SHC Antimicrobial Dosing Guide for Obesity

Definitions and Equations

BMI = weight (kg) / height^2 (m^2)

WHO BMI Classification	Definition
Obese Class I and II (obese)	BMI 30-40 kg/m^2
Obese Class III (morbidly obese)	BMI ≥ 40 kg/m^2

Body Weight	Equation[1]
IBW (kg)	Male: $50.0 + 2.3 \times (number\ of\ inches\ over\ 5\ ft)$ Female: $45.5 + 2.3 \times (number\ of\ inches\ over\ 5\ ft)$
ABW (kg)	IBW + C × (TBW – IBW) C = either 0.3 or 0.4 ($ABW_{0.3}$ or $ABW_{0.4}$)
LBW_{2005} (kg)	Male: $\frac{9270 \times \mathrm{TBW}}{6680 + 216 \times \mathrm{BMI}}$ Female: $\frac{9270 \times \mathrm{TBW}}{8780 + 244 \times \mathrm{BMI}}$
LBW (for anti-tuberculosis medications):	• Obesity: ATS/CDC Guidelines recommend dosing based on estimated lean body weight. • Lean Body Weight (men) = (1.10 x Weight(kg)) - 128 x (Weight^2/(100 x Height(m))^2) • Lean Body Weight (women) = (1.07 x Weight(kg)) - 148 x (Weight^2/(100 x Height(m))^2)

Table 1.[1] Recommended Antibiotic Dosing in Obesity (BMI ≥ 30 kg/m^2)

Drug	Maximum Dose[a]	Study Type[b]			Comments
		Case studies	PK/PD studies	Clinical outcomes	
β-lactams					
Amoxicillin	No Data				- Consider upper limit of normal dosing in severe infections,[c] e.g. up to 1g PO TID
Ampicillin	Insufficient data	●			- Consider upper limit of normal dosing in severe infections,[c] e.g. up to 2g q4h - Single study with 6 patients: higher V_d but decreased Vd/kg_{TBW}, CL unchanged[2]
Nafcillin	Insufficient data	●			- Single case report in critically ill, obese patient[3]: consider upper end of normal dosing in severe infections,[c] e.g. up to 2 g q4h
Piperacillin-tazobactam[4-14]	Up to 4.5 g q8h (prolonged infused over 4 hours) or 4.5 g q6h (30 min infusion)	●	●	●	- Prolonged infusions preferred for critically ill, obese patients - High dose, prolonged infusion if critically ill, obese, with CrCl > 100 ml/min
Cefazolin[15-21]	Insufficient data	●	●		- Consider upper limit of normal dosing in severe infections, e.g. up to 2 g q8h (option for continuous infusion)[22], or 1.5-2 g q6h intermittent dosing - In post-trauma critically ill patients, data suggests 2g q6h if CrCl > 215 ml/min.[23]
Cephalexin	No data				- Consider upper end of normal dosing in severe infections,[c] e.g. 500-1000 mg q6h
Cefepime, ceftazidime[14,24,25]	Up to 2g q8h prolonged infusion	●			

Ceftazidime/ avibactam[26,27]	No change		●		
Ceftolozane/ tazobactam[28]	No change		●		
Doripenem[14,29-31]	No change		●		- Consider extended infusion if targeting a higher PD endpoint of 100% fT>MIC or with less susceptible pathogens (i.e. MIC > 2)
Ertapenem[13,18,32-35]	No change		●	●	
Imipenem	No data				- Use caution in renal impairment and with high doses (1g q6h): increased risk of seizures
Meropenem[4,9,18,30,36-42]	Same dose: consider prolonged infusion for critically ill patients	●	●		- Prolonged infusion if critically ill, obese with CrCl > 100 ml/min, if targeting a higher PD endpoint of 100% fT>MIC, or infections with less susceptible pathogens (i.e. MIC > 2)
Monobactam					
Aztreonam	Insufficient data	●			- Single case report suggests higher dosing needed[43] - Consider upper end of normal dosing in severe infections,[c] e.g. 2g q6-8h
Fluoroquinolones					
Ciprofloxacin[44-47]	In critically ill, septic patients on CRRT with organisms with MICs > 0.5mg/L (e.g. *P.aeruginosa, A.baumannii*): > 90kg: 400 mg IV q8h	●	●		- Insufficient data except as noted in critically ill, septic patients on CRRT. - Consider upper end of normal dosing in severe infections,[c] e.g. up to 400 mg IV q8h or 750mg PO BID
Levofloxacin[48-51]	750 mg q24h	●	●		- PK reportedly unaltered by obesity, however, serum levels may be sensitive to CrCl: 1,000 mg q24h has been suggested for $CrCl_{IBW}$ > 110 ml/min to target gram negative pathogens
Moxifloxacin[52-54]	No change		●		
Aminoglycosides					
Amikacin[55-57]	Use adjusted body weight ($ABW_{0.4}$) for initial dose		●		- Adjust by TDM
Gentamicin[55-61]	Use adjusted body weight ($ABW_{0.4}$) for initial dose		●		- Adjust by TDM
Tobramycin[55-57,61,62]	Use adjusted body weight ($ABW_{0.4}$) for initial dose		●		- Adjust by TDM
Polymyxins					
Colistin methanesulfonate[63-67]	Use IBW		●		- Maximum dose of 360 mg daily to limit the risk of nephrotoxicity
Polymyxin B[67-70]	Limited data. Consider adjusted body weight ($ABW_{0.4}$), especially in upper end of dosing range		●		- Consider maximum dose 200 mg or 2 million units daily to limit risk of toxicity
Anti-MRSA agents					
Ceftaroline[71-73]	No change		●	●	- Consider q8h if targeting 50% fT>MIC for MRSA
Clindamycin[18,74-76]	IV: 600 mg q6h or 900 mg q8h PO: 450 - 600 mg q6h or 600- 900 mg Q8H		●	●	- Studies from prosthetic joint infection and SSTI suggest increased doses warranted - Manufacturer maximum: 2,700 mg/day in severe infections; 4,800 mg/day given by intermittent or continuous infusion for life-threatening infections[77]

