

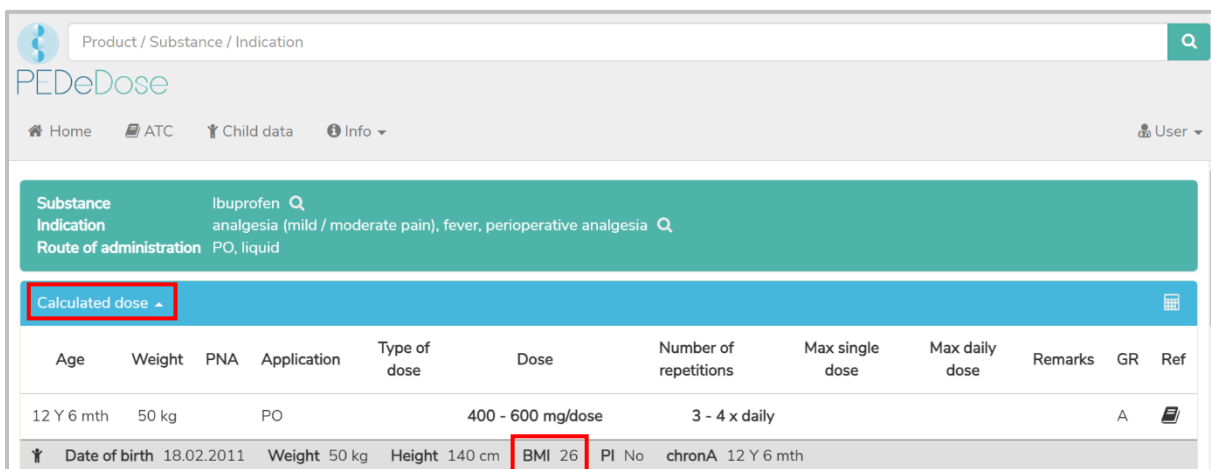
# Factsheet

## Drug dosing in overweight children

### Limitation of drug dosing based on total body weight

The dosages provided by PEDeDose apply to normal-weight children and their age-dependent body composition. The dose calculation is based on total body weight (TBW) and in some cases on body surface area (BSA). Thus, the dosages in PEDeDose do not consider altered physiological states, such as overweight, obesity, or ascites, where the increase in body weight is not linear to the ratio of body composition. The altered body composition as well as related comorbidities and substance-specific factors can influence the pharmacokinetics and pharmacodynamics of a drug. As a result of this, the dosages calculated by PEDeDose may be inappropriate and could, for example, lead to an overdose.

In order to provide healthcare professionals with an indicator for a patient's overweight or obesity status PEDeDose calculates the body mass index (BMI). The BMI is displayed together with the "Calculated dose" in the list of individual child data (see Figure 1). The Swiss Society of Paediatrics defines overweight as BMI >90th percentile and obesity as BMI >97th percentile<sup>1</sup>. In this factsheet the term "overweight" includes "obesity". Swiss BMI reference values and the growth curves for the paediatric population have been developed by Braegger et al. (2011)<sup>2</sup>.



Product / Substance / Indication											
PEDeDose											
Substance: Ibuprofen Indication: analgesia (mild / moderate pain), fever, perioperative analgesia Route of administration: PO, liquid											
Calculated dose											
Age	Weight	PNA	Application	Type of dose	Dose	Number of repetitions	Max single dose	Max daily dose	Remarks	GR	Ref
12 Y 6 mth	50 kg		PO		400 - 600 mg/dose	3 - 4 x daily				A	
Date of birth: 18.02.2011    Weight: 50 kg    Height: 140 cm <b>BMI: 26</b> PI: No    chronA: 12 Y 6 mth											

Figure 1: The body mass index (BMI) is displayed in PEDeDose in the tab "Calculated dose".

## Drug dosing in overweight children

Currently, label information on dose adjustment in overweight is rarely available. Some pharmacokinetic studies on specific active substances are available in the literature. However, missing external validation or inadequate sample sizes often remain a limitation. Therefore, in most cases the dosage in overweight children can only be derived empirically.

