The study listed below is a pharmacokinetic study proposing new, de-escalated dosing strategies for ampicillin for the indication of non-meningitis neonatal sepsis to reduce the risk toxicity associated with high doses of ampicillin in neonates.

Study	Characterization of the Population Pharmacokinetics of Ampicillin in Neonates Using an Opportunistic Study Design
Citation	Tremoulet A, Le J, Poindexter B, et al. Characterization of the population pharmacokinetics of ampicillin in neonates using an opportunistic study design. Antimicrob Agents Chemother. 2014;58(6):3013-3020. doi:10.1128/AAC.02374-13
Objectives	- Characterize the developmental PK of ampicillin prescribed per standard of care to neonates across a wide age spectrum - Compare the pharmacodynamic target attainments of various dosing strategies
Study Design	- Open-label, multicenter, opportunistic, prospective PK study of ampicillin in neonates stratified by gestational age - 9 centers - N = 73 participants, 142 observed drug concentrations
Methods	- Drug concentrations measured by tandem mass spectrometry - OK Data analyzed using population nonlinear mixed-effects modeling - Monte Carlo simulations were conducted to determine the probability of target attainment for the time in which the total steady-state ampicillin concentrations remained above the MIC for 50%, 75%, and 100% of the dosing interval - N = 73 participants, 142 observed drug concentrations

Results	- Gestational Age ≤ 34 weeks
	  o Postnatal Age 0-7 days - 50 mg/kg/dose, Intravenous, EVERY 12 HOURS
	  o Postnatal Age >7 days – 75 mg/kg/dose, Intravenous, EVERY 12 HOURS
	- Gestational Age >34 weeks – 50 mg/kg/dose, Intravenous, EVERY 8 HOURS

Use for new UW Health order panel	Will be used for de-escalation from meningitis dosing

The following organizations and studies were used in the NeoFax and Lexicomp recommendations and are considered high quality of evidence and strong recommendations per the GRADE criteria:

<table>
<tr><th>Organization</th><th>Citation</th><th>Recommendation</th><th>Notes</th></tr>
<tr><td>American Academy of Pediatrics</td><td>Puopolo KM, Lynfield R, Cummings JJ; American Academy of Pediatrics, Committee on Fetus and Newborn, Committee on Infectious Diseases. Management of Infants at Risk for Group B Streptococcal Disease. Pediatrics. 2019;144(2):e20191881</td><td>Ampicillin – Non-meningitis Dosing<table><tr><th>GA</th><th>PNA</th><th>Dosing</th><th>Frequency</th></tr><tr><td>≤ 34 weeks</td><td>0-7 days</td><td>50 mg/kg</td><td>Every 12 Hours</td></tr><tr><td></td><td>>7 days</td><td>75 mg/kg</td><td>Every 12 Hours</td></tr><tr><td>>34 weeks</td><td>0-28 days</td><td>50 mg/kg</td><td>Every 8 Hours</td></tr></table></td><td>Used for NeoFax recommendation</td></tr>
<tr><td>Nelson's Pediatric Antimicrobial Therapy</td><td>Bradley JS, Nelson JD, Barnett ED, et al, eds. Nelson's Pediatric Antimicrobial Therapy. 28th ed. American Academy of Pediatrics; 2022:chap 2.</td><td rowspan="2">Gentamicin – Neonatal Dosing<table><tr><th>GA</th><th>PNA</th><th>Dose</th><th>Frequency</th></tr><tr><td>< 30 weeks</td><td>≤ 14 days</td><td>5 mg/kg</td><td>Every 48 Hours</td></tr><tr><td></td><td>≥ 15 days</td><td>5 mg/kg</td><td>Every 36 Hours</td></tr><tr><td>30 – 34 weeks</td><td>≤ 10 days</td><td>5 mg/kg</td><td>Every 36 Hours</td></tr><tr><td></td><td>11-60 days</td><td>5 mg/kg</td><td>Every 24 Hours</td></tr><tr><td>≥ 35 weeks</td><td>≤ 7 days</td><td>4 mg/kg</td><td>Every 24 Hours</td></tr><tr><td></td><td>8-60 days</td><td>5 mg/kg</td><td>Every 24 Hours</td></tr></table></td><td>Used in Lexicomp and NeoFax recommendation</td></tr>
<tr><td>American Academy of Pediatrics (Red Book: 2021-2024 Report of the Committee on Infectious Diseases. 32nd ed. American Academy of Pediatrics; 2021)</td><td>Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book: 2021-2024 Report of the Committee on Infectious Diseases. 32nd ed. American Academy of Pediatrics; 2021.</td><td>Used in Lexicomp and NeoFax recommendation</td></tr>
<tr><td>Ampicillin Dose for Early and Late-Onset Group B Streptococcal Disease in Neonates</td><td>Lim SY, Miller JL. Ampicillin Dose for Early and Late-Onset Group B Streptococcal Disease in Neonates. Am J Perinatol. 2022;39(7):717-725. doi:10.1055/s-0040-1718880</td><td>Postnatal Age ≤ 7 days – 100 mg/kg/dose, Intravenous, EVERY 8 HOURS

