ANTIMICROBIAL DOSING IN EXTREMES OF BODY WEIGHT IN ADULTS

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CONTENTS

INTRODUCTION

Many aspects of drug handling are altered in patients with increased body weight who present with infection, risking therapeutic failure and antimicrobial resistance due to inadequate drug exposure. Conversely, in underweight patients, standard dosing risks exposing patients to drug toxicity.

Unfortunately, evidence is generally lacking when it comes to dosing in obese or underweight patients, with dose recommendations often based on case reports or small studies. Each case should be considered on an individual basis, taking into account other factors that will affect drug handling, including renal function.

Please note this guidance does **not** include information on dosing in surgical prophylaxis.

PARAMETERS USED FOR DOSING

There are many parameters that can be used when calculating antimicrobial doses. For simplicity these guidelines recommend doses based on actual body weight, ideal body weight and adjusted body weight, to minimise the risk of confusion for clinical staff.

BODY MASS INDEX (BMI)

Body mass index is not used to calculate drug dosage, but can guide dose adjustment when necessary. It may be calculated using the BNF calculator or with the equation below:

- https://www.medicinescomplete.com/mc/bnflegacy/current/
- **BMI (kg/m^2) = weight (kg)/(height(m)^2)**

NICE defines patients with a body mass index (BMI) over 30kg/m^2 as obese (CG189, 2014).

ACTUAL BODY WEIGHT

Actual body weight is defined as the patient's weight as measured and is sometimes referred to as total body weight. Abbreviation is not recommended to avoid confusion with adjusted body weight.

IDEAL BODY WEIGHT

Ideal body weight (IBW) is based on a patient's height and can be calculated using the formulae below. For ease of use, a reference table is provided.

- **Males: Ideal body weight (kg) = 50kg + 0.9kg for every cm height over 152cm**
- **Females: Ideal body weight (kg) = 45.5kg + 0.9kg for every cm height over 152cm**

ADULT FEMALES (> 16 yrs)		ADULT MALES (>16 yrs)	
Height	IBW (kg)	Height	IBW (kg)
≥191cm (6'3")	≥80.6	≥191cm (6' 3")	85.1
188cm (6'2")	77.9	188cm (6' 2")	82.4
185cm (6'1")	75.2	185cm (6' 1")	79.7
183cm (6')	73.4	183cm (6')	77.9
180cm (5'11")	70.7	180cm (5' 11")	75.2
178cm (5'10")	68.9	178cm (5' 10")	73.4
175cm (5'9")	66.2	175cm (5' 9")	70.7
173cm (5' 8")	64.4	173cm (5' 8")	68.9
170cm (5' 7")	61.7	170cm (5' 7")	66.2
168cm (5' 6")	59.9	168cm (5' 6")	64.4
165cm (5' 5")	57.2	165cm (5' 5")	61.7
163cm (5' 4")	55.4	163cm (5' 4")	59.9
160cm (5' 3")	52.7	160cm (5' 3")	57.2
157cm (5' 2")	50	157cm (5' 2")	54.5
155cm (5' 1")	48.2	155cm (5' 1")	52.7
≤152cm (5')	≤45.5	≤152cm (5')	≤50

ADJUSTED BODY WEIGHT

Whilst ideal body weight does not take into account any excess weight the patient is carrying, adjusted weight uses a correction factor to account for the vasculature and fluid present in adipose tissue.

If a patient's actual body weight is 30% more than the IBW, the adjusted body weight can be calculated using:

- **Adjusted ideal body weight (kg) = IBW + 0.4 (Actual body weight – IBW)**

DOSE RECOMMENDATIONS

ACICLOVIR

OBESE PATIENTS

Usually dose IV aciclovir using ideal body weight, taking renal function into account (1,2,4). Consider using adjusted body weight and the higher 10mg/kg dose for serious infections (e.g. herpes encephalitis) and for patients who are morbidly obese, with appropriate hydration and close monitoring of renal function (5).

UNDERWEIGHT PATIENTS

No information available

AMBISOME

OBESE PATIENTS

Dose using actual body weight (1,2,3), suggest monitoring for toxicity in obese patients including renal function and electrolytes (4).