Depending on the physicochemical properties of an active substance (solubility or distribution in fat/water), the pharmacokinetic parameters can change in overweight patients and influence the duration and/or intensity of the effect. Particularly relevant in this regard are two pharmacokinetic parameters: the volume of distribution (Vd), which reflects how a drug is distributed in the body, and the clearance (Cl), which describes the volume of plasma cleared from the drug per time unit<sup>3</sup>. Because of this, also the dose types – e.g., loading dose versus maintenance dose – must be taken into consideration. Thus, for the empirical dosing of drugs in overweight children, it can be stated that the body composition, the dose type, the physicochemical properties of the drug and its pharmacokinetic parameters as well as comorbidities must be considered. The position paper of the Pediatric Pharmacy Advocacy Group<sup>4</sup> and the article by Xiong et al.<sup>5</sup> are helpful for understanding and approaching dose adjustment in overweight children.

As a practical approach for empirical dosing, the literature describes various body size descriptors, which can be used instead of TBW for the calculation of drug doses in overweight children<sup>5,6</sup>. An overview of reported body size descriptors can be found in Table 1.

Table 1: List of body size descriptors. Literature references: <sup>5-8</sup>

Body Size Descriptor	Description
Total Body Weight (TBW)	The actual body weight
Lean Body Weight (LBW) / Fat Free Mass (FFM)	Sum of the weight of organs, muscles, bones, and extracellular fluids
Ideal Body Weight (IBW)	Weight at the 50 <sup>th</sup> percentile of the growth chart for the child's age (accounts for sex differences)
Adjusted Body Weight (AdjBW)	AdjBW = IBW + k * (TBW – IBW) k = adjustment factor
Body Surface Area (BSA) by Mosteller	$BSA = (TBW * height [cm] / 3600)^{1/2}$

## Approaches for daily practice

Dosing recommendations for overweight patients may be found in the label information. However, as this information is rarely available, published guidelines (Table 2) and a list of review articles grouped by medical subspecialty (Table 3) are provided below. They report substance-specific body size descriptors that may be appropriate for the empirical calculation of drug dosages in overweight children.

A list of key questions that should be addressed for drug dosing in overweight individuals derived from the literature<sup>4,5,9</sup> and from pharmacological rationale, are presented in Figure 2.

