Meropenem
- Piperacillin-tazobactam
- Tobramycin (IV only)

Broad spectrum antibacterial agents predominantly used for community-acquired infections

- Cefaclor
- Cefdinir

- Cefixime
- Cefotaxime
- Cefpodoxime
- Cefprozil
- Ceftriaxone
- Cefuroxime
- Ciprofloxacin
- Ertapenem
- Gamifloxacin
- Levofloxacin
- Moxifloxacin

Antibacterial agents predominantly used for resistant Gram-positive infections (e.g., MRSA)

- Ceftaroline
- Dalbavancin
- Daptomycin
- Linezolid
- Oritavancin
- Quinupristin/Dalfopristin
- Tedizolid
- Telavancin
- Vancomycin (IV only)

Narrow spectrum beta-lactam agents

- Amoxicillin
- Amoxicillin-clavulanate
- Ampicillin
- Ampicillin-sulbactam
- Cefadroxil
- Cefazolin
- Cefotetan
- Cefoxitin
- Cephalexin
- Dicloxacillin
- Nafcillin
- Oxacillin
- Penicillin G
- Penicillin V

Antibacterial agents posing the highest risk for *C. difficile* infection (not mutually exclusive)

- Cefdinir
- Cefepime
- Cefixime
- Cefotaxime
- Cefpodoxime
- Ceftazidime

- Ceftriaxone
- Ciprofloxacin
- Clindamycin
- Gemifloxacin
- Levofloxacin
- Moxifloxacin

Antifungal agents predominantly used for invasive candidiasis

- Anidulafungin
- Caspofungin
- Fluconazole
- Micafungin

Antibacterial agents predominantly used for extensively antibiotic resistant bacteria

- Ceftazidime-avibactam
- Ceftolozane-tazobactam
- Colistimethate (IV only)
- Polymyxin B (IV only)
- Tigecycline