UNDERWEIGHT PATIENTS

Dose as per SPC on a mg/kg basis (1)

AMIKACIN

OBESE PATIENTS

Dose using adjusted body weight (2, 4, 5, 7) then adjust according to levels.

UNDERWEIGHT PATIENTS

No information available

AMOXICILLIN

OBESE PATIENTS

Dosing should be at the higher end of the recommended treatment ranges, e.g. IV 2g every 4 hours or Po 1g TDS, particularly in morbidly obese patients with severe infections (4). A 1g TDS IV dose may suffice for non-severe infections (8) Amoxicillin concentrates in the urine such that increased doses may not be necessary for urinary tract infections. Consider using a front-loading strategy, where antibiotics are given at higher doses initially and then reduced to standard dosing, depending on culture results, organ function and response to therapy (4)

UNDERWEIGHT PATIENTS

No information available

AMPICILLIN

OBESE PATIENTS

Dosing should be at the higher end of the recommended treatment ranges, e.g. IV 2g every 4 hours, particularly in morbidly obese patients with more severe infections. Take into account renal function. Consider using a front-loading strategy, where antibiotics are given at higher doses initially and then reduced to standard dosing, depending on culture results, organ function and response to therapy (4)

UNDERWEIGHT PATIENTS

No information available

ANIDULAFUNGIN

OBESE PATIENTS

No dose adjustment necessary (1), however consider a 25% increase in loading and maintenance doses in patients weighing more than 140kg; to minimise wastage this may be achieved by giving in repetitive cycles of 200mg followed by 3 doses of 100mg over the duration of the course length (which will provide equivalent cumulative exposure over 4 days) (9). A dose increase of 50% can be considered in patients weighing 200kg or more if the perceived benefit outweighs the risk (8)

UNDERWEIGHT PATIENTS

No change to manufacturer's recommended dosage (1)

AZITHROMYCIN

OBESE PATIENTS

Use higher end of normal doses (4).

UNDERWEIGHT PATIENTS

No information available

AZTREONAM

OBESE PATIENTS

A single case report suggests higher dosing is needed. Consider upper end of normal dosing in severe infections (e.g. 2g TDS-QDS) (7)

UNDERWEIGHT PATIENTS

No information available.

BENZYLPENICILLIN

OBESE PATIENTS

Dosing should be at the higher end of the recommended treatment ranges, e.g. IV 1.2-2.4g every 4 hours, particularly in morbidly obese patients with severe infections. Take renal function into account. Consider using a frontloading strategy, where antibiotics are given at higher doses initially and then reduced to standard dosing, depending on culture results, organ function and response to therapy (1, 4).

UNDERWEIGHT PATIENTS

No information available

CASPOFUNGIN

OBESE PATIENTS

Dose of 150mg daily has been recommended (off label). While data supporting this dose specifically in obese individuals is lacking, this approach has been compared to traditional dosing and should produce an AUC that is approximately double that of a 70mg/day regimen. Doses of up to 200mg/day have been administered, with no reports of dose limiting toxicity (9)

UNDERWEIGHT PATIENTS

No information available

CEFALEXIN

OBESE PATIENTS

Consider upper end of normal dosing in severe infections, e.g. 500mg-1g QDS (7)

UNDERWEIGHT PATIENTS

No information available

CEFOTAXIME

OBESE PATIENTS

Use standard doses up to a maximum of 12g a day (4)

UNDERWEIGHT PATIENTS

No information available

CEFTAZIDIME

OBESE PATIENTS

Use 2g TDS IV, preferably by prolonged infusion (4, 7)

UNDERWEIGHT PATIENTS

No information available

CEFTAZIDIME/AVIBACTAM

OBESE PATIENTS

No dose adjustment necessary (7)

UNDERWEIGHT PATIENTS

No information available

CEFTOLOZANE/TAZOBACTAM

OBESE PATIENTS

No dose adjustment necessary (7)

UNDERWEIGHT PATIENTS

No information available

CEFTRIAXONE

OBESE PATIENTS

Dose at top end of licensed dose, up to a maximum of 2g BD. Take into account renal function. (1, 4)

