

## Antimicrobial stewardship recommendations for antimicrobials in neonates: ANMF majority consensus

### **Background**

Antimicrobials are the most prescribed drugs in the Neonatal Intensive Care Units (NICUs). Prolonged use of broad spectrum antimicrobials in NICUs increases the risk of *Candida* colonization and invasive infection, necrotizing enterocolitis, late onset neonatal sepsis and death.(1)

Antimicrobial stewardship (AMS) is defined as an ongoing effort by a health service organisation to optimise antimicrobial use among patients 'to improve patient outcomes, ensure cost-effective therapy and reduce adverse sequelae of antimicrobial use (including antimicrobial resistance).(2)

Effective AMS programs reduce inappropriate antimicrobial use, improve patient outcomes and reduce adverse consequences of antimicrobial use (including antimicrobial resistance, toxicity and unnecessary costs). Along with infection prevention and control, hand hygiene and surveillance, AMS programs are a key strategy in preventing antimicrobial resistance and decreasing preventable infections. The emergence of antimicrobial-resistant bacteria is closely linked with inappropriate antimicrobial use. (2)

AMS programs may however need to be tailored in each organisation. The types of strategies and activities used depend on the specific organisational context, and factors such as the complexity, size and resources available for implementation, monitoring and evaluation.(2)

### **Australasian Neonatal Medicines Formulary (ANMF) consensus**

ANMF steering group, in consultation with Clinical Excellence Commission (CEC) and the Sydney Children's Hospital Network (SCHN) Antimicrobial Stewardship (AMS) pharmacists undertook a process of harmonisation of antimicrobial stewardship categorisation for neonates in New South Wales.

This consensus document is a guide only. It is based on majority consensus of the ANMF steering group in consultation with Clinical Excellence Commission and many tertiary NICUs in New South Wales. The aim is to bring consistency and facilitate implementation of antimicrobial stewardship across neonatal facilities. During the development of this document, a number of tertiary NICUs highlighted the gaps in implementation of AMS at local level due to the resource constraints.

ANMF group and CEC recognize that the level of resources available in NSW hospitals varies significantly, as does the range of antimicrobial agents kept and the types of infectious diseases treated. The availability of staff with expertise in the treatment of infectious diseases, and their capacity to provide guidance on antimicrobial use, may also affect the choice and extent of restrictions that are put in place at a local level.(3)

The choice of appropriate antimicrobial treatment should be based on the epidemiological and microbiological data of each NICU.(1) At local level, continuous epidemiological surveillance of responsible pathogens and their antimicrobial resistant patterns are of paramount importance while implementing the AMS program.

ANMF steering group recommends development of AMS teams consisting of infectious diseases specialists, microbiologists, pharmacists, infection control nurses and representatives of the Intensive Care Units. These teams could perform weekly visits in NICUs where all the antimicrobials administered to the newborns (e.g. administration indication, dose, duration of treatment) are checked and suggestions are made for optimal use of these. Also, this group could be responsible for the preauthorization of drugs.(1)

ANMF group followed the traffic light system to categorise antimicrobials for neonates. Traffic light system is a well recognised system for AMS implementation across Australian hospitals. The implementation of antimicrobial restriction policy should not prevent timely access to antimicrobials for lifesaving conditions. Care must be taken to ensure patients receive appropriate therapy at scheduled administration times, particularly if restricted agents are not available in ward imprest rooms or cupboards. If restricted antimicrobials are solely kept in the pharmacy department, consideration must be given to how these antimicrobials can be accessed outside of pharmacy hours.(3)

### **Green – Unrestricted**

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Green antimicrobial agents should be prescribed sensibly and appropriately, but have no specific restrictions on their use.

Table 1. Unrestricted anti-infective medications (Green category)\*

Drug name	Restriction category
Amoxicillin	Unrestricted
Amoxicillin/clavulanic acid	Unrestricted
Ampicillin	Unrestricted
Benzylpenicillin	Unrestricted
Cefaclor	Unrestricted
Cefalexin	Unrestricted
Cefazolin	Unrestricted
Cefuroxime	Unrestricted
Erythromycin ethylsuccinate (PO)	Unrestricted
Flucloxacillin	Unrestricted
Metronidazole	Unrestricted
Miconazole	Unrestricted
Nystatin	Unrestricted
Sulfamethoxazole/trimethoprim (PO)	Unrestricted

\*Unrestricted anti-infective medication is to be used in accordance with its Therapeutic Goods Administration (TGA) listed indications and the Therapeutic Guidelines (TGs) or other NSW endorsed guideline.