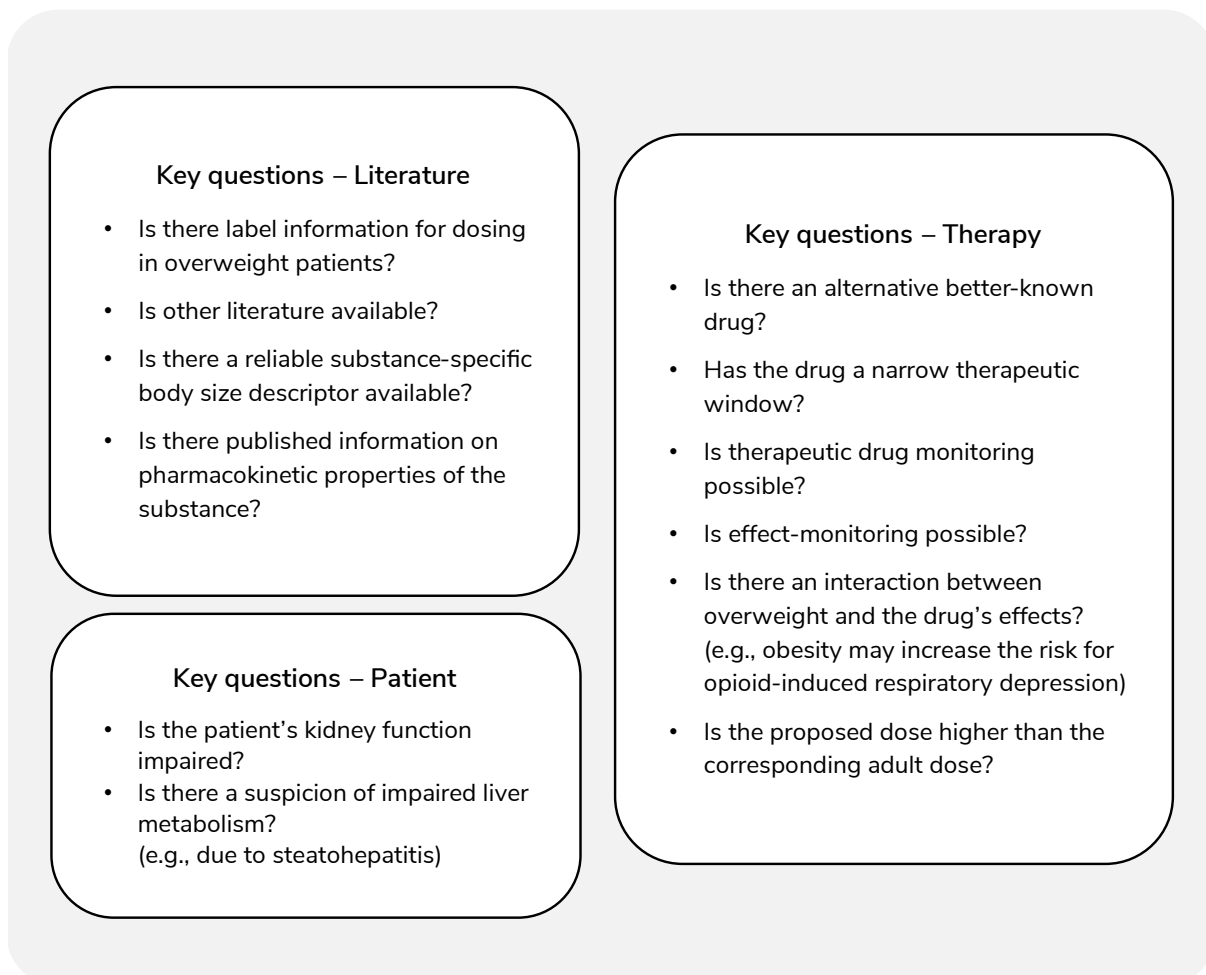


Figure 3: Key questions that should be considered for drug dosing in overweight individuals.

## Guidelines

Table 2: Clinical practice guidelines for drug dosing in overweight children and adults. Links last accessed on 2023-08-16

### For children

#### UK Specialized Pharmacy Service Guideline

<https://www.sps.nhs.uk/articles/how-should-medicines-be-dosed-in-children-who-are-obese/>

Guideline with specific dosing recommendations from the UK Specialized Pharmacy Service. Mainly based on the reviews of Ross et al. (2015)<sup>10</sup>, Kendrick et al. (2015)<sup>11</sup>, and the British National Formulary for Children.

### For adults

#### Stanford Health Care Antimicrobial Dosing Guide – Obesity

<https://med.stanford.edu/bugsanddrugs/guidebook.html>

Guide from the Stanford Antimicrobial Safety and Sustainability Program. Contains antimicrobial and antiviral dosing recommendations for obese adults (BMI  $\geq 30$  kg/m<sup>2</sup>).

## Review articles

Table 3: Review articles describing substance-specific body size descriptors for the calculation of drug dosages in overweight children.

Literature reference	Title and PubMed-Link
<b>General medicine</b>	
Harskamp-van Ginkel et al. (2015) <sup>12</sup>	Drug dosing and pharmacokinetics in children with obesity: a systematic review <a href="#">PMID: 25961828</a>
Kendrick et al. (2015) <sup>11</sup>	Pediatric obesity: pharmacokinetics and implications for drug dosing <a href="#">PMID: 26361823</a>
Kyler et al. (2019) <sup>13</sup>	Drug dose selection in pediatric obesity: available information for the most commonly prescribed drugs to children <a href="#">PMID: 31432433</a>
Mulla and Johnson (2010) <sup>6</sup>	Dosing dilemmas in obese children <a href="#">PMID: 20585055</a>
<b>Anaesthesia</b>	
Chidambaran et al. (2017) <sup>9</sup>	Anesthetic and pharmacologic considerations in perioperative care of obese children. <a href="#">PMID: 29275265</a>
Mortensen et al. (2011) <sup>8</sup>	Anesthetizing the obese child <a href="#">PMID: 21429056</a>

Literature reference	Title and PubMed-Link
<b>Antimicrobials</b>	
Natale et al. (2017) <sup>14</sup>	Pediatric obesity: pharmacokinetic alterations and effects on antimicrobial dosing <a href="#">PMID: 28079262</a>
<b>Emergency care</b>	
Wells and Goldstein (2020) <sup>15</sup>	The utility of pediatric age-based weight estimation formulas for emergency drug dose calculations in obese children <a href="#">PMID: 33145545</a>
<b>Intensive care</b>	
Ross et al. (2015) <sup>10</sup>	Development of recommendations for dosing of commonly prescribed medications in critically ill obese children <a href="#">PMID: 25788508</a>