UNDERWEIGHT PATIENTS

No information available

CEFUROXIME

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

CIPROFLOXACIN

OBESE PATIENTS

May benefit from increased dosing. Weight based doses have been suggested using actual body weight and a 4mg/kg/dose, up to a maximum of 800mg BD. TDS dosing may be considered in critically ill patients, though it has also been suggested that 600mg BD is better than 400mg TDS as this improves Cmax:MIC ratio. It is extremely important that obese patients receiving high dose fluoroquinolones are closely monitored for cardiovascular, neurological and metabolic adverse effects, including QTc prolongation (1, 4, 6)

UNDERWEIGHT PATIENTS

No information available, however mg/kg dosing can be used.

CLARITHROMYCIN

OBESE PATIENTS

Use higher end of normal doses (4)

UNDERWEIGHT PATIENTS

No information available

CLINDAMYCIN

OBESE PATIENTS

For standard infections in patients >75kg give 900mg TDS (Po or IV) (4, 7). For serious/life-threatening infections suggest doses of up to 4.8g/day in divided doses (1,6,7). Doses of <10mg/kg/24 hours have demonstrated worse outcomes in obese patients (1)

UNDERWEIGHT PATIENTS

No information available

CO-AMOXICLAV

OBESE PATIENTS

For oral doses consider supplementing 625mg co-amoxiclav with 500mg amoxicillin to ensure adequate amoxicillin exposure (8)

UNDERWEIGHT PATIENTS

No information available

COLISTIMETHATE SODIUM (COLISTIN)

OBESE PATIENTS

Loading dose based on ideal body weight, then maintenance dose based on creatinine clearance and TDM (discuss with microbiology) (4, 6, 7). Excessive dosing as a result of using actual body weight has been associated with higher rates of nephrotoxicity in obese patients (6).

UNDERWEIGHT PATIENTS

Dose based on actual body weight (4)

CO-TRIMOXAZOLE

OBESE PATIENTS

Use higher end of normal doses (4). Consider using adjusted body weight when calculating higher doses (7). Inadequate oral doses (<30mg/kg/day, equivalent to <5mg/kg trimethoprim/day) had worse outcomes in morbidly obese patients. For treatment of Pneumocystis pneumonia doses of up to 120mg/kg/day (equivalent to 20mg/kg trimethoprim/day) have been used. Take renal function into account (1). Monitor potassium (risk of hyperkalaemia) and FBC

UNDERWEIGHT PATIENTS

No information available

DAPTOMYCIN

OBESE PATIENTS

Dose using actual body weight if BMI is less than 35 kg/m2, but use adjusted body weight if the BMI is over 35 kg/m2. Monitor for toxicity, including CK levels to identify patients at high risk of developing myopathy. Adjust dose for renal impairment if necessary. (1, 2, 4, 5, 7)

UNDERWEIGHT PATIENTS

No information beyond standard mg/kg dosing (1)

DOXYCYCLINE

OBESE PATIENTS

Use higher end of normal doses (4)

UNDERWEIGHT PATIENTS

No information available

ERTAPENEM

OBESE PATIENTS

A standard 1g dose may not provide adequate drug exposure in obese patients for organisms with a minimum inhibitory concentration (MIC) in excess of 0.25-0.5µg/ml, which may include species such as *Strep pneumoniae*, *Pseudomonas aeruginosa*, *Aceinebacter* spp, *Bacteroides fragilis* and oxacillin susceptible coagulase negative *Staphylococci* (1,6,11). In such cases consider 1g bd or discuss with microbiology. (4)

UNDERWEIGHT PATIENTS

No information available

ERYTHROMYCIN

OBESE PATIENTS

Use higher end of normal doses (4)

UNDERWEIGHT PATIENTS

No information available

FIDAXOMICIN

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

FLUCLOXACILLIN

OBESE PATIENTS

Dosing should be at the higher end of the recommended treatment ranges, e.g. 2g every 4-6 hours IV, particularly in morbidly obese patients with more severe infections. Take into account renal function. Consider using a frontloading strategy, where antibiotics are given at higher doses initially and then reduced to standard dosing, depending on culture results, organ function and response to therapy (1, 4)

UNDERWEIGHT PATIENTS

No information available

FLUCONAZOLE

OBESE PATIENTS

Recommendation based on limited information. Use the higher end of the 6-12mg/kg dose range (oral or IV), based on actual body weight up to 1200mg/day (off label dose) (8).

