

## How should medicines be dosed in children who are obese?

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### Background

Childhood obesity is increasing in the UK and represents a serious and increasing global health problem (1,2). In England, about 3 in 10 children aged 2-15 years are overweight or obese (2,3). Obesity is directly linked to many health problems including cardiovascular disease, type 2 diabetes and obstructive sleep apnoea. It can also contribute to psychological and psychiatric morbidities. As a result, healthcare professionals are increasingly likely to have under their care children with obesity-associated conditions requiring drug therapy (2).

Childhood obesity is defined on the basis of weight and height, using body mass index (BMI). BMI (adjusted for age and gender) should be used as a practical estimation of body fat in children and young people (2,4). However, it should be interpreted with caution as it is not a direct measure of adiposity (2). Assessing the BMI of children is more complicated than for adults because it changes as they grow and mature, with different growth patterns seen between boys and girls (4). Public Health England advises that the British 1990 (UK90) growth reference charts should be used to determine the weight status of children. A child  $\geq$  the 91<sup>st</sup> centile is classified as overweight, and as obese if  $\geq$  the 98<sup>th</sup> centile (4). The Royal College of Paediatrics and Child Health (RCPCH) [BMI chart or UK-WHO growth charts](#) can be used to determine a child's BMI centile.

Findings from a study by Collier *et al.* suggests that the majority of paediatric prescribers do not calculate BMI to determine whether a child is obese when prescribing medication (1). Currently, height is not routinely measured at the point of admission to hospital (5). Without a recent height it is not possible to determine a child's BMI centile to identify if they are obese.

Identifying whether a child is obese is important as body composition and physiological changes in obesity can affect drug pharmacokinetics and the distribution of drugs into tissues (6,7).

Traditionally, children are dosed according to their body-weight or age, as a surrogate of 'normal' size and function (6). However, as the increase in weight in children living with obesity is not composed of similar proportions of fat and lean tissue, there is a risk of overdose if total body weight (TBW) is used during weight-based dosing of certain drugs (5,6).

There is a lack of pharmacokinetic studies on individual drugs in children who are obese and these patients are rarely included in trials during drug development (6,8). Determining whether drug dose adjustments are necessary is becoming an ever-increasing dilemma and in the absence of clear guidance, decisions are often left at the discretion and experience of prescribers (9).

Due to the potential for differences in drug handling and pharmacokinetics in infants and neonates, this Q&A is not applicable to children under the age of 2.

### Answer

#### Pharmacokinetics in paediatric obesity

Pharmacokinetic (PK) alterations occur in obesity due to changes in body composition and physiology. It is important to consider the consequences of these changes as failure to adjust doses appropriately in patients who are obese may result in therapeutic failure or drug-related toxicity (5,10).

Wells *et al.* compared body composition in overweight, obese and 'normal' weight children (11). Children living with obesity were on average 3.9 cm taller and had significantly higher total body water, body volume, lean mass, fat mass and bone mineral content than normal-weight children. They also had an increased hydration of lean mass which they attributed to increased extracellular water. The increases in fat mass were substantially more than that of lean mass. While this varies between individuals and ethnic groups, approximately 75% of excess weight may be assumed to be fat mass and the remaining 25% to be lean mass (11).

Physiological and pathological changes associated with obesity include increased cardiac output and circulating blood volume, reduced tissue perfusion, and altered liver and kidney function (12).

While it may be presumed that excess body weight in children who are obese leads to alterations in PK parameters of many drugs (13), relatively little is known about the effect of obesity on drug pharmacokinetics in children (13,14). Some PK alterations associated with obesity are discussed below.

### Absorption

Drug absorption appears unaltered in obesity based on limited available data in adults (15).

### Volume of Distribution

Apparent volume of distribution ( $V_d$ ) is a theoretic parameter that reflects how a drug is distributed in the body (12). Although it often changes with obesity, the direction and magnitude is not always predictable (16).  $V_d$  is influenced by the physicochemical properties of a drug, such as lipid solubility and plasma protein binding, as well as physiological changes of obesity, which alters body mass, blood volume, extracellular water and tissue perfusion (12).

### Clearance

Clearance is based on metabolism and organ perfusion (6). In individuals living with obesity, it can be affected by weight-related changes in renal function or changes in the activity of drug-metabolising enzymes (15).