## References

1. Braegger C, Jenni O, Daniel K, Luciano M. New Swiss growth charts. *Paediatrica*. 2011;1. <https://www.paediatricschweiz.ch/neue-wachstumskurven-fur-die-schweiz/>
2. Braegger C, Jenni O, Daniel K, Luciano M. Growth Charts - Recommended by the Swiss Society of Paediatrics. Swiss Society of Paediatrics. [https://www.pededose.ch/de/file/show?filename=Perzentilen\\_SGP\\_DE](https://www.pededose.ch/de/file/show?filename=Perzentilen_SGP_DE)
3. Brill MJE, Diepstraten J, van Rongen A, van Kralingen S, van den Anker JN, Knibbe CAJ. Impact of Obesity on Drug Metabolism and Elimination in Adults and Children. *Clin Pharmacokinet*. 2012;51(5):277-304. doi:10.2165/11599410-000000000-00000
4. Matson KL, Horton ER, Capino AC, on behalf of the Advocacy Committee for the Pediatric Pharmacy Advocacy Group. Medication Dosage in Overweight and Obese Children. *J Pediatr Pharmacol Ther*. 2017;22(1):81-83. doi:10.5863/1551-6776-22.1.81
5. Xiong Y, Fukuda T, Knibbe CAJ, Vinks AA. Drug Dosing in Obese Children: Challenges and Evidence-Based Strategies. *Pediatr Clin of North Am*. 2017;64(6):1417-1438. doi:10.1016/j.pcl.2017.08.011
6. Mulla H, Johnson TN. Dosing dilemmas in obese children. *Arch Dis Child*. 2010;95(4):112-117. doi:10.1136/adc.2009.163055
7. Gade C, Christensen HR, Dalhoff KP, Holm JC, Holst H. Inconsistencies in dosage practice in children with overweight or obesity: A retrospective cohort study. *Pharmacol Res Perspect*. 2018;6(3):e00398. doi:10.1002/prp2.398
8. Mortensen A, Lenz K, Abildstrøm H, Lauritsen TLB. Anesthetizing the obese child. *Pediatr Anesth*. 2011;21(6):623-629. doi:10.1111/j.1460-9592.2011.03559.x
9. Chidambaran V, Tewari A, Mahmoud M. Anesthetic and pharmacologic considerations in perioperative care of obese children. *J Clin Anesth*. 2018;45:39-50. doi:10.1016/j.jclinane.2017.12.016
10. Ross EL, Heizer J, Mixon MA, et al. Development of recommendations for dosing of commonly prescribed medications in critically ill obese children. *AJHP*. 2015;72(7):542-556. doi:10.2146/ajhp140280
11. Kendrick JG, Carr RR, Ensom MHH. Pediatric Obesity: Pharmacokinetics and Implications for Drug Dosing. *Clin Ther*. 2015;37(9):1897-1923. doi:10.1016/j.clinthera.2015.05.495
12. Harskamp-van Ginkel MW, Hill KD, Becker KC, et al. Drug Dosing and Pharmacokinetics in Children With Obesity: A Systematic Review. *JAMA Pediatr*. 2015;169(7):678-685. doi:10.1001/jamapediatrics.2015.132
13. Kyler KE, Wagner J, Hosey-Cojocari C, Watt K, Shakhnovich V. Drug Dose Selection in Pediatric Obesity: Available Information for the Most Commonly Prescribed Drugs to Children. *Pediatr Drugs*. 2019;21(5):357-369. doi:10.1007/s40272-019-00352-8
14. Natale S, Bradley J, Nguyen WH, et al. Pediatric Obesity: Pharmacokinetic Alterations and Effects on Antimicrobial Dosing. *Pharmacotherapy*. 2017;37(3):361-378. doi:10.1002/phar.1899
15. Wells M, Goldstein L. The utility of pediatric age-based weight estimation formulas for emergency drug dose calculations in obese children. *JACEP Open*. 2020;1(5):947-954. doi:10.1002/emp2.12099