**Orange – Restricted**

Many orange antimicrobials are restricted to use for selected indications or for a limited amount of time (e.g. 72 hours) prior to seeking approval from an ID physician or clinical microbiologist, or a nominated medical officer. These agents often require approval after initiation of therapy. Some agents may be classified as orange for specific indications and red for all other indications.

Table 2. Restricted anti-infective medications after 72 hours (Amber category)\*

Drug name	Restriction category
Amikacin <sup>5</sup>	Restricted after 72 hours
Meropenem	Restricted after 72 hours
Aciclovir (IV)	Restricted after 72 hours
Azithromycin	Restricted after 72 hours
Cefepime	Restricted after 72 hours
Cefotaxime	Restricted after 72 hours
Ceftazidime	Restricted after 72 hours
Ceftriaxone	Restricted after 72 hours
Clindamycin	Restricted after 72 hours
Fluconazole	Restricted after 72 hours
Ganciclovir (IV)	Restricted after 72 hours

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Gentamicin (IV/IP)	Restricted after 72 hours
Piperacillin/tazobactam <sup>#</sup>	Restricted after 72 hours <sup>#</sup>
Sulfamethoxazole/trimethoprim (IV)	Restricted after 72 hours
Tobramycin	Restricted after 72 hours
Valganciclovir (ORAL)	Restricted after 72 hours
Vancomycin	Restricted after 72 hours

\***Anti-infective medications** in this list are unrestricted for empiric therapy for up to 72 hours. For continuation of therapy after 72 hours, consult with Infectious diseases specialist or microbiology specialist or their specialist as per the local antimicrobial stewardship team policy for ongoing treatment., unless prescribed by an appropriate specialist or recommended by Infectious diseases or Microbiology specialist.

<sup>#</sup>**Piperacillin/tazobactam** can be prescribed up to 7 days without AMS approval for the treatment of Intra-abdominal infections, including necrotising enterocolitis.

**Red – Highly restricted**

Most red antimicrobials require discussion with an infectious disease (ID) physician or clinical microbiologist (or a nominated medical officer) prior to use, however some restriction may be criteria-based where appropriate. Consideration must be given on how to manage requests for highly restricted antimicrobials in life-threatening and/or urgent situations 24 hours a day, 7 days a week.

Table 3: Restricted anti-infective medications (Red category)

<b>Drug name</b>	<b>Restrictions</b>
Amphotericin B Liposomal	Restricted
Amphotericin B Conventional (IV) [Special Access Scheme (SAS)]	Restricted Special Access Scheme form must be submitted and informed consent for use obtained
Anidulafungin	Restricted
Cefiderocol (SAS)	Restricted Special Access Scheme form must be submitted and informed consent for use obtained
Ceftaroline	Restricted
Ceftazidime-Avibactam	Restricted
Ceftolozane-tazobactam	Restricted
Cidofovir	Restricted
Ciprofloxacin (IV/PO)	Restricted
Daptomycin	Restricted
Flucytosine (SAS; PO)	Restricted Special Access Scheme form must be submitted and informed consent for use obtained
Fosfomycin (SAS)	Restricted Special Access Scheme form must be submitted and informed consent for use obtained
Imipenem/Cilastatin	Restricted
Linezolid	Restricted
Meropenem-vaborbactam (SAS)	Restricted

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	Special Access Scheme form must be submitted and informed consent for use obtained
Micafungin	Restricted
Pyrimethamine (SAS)	Restricted Special Access Scheme form must be submitted and informed consent for use obtained
Remdesivir	Restricted
Sulfadiazine (SAS; PO)	Restricted Special Access Scheme form must be submitted and informed consent for use obtained
Teicoplanin	Restricted
Voriconazole	Restricted

\*Anti-infectives in red category can only be prescribed upon the advice from local antimicrobial stewardship services or other relevant specialist medical practitioners as determined by local Drug and Therapeutics Committee or local AMS policy before use.

### Summary

ANMF group, in consultation with CEC, undertook a process of harmonisation of AMS categorisation for 38 antimicrobials used in neonatal population in New South Wales. This majority consensus-based recommendation aims to bring consistency and facilitate the implementation of antimicrobial stewardship across NSW.

### References

1. Gkentzi D, Dimitriou G. Antimicrobial stewardship in the neonatal intensive care unit: an update. *Current pediatric reviews*. 2019;15(1):47-52.
2. Australian commission on safety and quality in healthcare. Antimicrobial stewardship. <https://www.safetyandquality.gov.au/standards/nsqhs-standards/preventing-and-controlling-infections-standard/antimicrobial-stewardship>. Accessed online on 25 March 2024. .
3. Clinical Excellence Commission. AMS toolkit - List of recommended antimicrobial restrictions. SHPN (CEC) 170180. April 2017. Accessed online on 25 March 2024.

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