The impact of obesity on drug metabolism differs greatly, depending on the metabolic pathway involved (12,17). Obesity may alter the activity of both phase I and phase II reactions however its effect on expression and function of CYP enzymes are inconclusive with the exception of CYP3A4 and CYP2E1 (17). The activity of CYP3A4, which is responsible for over 50% of phase I reactions, is reduced in patients who are obese (12,17) and expression of CYP2E1 has been reported to be increased (16,17). However, limited data exist about phase I and phase II metabolism in these children (17).

Obesity during childhood has been associated with an increased risk for non-alcoholic fatty liver disease (7) potentially impairing hepatic blood flow, which might in turn have an impact on hepatic drug clearance (18). However, increased liver blood flow owing to increased cardiac output and blood volume may counteract this (12,16). The effect of obesity on renal clearance is unclear (17). Increases in glomerular filtration and renal blood flow have been reported as well as evidence of unaltered renal function (15,16).

### Which measure of weight should be used?

Methods for dosing medication in children include: age-based dosing, allometric scaling, body surface area (BSA)-based dosing, and weight-based dosing (7).

The majority of children's doses in the *BNF for Children* (BNFC) are standardised by body-weight (4). Calculation by body-weight in children who are obese may result in much higher doses being administered than necessary (4). To accommodate for changes in body composition, dose adjustments using an appropriate size descriptor such as ideal body weight (IBW) or adjusted body weight (AdjBW) may be necessary for certain drugs (5,6). For children >120% of IBW, the choice of size descriptor becomes more important since the calculated dose of medicine could vary considerably (19). In an emergency setting, actual body weight (or estimated body weight) may be used to prevent delay of treatment. However, dosing should be reviewed as soon as possible to ensure excess dosing does not accumulate.

### Size descriptors and how to calculate

**Table 1: Common measures of weight used when dosing medicines in childhood obesity**

Weight (kg)	How/What to measure/calculate
<b>Total Body Weight (TBW)</b>	Weight in kg (no adjustment necessary)
<b>Body Mass Index (BMI)</b>	TBW(kg)/ (height in m) <sup>2</sup>
<b>Ideal Body Weight (IBW)</b> <sup>20,21</sup>	Moore's Method - Using <a href="#">STAMP</a> tool or <a href="#">UK WHO growth charts</a> , cross reference height centile to weight for that centile
<b>Adjusted Body Weight (AdjBW)</b> <sup>18</sup>	IBW + Adjustment Factor (0.3) x (TBW-IBW)

### Ideal Body Weight

For certain medications, IBW is the recommended weight to be used for dose calculations, especially for those with a low volume of distribution and narrow therapeutic window (1,19). The BNFC indicates which drugs require dose calculations based on IBW; however, it does not provide guidance on how to calculate it (1,4).

There are numerous methods of obtaining IBW in children including Moore's method, McLaren method and the reverse BMI method (20). In children <8 years, all of these methods provide relatively similar results across all percentiles. In older children, especially at the lowest and highest percentiles, the different methods provide dissimilar results. Whilst the BMI method may be the most accurate measure it requires experience to calculate and many Trusts/Health boards use the Moore's method as it uses a validated tool for measuring centiles and it is easy to calculate. There are practical difficulties with the Moore's method in approximating where the IBW falls between percentiles and it does not allow calculation of IBW in patients at the extreme ends of the height scale, ie, above the 97<sup>th</sup> or below the 3<sup>rd</sup> percentile (20). On those occasions where the height falls between two centiles, the difference in distance between the centiles should be gaged and the same distance used for the weight centiles. For example, if the height fell a third of the way between the 50<sup>th</sup> and 75<sup>th</sup> centile, then the weight a third of the way between the 50<sup>th</sup> and 75<sup>th</sup> centile should be chosen for the age of the child. Advice and judgement from an experienced clinician/pharmacist may be required in situations of extreme obesity and for high risk medication.

### Moore's Method<sup>21</sup>

IBW is determined by first measuring the height of the child in centimetres and using that to identify the height centile for their age. Length may need to be used if the child is too sick to stand up or if the child has some form of disability, or ask the parent/carer to provide a recent height estimate. Their IBW weight is then selected according to the weight at the same centile as their height for their age. The [UK WHO growth charts](#) or the Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP) centile reference tables can be used for the determination of height and weight centiles

(22). More information on using the STAMP tool can be found here:

[http://www.stampscreeningtool.org/data/pdfs/stamp\\_tool.pdf](http://www.stampscreeningtool.org/data/pdfs/stamp_tool.pdf)

Box 1: Example of IBW calculation using Moore's method

A 7 year old girl who is 1.2m tall and weighs 32kg

Step 1: Identify the height centile using STAMP centile reference table/UK WHO growth charts

The height is around the 50<sup>th</sup> centile.