Postnatal Age > 7 days – 75 mg/kg/dose, Intravenous, EVERY 6 HOURS</td><td>Ampicillin meningitis dosing as outlined up the new 2018 Red Book dosing</td></tr>
</table>

Recommended Dosing Tables

Ampicillin – Meningitis Dosing		
PNA	**Dose**	**Frequency**
≤ 7 days	100 mg/kg	Every 8 Hours
>7 days	75 mg/kg	Every 6 Hours

Ampicillin – Non-meningitis Dosing			
GA	**PNA**	**Dosing**	**Frequency**
≤ 34 weeks	0-7 days	50 mg/kg	Every 12 Hours
	>7-28 days	75 mg/kg	Every 12 Hours
>34 weeks	0-28 days	50 mg/kg	Every 8 Hours

Ampicillin – Non-meningitis Dosing		
PNA	**Dosing**	**Frequency**
> 28 days	50 mg/kg	Every 6 Hours

Gentamicin – Neonatal Dosing			
GA	**PNA**	**Dose**	**Frequency**
< 30 weeks	≤ 14 days	5 mg/kg	Every 48 Hours
	≥ 15 days	5 mg/kg	Every 36 Hours
30 – 34 weeks	≤ 10 days	5 mg/kg	Every 36 Hours
	11-60 days	5 mg/kg	Every 24 Hours
≥ 35 weeks	≤ 7 days	4 mg/kg	Every 24 Hours
	8-60 days	5 mg/kg	Every 24 Hours

Acyclovir – Neonatal Dosing		
PMA	**Dose**	**Frequency**
<30 weeks	20 mg/kg	Every 12 Hours
≥30 weeks	20 mg/kg	Every 8 Hours

Metronidazole – Neonatal Dosing		
Loading Dose: 15 mg/kg ONCE		
PMA	**Dose**	**Frequency**
<34 weeks	7.5 mg/kg	Every 12 Hours
34-40 weeks	7.5 mg/kg	Every 8 Hours
>40 weeks	10 mg/kg	Every 8 Hours