UNDERWEIGHT PATIENTS

No information available

FLUCYTOSINE

OBESE PATIENTS

Dose using ideal body weight (3, 5, 9)

UNDERWEIGHT PATIENTS

No information available

FOSFOMYCIN

OBESE PATIENTS

No information available for oral fosfomycin. For IV fosfomycin, use the higher end of the dosing range, especially for indications other than urinary tract infections (12).

UNDERWEIGHT PATIENTS

No information available

GANCICLOVIR

OBESE PATIENTS

Dose using ideal body weight. Monitor renal function and FBC as dose-dependent risk of neutropenia (4)

UNDERWEIGHT PATIENTS

No information available

GENTAMICIN

OBESE PATIENTS

Dose initially using adjusted body weight (2, 3, 4, 5, 7) then adjust according to levels

UNDERWEIGHT PATIENTS

No information available

IMIPENEM/CILASTATIN

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

ITRACONAZOLE

OBESE PATIENTS

Recommend 200mg BD in obese patients (or higher if recommended, e.g. histoplasmosis) then use therapeutic drug monitoring to adjust the dose (9)

UNDERWEIGHT PATIENTS

No information available

LEVOFLOXACIN

OBESE PATIENTS

Too little information to give a definitive dose recommendation (1,6). One source recommends no dose adjustment (5) whilst another advises an initial starting dose of 500-750mg BD (off-label) (4). It is extremely important that obese patients receiving high dose fluoroquinolones are closely monitored for cardiovascular, neurological and metabolic adverse effects, including QTc prolongation (4)

UNDERWEIGHT PATIENTS

No information available (1)

LINEZOLID

OBESE PATIENTS

Dosage adjustments based on BMI alone are not required and standard doses for patients with body weights up to approximately 150kg should provide AUC values similar to those seen in non-obese patients. 600mg twice daily was sufficient for the treatment of skin and soft tissue infections in obese adults (1, 5, 7)

UNDERWEIGHT PATIENTS

No studies carried out on underweight adults in any clinical trials. In a compassionate use programme of adult patients, those who weighed more than 40kg were treated at a dose of 600mg Po/IV every 12 hours; adult patients ≤40kg received a dose of 10mg/kg every 12 hours Po/IV (1)

MEROPENEM

OBESE PATIENTS

No dose adjustment required (13). Use upper end of normal dose range, i.e. 1g TDS IV or for CNS or cystic fibrosis infections 2g TDS IV (4). Consider prolonged infusion for critically ill patients (7)

UNDERWEIGHT PATIENTS

No information available

METRONIDAZOLE

OBESE PATIENTS

Use standard dosing (1). Consider higher doses in morbidly obese patients for serious systemic infections and brain abscesses (4)

UNDERWEIGHT PATIENTS

No specific information available; mg/kg dosing could be used (1). Consult product literature for mg/kg doses: https://www.medicines.org.uk

MICAFUNGIN

OBESE PATIENTS

For patients up to 200kg dose using the formula: Dose (mg) = weight (kg) + 42, rounded to the nearest 25mg (doses of up to 300mg/day for 7 days have been reported without adverse events) (9)

UNDERWEIGHT PATIENTS

Consult product literature for mg/kg doses for patients weighing less than 40kg: https://www.medicines.org.uk

MOXIFLOXACIN

OBESE PATIENTS

Given the limited information on moxifloxacin dosing and high risk of QTc prolongation, use of ciprofloxacin or levofloxacin is recommended to treat non-tuberculosis regimens in obese patients (4). If treatment with moxifloxacin is preferred do not adjust the dose (5, 7), however monitor for potential treatment failure, as one reference states that a standard dose of 400mg in patients is not sufficient for patients with a lean body weight over 78kg (4).