Step 2: Identify the weight at the 50<sup>th</sup> centile using STAMP centile reference table/UK WHO growth charts

50<sup>th</sup> centile weight for a 7 year old girl is 23kg.

### Adjusted Body Weight

To calculate AdjBW, the IBW of the child is used in addition to a specified cofactor, which is a fraction of the excess weight gain between IBW and TBW (5). The following example uses an AdjBW cofactor of 0.35. While a variety of correction factors are suggested in the literature, **NPPG recommend using an adjustment factor of 0.35 in most cases as a pragmatic solution to calculating adjusted body weight in children living with obesity.**

$$\text{AdjBW} = \text{IBW} + 0.35 \times (\text{TBW} - \text{IBW})$$

Box 2: Example of AdjBW calculation using IBW

A 7 year old girl who weighs 32kg and is 1.2m tall has an IBW of 23kg (calculated using Moore's Method)

IBW using Moore's method = 23kg

$$\text{AdjBW} = \text{IBW} + 0.35 \times (\text{TBW} - \text{IBW})$$

$$\text{AdjBW} = 23\text{kg} + 0.35 \times (32\text{kg} - 23\text{kg}) = 26.2\text{kg}$$

### Estimated weight

Other methods exist for estimation of weight including linear equations such as the three Advanced Paediatric and Life Support (APLS) age-based formulae or the UK Resuscitation Council aged based formula (23).

UK Resuscitation Council for ages 1-10 years

$$\text{Weight (kg)} = 2 \times (\text{age in years} + 4)$$

APLS Formulae for ages 1 month-12 years

$$1-12 \text{ months: Weight (kg)} = (0.5 \times \text{age in months}) + 4$$

$$1-5 \text{ years: Weight (kg)} = (2 \times \text{age in years}) + 8$$

$$6-12 \text{ years: Weight (kg)} = (3 \times \text{age in years}) + 7$$

The APLS formulae give higher estimates of expected weight for a wider age range which may be a more accurate reflection of actual body weight due to the increasing prevalence of childhood obesity (23). The UK Resuscitation Council formula appears to result in a lower estimate of weight, which

may relate more closely to IBW than actual body weight (23).

### Drug dosing in children living with obesity – things to consider

While we may reasonably assume that the increase in fat mass in obesity has the potential to alter the distribution of lipophilic drugs and the increase in lean mass to alter drug clearance, we cannot reliably predict the magnitude of dose change, if any, for a specific drug based simply on its physico-chemical properties or known pharmacokinetics in normal weight patients (6). In the absence of clinical data in children living with obesity, it will be necessary to determine the most appropriate size descriptor to guide dosing. In these cases, the following should be considered:

#### Loading dose

Loading doses are based on  $V_d$  (6). The larger the  $V_d$ , the higher the initial dose required to achieve therapeutic plasma concentrations (23). For relatively hydrophilic drugs that distribute mainly into lean body tissue, loading doses are generally based on IBW (19). For drugs that partially distribute into adipose tissue, AdjBW may be a more conservative measure (8). Lipophilic drugs that distribute predominantly into adipose tissue are expected to have an increased  $V_d$  (15), therefore a larger dose may be needed for an adequate response. Loading doses of these drugs should generally be based on TBW (19) however, this should be assessed on a case by case basis as the relationship between a drug's lipophilicity and its distribution to adipose tissue is not always consistent and predictable, especially for highly lipophilic drugs (15).

#### Maintenance dose

Maintenance doses are based on drug clearance (6), predominantly determined by renal and hepatic function (24). Since clearance of drugs does not increase proportionally with bodyweight in individuals living with obesity, it has been suggested that an altered weight that adjusts for the difference between lean and total body weight be used to calculate maintenance drug doses.