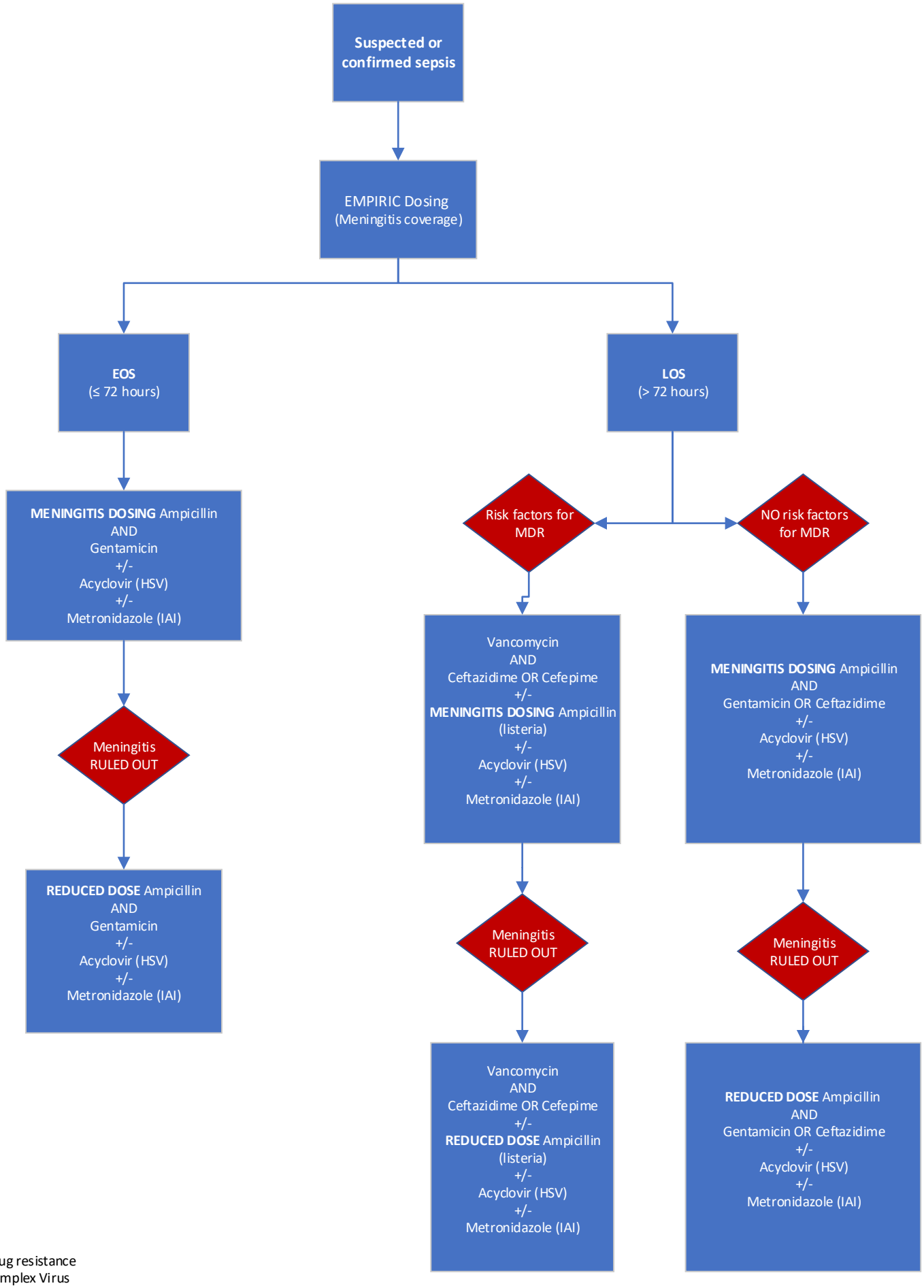
Ceftazidime – Neonatal Dosing		
PNA	**Dose**	**Frequency**
≤7 days	50 mg/kg	Every 12 Hours
8-28 days	50 mg/kg	Every 8 Hours

Vancomycin – Neonatal Dosing			
PMA	**PNA**	**Dose**	**Frequency**
≤29 weeks	0-14 days	15 mg/kg	Every 18 Hours
	>14 days	15 mg/kg	Every 12 Hours
30-36 weeks	0-14 days	15 mg/kg	Every 12 Hours
	>14 days	15 mg/kg	Every 8 Hours
37-44 weeks	<7 days	15 mg/kg	Every 12 Hours
	>7 days	15 mg/kg	Every 8 Hours

Cefepime – Neonatal Dosing		
PMA	**Dose**	**Frequency**
<44 weeks	50 mg/kg	Every 12 Hours

Gestational Age (GA): Time elapsed between the first day of the last menstrual period and the day of delivery; reported in weeks
Postnatal Age (PNA): time elapsed after birth-often considered the chronological age; reported in days, weeks, months
Postmenstrual Age (PMA): gestational age plus postnatal age; reported in weeks

Antibiotic Selection Algorithm below.



-MDR: Multi-drug resistance
-HSV: Herpes Simplex Virus
-IAI: Intra-abdominal Infection
-Risk factors for MDR: previous antibiotic use (specifically broad spectrum/cephalosporin), previous NICU stay, prolonged hospitalization, prolonged antibiotic therapy, presence of a central line or other invasive device, previous infection with MDR organism, neutropenia, underlying renal dysfunction
-Narrow antibiotic therapy appropriately when/if culture results available
-Broaden to other broad spectrum antibiotic if hx of MDR organism resistant to vanco +/- ceftaz or cefepime (ex: zosyn, meropenem)