UNDERWEIGHT PATIENTS

No information available

NITROFURANTOIN

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

OSELTAMIVIR

OBESE PATIENTS

No dose adjustment recommended for routine prophylaxis and treatment of influenza (4, 5)

UNDERWEIGHT PATIENTS

No information available

PHENOXYMETHYLPENICILLIN (PENICILLIN V)

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

PIPERACILLIN/TAZOBACTAM

OBESE PATIENTS

4.5g QDS (dependent on renal function) is the recommended standard dose for all critically ill patients, neutropenic sepsis and *Pseudomonas* infections irrespective of weight. Some sources recommend standard dosing is suffice in obesity (6), but others suggest 4.5g QDS (1) or even higher off-label doses of 6.75 g QDS for patients 105–139 kg, and up to 9 g QDS for patients ≥ 140 kg (14), should be considered, dependent on renal function. Continuous infusion or prolonged infusion over 4 hours is preferred (off-label use), especially in critically ill patients (7, 14). In patients with augmented renal clearance (> 130 mL/min) continuous infusion may be the only way of achieving target levels in obesity (14). Consider using a front-loading strategy, where antibiotics are given at higher doses initially and then reduced to standard dosing, depending on culture results, organ function and response to therapy (4)

UNDERWEIGHT PATIENTS

No specific advice available, suggest mg/kg dosing as per BNF for Children in patients under 40kg, or 50kg if neutropenic (1)

PIVMECILLINAM

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

POSACONAZOLE

OBESE PATIENTS

For patients over 140kg increase both IV and oral doses to 400mg for both the twice daily loading and the daily maintenance doses, then adjust according to therapeutic drug monitoring levels. For prophylaxis, a 300 mg dose is adequate in patients up to 190 kg (15)

UNDERWEIGHT PATIENTS

No information available

RIFAMPICIN

OBESE PATIENTS

Dose using ideal body weight, up to 1200mg/day in divided doses (1)

UNDERWEIGHT PATIENTS

No information available

SODIUM FUSIDATE

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

TEDIZOLID

OBESE PATIENTS

No dose adjustment required (5, 7)

UNDERWEIGHT PATIENTS

No information available

TEICOPLANIN

OBESE PATIENTS

Dose using actual body weight and monitor levels (2, 6)

UNDERWEIGHT PATIENTS

No information available

TEMOCILLIN

OBESE PATIENTS

No information available

UNDERWEIGHT PATIENTS

No information available

TIGECYCLINE

OBESE PATIENTS

In clinical trials, patient weight has ranged from 34kg to 200kg, and analysis of AUC and clearance did not appear to be different, suggesting there is no pharmacokinetic justification for dose adjustment based on patient weight (1). However, morbidly obese patients may be at the risk of therapy failure for certain Gram negative pathogens (16). Consider 100mg BD to treat multi-drug resistant pathogens in obese patients (17)

UNDERWEIGHT PATIENTS

In clinical trials, patient weight has ranged from 34kg to 200kg, and analysis of AUC and clearance did not appear to be different, suggesting there is no pharmacokinetic justification for dose adjustment based on patient weight (1)

TOBRAMYCIN

OBESE PATIENTS

Dose initially using adjusted body weight (3, 4, 5, 7) then adjust according to levels

UNDERWEIGHT PATIENTS

No information available

TRIMETHOPRIM

OBESE PATIENTS

Use higher end of normal doses (4). Monitor potassium (risk of hyperkalaemia)

UNDERWEIGHT PATIENTS

No information available

VANCOMYCIN IV

OBESE PATIENTS

Refer to local guidance

UNDERWEIGHT PATIENTS

No information available

VORICONAZOLE

OBESE PATIENTS

Dose IV using adjusted body weight (1, 4, 8). No dose adjustment required for oral voriconazole (5, 8). Given strong association between supra-therapeutic concentrations in morbidly obese patients receiving 4mg/kg actual body weight, consider therapeutic drug monitoring (1,4,8).

UNDERWEIGHT PATIENTS

Dose as per SPC and renal drug handbook (1)

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ABBREVIATIONS

AUC	Area under curve
BMI	Body mass index
CK	Creatine kinase
C max:MIC	Maximum concentration to minimum inhibitory concentration ratio
CNS	Central nervous system
IBW	Ideal body weight
QTc	QT interval
TDM	Therapeutic Drug Monitoring