#### Patient characteristics

- Nature and severity of illness. For example, if risk of undertreating is greater than over-treating, consider a more liberal size descriptor (19).
- Extent of obesity
- Any comorbidities and underlying organ function (13)

#### Drug characteristics

- What is the therapeutic range of the drug? The narrower the range, the greater the need for caution (25). Consider therapeutic drug monitoring and subsequent dose adjustment to optimise treatment.
- What is the side effect profile of the drug? The greater the risk of serious toxicity, the greater the need for care (25).
- Is the drug being used acutely or for a chronic condition?
- Are there other medications in the same drug class with stronger data? (19)
- Are there PK data available for the drug in adults who are obese? Prescribers may need to extrapolate from adult data while considering the effects of growth and development on pharmacokinetics (13). However important differences in clearance and other PK parameters

may exist between adults and children who are obese which means that conducting PK studies specifically in children who are obese is needed (14).

### Dosage recommendations

As previously mentioned, there are limited published data available on drug dosing in children living with obesity. Table 2 below contains currently available data; however, some of the information has been derived from adult obesity data. It is intended to generate discussion and for paediatric teams to agree a consensus locally. This list is not exhaustive and absence does not imply that no dose adjustment is needed in children who are obese. This information does not apply to children under the age of 2. Patient-specific factors such as underlying organ function, illness severity and extent of obesity should be taken in to account when determining appropriate drug doses for individual patients (7). Drug levels should be monitored wherever possible. For children  $\geq 40$ kg, care and familiarity with adult dosage regimens is needed as calculated doses should not normally exceed the maximum recommended dose for an adult (4,25). In all cases, treatment should not rely purely on calculated dose but be clinically reviewed regularly to ensure that the child is receiving the correct dose in terms of both efficacy and safety.

**NPPG recommend using a standard adjustment factor of 0.35 to calculate adjusted body weight for those drugs where it is required.**

**Table 2: A summary of published evidence on size descriptors to base doses of a range of drugs commonly used in children**

Drug	Dosing scalar from literature	Comments	NPPG recommendation	Literature Refs
<b>Antimicrobials</b>				
Aciclovir	IBW		IBW	4, 6, 19
Carbapenems	No dose adjustment necessary	Up to adult maximum dose	No dose adjustment necessary	13, 18, 26
Cephalosporins	No dose adjustment necessary	Up to adult maximum dose	No dose adjustment necessary	7, 98, 27*
Ciprofloxacin	No dose adjustment or AdjBW (correction factor 0.45).	Conflicting data regarding pharmacokinetics in obesity. Dose adjustment may be required. Monitor for side effects.	No dose adjustment or AdjBW (correction factor 0.35).	6, 18, 26
Clindamycin	No dose adjustment necessary	Lack of literature support to alter current practice.	No dose adjustment necessary	18, 19, 28*
Fluconazole	No dose adjustment necessary	Lack of literature support to alter current practice.	No dose adjustment necessary	19
Gentamicin	AdjBW (correction factor 0.4) or no dose adjustment	Conflicting guidance. Monitor levels and adjust doses accordingly. In critically ill patients, consider basing the initial dose on their total body weight in order to ensure adequate serum concentrations.	AdjBW (correction factor 0.35) or no dose adjustment	4, 6, 7, 18, 19, 29*



Drug	Dosing scalar from literature	Comments	NPPG recommendation	Literature Refs
		The BNFC advise that IBW should be used to calculate doses with close monitoring of the serum concentrations.		
Metronidazole	No dose adjustment necessary	Up to adult maximum dose. Lack of literature support to alter current practice.	No dose adjustment necessary	19, 26
Penicillins	No dose adjustment necessary	Up to adult maximum dose	No dose adjustment necessary	7, 18, 19
Teicoplanin	No dose adjustment necessary		No dose adjustment necessary	4, 18
Tobramycin	AdjBW (correction factor 0.4) or no dose adjustment	Conflicting guidance. Monitor levels and adjust doses accordingly. In critically ill patients, consider basing the initial dose on total body weight in order to ensure adequate serum concentrations. The BNF advise that IBW should be used to calculate doses with close monitoring of the serum concentrations.	AdjBW (correction factor 0.35) or no dose adjustment	7, 8, 18, 19, 27*, 30
Vancomycin	No dose adjustment necessary	Up to adult maximum dose. Assumes normal renal function. Monitor levels.	No dose adjustment necessary	7, 8, 31-34*, 35
Voriconazole	IBW	Risk of toxicity if used total body weight	IBW	19
<b>Anticonvulsants and sedatives</b>				
Benzodiazepines	No dose adjustment for loading, IBW for maintenance	May require a loading dose based without adjusting the dose or multiple "mini" loading doses. Monitor clinically and titrate to effect.	No dose adjustment for loading, IBW for maintenance	13, 19, 36-37*, 38-39, 40-41*
Carbamazepine	IBW (maintenance)	Serum concentration should be closely monitored and dose should be adjusted as appropriate.	IBW (maintenance)	19, 42-43
Levetiracetam	AdjBW (0.25)	Volume of distribution is similar to that of total body water	AdjBW (0.35)	19
Phenytoin/ Fosphenytoin	No dose adjustment for loading dose (maximum 2g); IBW	Monitor levels. Consider clinical condition and extent of obesity when	No dose adjustment for loading dose (maximum 2g); IBW	13, 19