Dalbavancin[78-81]	No change		●	●	
Daptomycin[18,61,81-91]	Same weight-based dose but use adjusted body weight ($ABW_{0.4}$)	●	●	●	- Caution in renal insufficiency, dialysis. Monitor CKs and signs of myopathy
Linezolid[18,37,81,92-100]	No change	●	●	●	
Oritavancin[81]	No change		●		
Sulfamethoxazole/ trimethoprim[76,101]	SSTI or severe/complicated UTI: up to 320 mg PO BID or 8-10 mg/kg_{ABW}/day in divided doses		●	●	- Limited data to guide optimal dosing weight - Consider adjusted body weight when using high doses (e.g. >8 mg/kg/day)
Tedizolid[81,102,103]	No change		●		
Telavancin[1,81,104,105]	Same dose; consider a maximum of 1,000 mg/dose		●	●	- Increased systemic exposure may be related to AKI - These are tentative pending results of an ongoing Phase I trial (NCT02753855)
Tigecycline[61,81,106,107]	No change		●	●	
Vancomycin[18,37,61,108-132]	See Vancomycin Per Pharmacy Protocol (Appendix C) Load: 20-25 mg/kg_{TBW} (consider a maximum of 2.5 g) Maintenance: 10-15 mg/kg_{TBW} q12h* initially (consider a maximum of 2g/dose), then adjust by TDM - Consider 7.5-12.5 mg/kg_{TBW} q12h* if BMI ≥ 40 kg/m^2 **May convert to q8h regimen based on adequate renal function (e.g. CrCl > 120 ml/min) and age* Consider an initial maximum daily dose of 4.5 g	●	●		- Alternative approach using $ABW_{0.4}$: loading dose 25-30 mg/kg_{ABW}, initial maintenance dose approximately 15 mg/kg_{ABW} q12h*, then adjust by TDM - Loading doses commonly ranged from none to 3g; daily doses commonly ranged 2-4g or 20-30 mg/kg_{TBW}/day - Adjust doses by TDM (peak and trough) using software utilizing Bayesian methods and AUC targets. - If calculating without software, see Hong et al for equations.[119] - If only measuring troughs, more cautious and frequent initial monitoring of levels may be warranted

a. Does not include dose adjustments for renal and/or hepatic impairment. Doses listed are within usual safety margins. Lower doses may be sufficient in mild infections (e.g. UTI). Dosages are based on the provided references and/or the authors' opinion, and should not replace clinical judgment. CrCl assumes calculation using $ABW_{0.4}$ unless specified in table.
b. Dots represent types of studies available and not quantity
c. Dosing recommendations are for severe or deep-seated infections based on similarities in PK profile and dosing recommendations with other antibiotics of the same class when there is insufficient or no data in obese patients.

Table 2. Recommended Antifungal Dosing in Obesity (BMI ≥ 30 kg/m^2)

Drug	Maximum Dose[a]	Study Type[b]			Comments
		Case studies	PK/PD studies	Clinical outcomes	
Caspofungin [133-135]	70 mg x1, then 50-70 mg daily		●	●	- Retrospective study from 9 clinical studies found no significant difference in favorable responses in invasive candidiasis between obese and non-obese groups - PK studies showed no correlation with BMI and PK parameters, but did find negative correlation between caspofungin peak levels and body weight, suggests increased doses needed for higher TBW - In clinical trial of invasive candidemia, no safety concerns found with caspofungin 150mg daily
Fluconazole[135-139]	Candidiasis: 12mg/kg x1 load, then 6mg/kg q24h (TBW)	●	●	●	- Doses up to 1200 mg daily have been reported in the literature for Cryptococcus meningitis - In critically ill, esp with CrCl > 50, higher doses may be warranted to achieve PK/PD target of fAUC/MIC > 100, esp if MIC > 2 *Candida spp* - Consider TDM for severe infections
Liposomal Amphotericin[135]	Use total or adjusted body weight		●	●	- No PK data in obese humans; in general pop PK studies, linear increase in Vd and CL with weight - Safety data: at doses 7.5-15mg/kg/day, similar discontinuation rates; PK became non-linear (max Cmax and AUC at 10mg/kg/day)
Voriconazole, [135,140-145]	Use adjusted body weight or LBW_{2005}	●	●		- Adjust dosing based on TDM - Retrospective TDM studies frequently showed supratherapeutic levels in obese subjects when dosed by TBW - Steady state plasma PK of voriconazole did not suggest weight-based dose adjustments necessary

Table 3. Recommended Antiviral Dosing in Obesity (BMI ≥ 30 kg/m^2)

Drug	Maximum Dose[a]	Study Type[b]			Comments
		Case studies	PK/PD studies	Clinical outcomes	
Acyclovir[146-148]	Use ideal or adjusted body weight		●	●	- PK study: 5mg/kg IV x1 showed that dosing based on IBW in obese patients led to lower AUC than dosing by TBW in normal-weight patients. Authors suggest using ABW - Renal function may be a more important consideration than weight-based dosing in obese patients
Cidofovir[149]	Use adjusted body weight				- No data - Based on similar PK profile and physiochemical properties as acyclovir, long intracellular half-life (except foscarnet, which deposits in bone), dose-limiting toxicity (e.g. myelosuppression)
Foscarnet[149]	Use adjusted body weight				
Ganciclovir[149]	Use adjusted body weight				

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