Drug	Dosing scalar from literature	Comments	NPPG recommendation	Literature Refs
	or AdjBW (correction factor 0.3) for maintenance	determining loading doses.	or AdjBW (correction factor 0.35) for maintenance	
Phenobarbital	No dose adjustment necessary	Monitor levels. Titrate to effect.	No dose adjustment necessary	19
Sodium valproate/ Valproic acid	No dose adjustment necessary up to adult max	Wide therapeutic range and concentration monitoring	No dose adjustment necessary up to adult max	19
<b>Analgesics</b>				
Ibuprofen	AdjBW (correction factor 0.4) up to adult max	Very limited information available.	AdjBW (correction factor 0.35) up to adult max	19
Fentanyl	AdjBW (correction factor 0.35)	Titrate to effect.	AdjBW (correction factor 0.35)	36*
Morphine	IBW	Titrate to effect.	IBW	19, 44
Paracetamol	AdjBW (correction factor 0.4) up to adult max	Limited information available.	AdjBW (correction factor 0.35) up to adult max	5, 19
<b>Miscellaneous</b>				
Aminophylline/Th eophylline	No dose adjustment for loading dose, IBW for maintenance	BNFC advises that IBW should be used to calculate doses of aminophylline with close monitoring of the serum concentrations.	No dose adjustment for loading dose, IBW for maintenance	4, 13, 45
Corticosteroids (dexamethasone and prednisolone) – see methylprednisolone separately	No dose adjustment necessary		No dose adjustment necessary	19, 46
Enoxaparin	No dose adjustment or AdjBW (correction factor 0.4).	Monitor coagulation parameters. Titrate to effect. Consider adult dosing for 16 years and over and > 100kg, dependent on bleeding and clotting risk factors.	No dose adjustment or AdjBW (correction factor 0.35).	5, 7, 19, 47- 48*
Furosemide	IBW, titrate to effect	Risk of ototoxicity		19
Heparin	TBW or AdjBW (correction factor 0.4).	Monitor coagulation parameters. Titrate to effect.	TBW or AdjBW (correction factor 0.35).	7, 18, 49, 50*
Immunoglobulin G (IVIG)/ Human normal immunoglobulin	IBW	Where clinically appropriate round doses to nearest vial size to minimise wastage	IBW	51
Methylprednisolone	IBW	Based on adult data. Clearance may be reduced in patients who are obese.	IBW	19
Metoclopramide	IBW		IBW	19



Drug	Dosing scalar from literature	Comments	NPPG recommendation	Literature Refs
Ondansetron	No dose adjustment necessary	Up to adult maximum dose. Lack of literature support to alter current practice.	No dose adjustment necessary	19, 47
Proton pump inhibitors	No dose adjustment necessary	May also be dosed based on AdjBW (0.3).	No dose adjustment necessary	19, 52*
Ranitidine	IBW		IBW	10, 19
Spirolactone	No dose adjustment necessary up to adult max		No dose adjustment necessary up to adult max	19

AdjBW, adjusted body weight; IBW, ideal body weight

\*Paediatric data available

## Summary

- Obesity results in physiological changes that can affect the volume of distribution and the clearance of drugs. The extent of these changes is variable and depends upon both patient – specific factors and the physico-chemical properties of the drug.
- There are a lack of pharmacokinetic data on the use of commonly used drugs in obese children, therefore knowledge of which size descriptor to use in determining the optimum dose for this group of patients is limited.
- Drug-dosing guidelines are typically derived from available data in adults who are obese.
- Height measurements are needed on admission to hospital to identify obesity and to calculate doses based on the appropriate size descriptor.
- Evidence-based, locally agreed guidance is required indicating which method to use for IBW calculation and which size descriptor to use for commonly used drugs in children to reduce variability and ensure optimal effectiveness and safety.
- Although this information is provided to guide prescribers on dosing, each patient is individual and they should be clinically monitored and regularly reviewed for side effects (safety) and treatment response (efficacy).
- In an emergency setting, actual body weight (or estimated body weight) may be used to prevent delay of treatment

## Limitations

- The information in this Q&A is based on very limited evidence therefore further studies are needed before definite recommendations can be made.
- There are no data for most drugs in children who are obese.
- Absence of a drug from Table 2 does not imply that no dose adjustment is necessary in children who are obese.
- A detailed discussion of the effect of obesity on the pharmacokinetics of drugs is beyond the scope of this Q&A.
- This Q&A is intended for paediatric patients only. Information is not applicable for children under the age of 2.

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## Quality Assurance

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### Date Prepared

7<sup>th</sup> May 2021

### Checked by

Gail Woodland, Senior Information Pharmacist, Welsh Medicines Information Centre, Cardiff  
Anna Burgess, NPPG Information Officer, Welsh Medicines Information Centre, Cardiff

### Date of check

28th May 2021

### Search strategy

General Embase search: [\*WEIGHT OR \*BODY WEIGHT OR\*OBESITY OR \*ADOLESCENT OBESITY OR \*CHILDHOOD OBESITY] AND [DOSE CALCULATION OR DRUG DOSE OR PHARMACOKINETICS] Limit to: Human and (child <unspecified age>) and English Language

### Specific Embase search:

1. [pharmacokinetics.mp. or exp \*pharmacokinetics/] or [tissue distribution.mp. or \*tissue distribution/] or [\*bioavailability/] or [exp \*drug dose/] or [\*dose calculation/]
2. [\*adolescent obesity/] or [\*obesity/] or [\*childhood obesity/] or [exp \*body weight/]
3. 1 and 2
4. [\*analgesic agent/] or [\*narcotic analgesic agent/] or [nsaid.mp. or \*nonsteroid antiinflammatory agent/] or [paracetamol.mp. or paracetamol/] or [ibuprofen.mp. or ibuprofen/] or [diclofenac/ or diclofenac.mp.] or [naproxen/ or naproxen.mp.] or [opiate agonist/] or [morphine sulfate/ or morphine.mp.] or [buprenorphine/ or buprenorphine.mp.] or [fentanyl.mp. or fentanyl/] or [oxycodone.mp. or oxycodone/] or [anticonvulsant.mp. or \*anticonvulsive agent/] or [\*hypnotic sedative agent/] or [\*benzodiazepine derivative/] or [carbamazepine/ or carbamazepine.mp.] or [levetiracetam.mp. or levetiracetam/] or [phenytoin/ or phenytoin.mp.] or [phenobarbital.mp. or phenobarbital/] or [sodium valproate.mp. or valproic acid/] or [clobazam.mp. or clobazam/] or [clonazepam/ or clonazepam.mp.] or [diazepam.mp. or diazepam/] or [lorazepam.mp. or lorazepam/] or [midazolam/ or midazolam.mp.] or [antibacterial.mp. or \*antiinfective agent/] or [\*antifungal agent/]

or [\*antivirus agent/] or [\*antibiotic agent/] or [\*aminoglycoside antibiotic agent/] or [\*beta lactam antibiotic/] or [\*carbapenem/] or [\*cephalosporin/] or [\*polypeptide antibiotic agent/] or [glycopeptide.mp.] or [\*macrolide/] or [\*penicillin derivative/] or [\*quinolone derivative/] or [aciclovir.mp. or aciclovir/] or [azithromycin/ or azithromycin.mp.] or [ciprofloxacin.mp. or ciprofloxacin/] or [clindamycin/ or clindamycin.mp.] or [gentamicin.mp. or gentamicin/] or [clarithromycin.mp. or clarithromycin/] or [erythromycin/ or erythromycin.mp.] or [metronidazole/ or metronidazole.mp.] or [penicillin.mp. or penicillin derivative/] or [rifampicin.mp. or rifampicin/] or [tobramycin/ or tobramycin.mp.] or [vancomycin.mp. or vancomycin/] or [nitrofurantoin.mp. or nitrofurantoin/] or [trimethoprim/ or trimethoprim.mp.] or [anticoagulant.mp. or \*anticoagulant agent/] or [\*low molecular weight heparin/ or \*heparin/ or heparin.mp.] or [enoxaparin.mp. or enoxaparin/] or [glucocorticoid.mp. or \*glucocorticoid/] or [corticosteroid.mp. or \*corticosteroid/] or [\*antiinflammatory agent/] or [dexamethasone/ or dexamethasone.mp.] or [hydrocortisone.mp. or hydrocortisone/] or [prednisolone.mp. or prednisolone/] or [antiulcer.mp. or \*antiulcer agent/] or [\*proton pump inhibitor/] or [\*histamine H2 receptor antagonist/] or [omeprazole.mp. or omeprazole/] or [lansoprazole/ or lansoprazole.mp.] or [ranitidine/ or ranitidine.mp.] or [esomeprazole.mp. or esomeprazole/ or teicoplanin]

5. 3 and 4

Limit 5 to: Human and English Language

General Medline search: [PEDIATRIC OBESITY OR OBESITY] AND [DRUG DOSAGE CALCULATIONS OR PHARMACOKINETICS] [MeSH terms] on 24/04/13 Limit to: Human and (“all child 0-18 years”) and English Language

Specific Medline search:

- [pharmacokinetics.mp. or \*PHARMACOKINETICS/] or [tissue distribution.mp. or \*Tissue Distribution/] or [\*ABSORPTION/] or [\*Biological Availability/] or [clearance.mp. or \*METABOLIC CLEARANCE RATE/] or [\*HEPATOBIILIARY ELIMINATION/ or \*RENAL ELIMINATION/ or elimination.mp.] or [dosage.mp. or \*DRUG DOSAGE CALCULATIONS/]
- [\*OBESITY/ or \*PEDIATRIC OBESITY/] or [\*Body Weight/]
- 1 and 2
- [analgesics.mp. or \*ANALGESICS, NON-NARCOTIC/ or \*ANALGESICS/ or \*ANALGESICS, OPIOID/] or [\*Anti-Inflammatory Agents, Non-Steroidal/] or [paracetamol.mp. or Acetaminophen/] or [ibuprofen.mp. or IBUPROFEN/] or [diclofenac.mp. or DICLOFENAC/] or [naproxen.mp. or NAPROXEN/] or [morphine.mp. or MORPHINE/] or [fentanyl.mp. or FENTANYL/] or [BUPRENORPHINE/ or buprenorphine.mp.] or [oxycodone.mp. or OXYCODONE/] or [antiepileptics.mp. or Anticonvulsants/] or [“Hypnotics and Sedatives”/] or [BENZODIAZEPINES/] or [carbamazepine.mp. or CARBAMAZEPINE/] or [levetiracetam.mp.] or [phenytoin.mp. or PHENYTOIN/] or [phenobarbital.mp. or PHENOBARBITAL/] or [sodium valproate.mp. or Valproic Acid/] or [clobazam.mp.] or [clonazepam.mp. or CLONAZEPAM/] or [DIAZEPAM/ or diazepam.mp.] or [midazolam.mp. or MIDAZOLAM/] or [lorazepam.mp. or LORAZEPAM/] or [aminoglycosides.mp. or exp \*AMINOGLYCOSIDES/] or [betalactams.mp. or exp \*beta-Lactams/] or [beta-lactams.mp.] or [carbapenems.mp. or exp \*CARBAPENEMS/] or [cephalosporins.mp. or exp \*CEPHALOSPORINS/] or [glycopeptides.mp. or exp \*GLYCOPEPTIDES/] or [macrolides.mp. or exp \*MACROLIDES/] or [penicillins.mp. or exp \*PENICILLINS/] or [fluoroquinolones.mp. or exp \*FLUOROQUINOLONES/] or [aciclovir.mp. or Acyclovir/] or [azithromycin.mp. or AZITHROMYCIN/] or [ciprofloxacin.mp. or CIPROFLOXACIN/] or [clindamycin.mp. or CLINDAMYCIN/] or [gentamicin.mp. or Gentamicins/] or [clarithromycin.mp. or CLARITHROMYCIN/] or [erythromycin.mp. or ERYTHROMYCIN/] or [metronidazole.mp. or METRONIDAZOLE/] or [penicillin.mp. or Penicillins/] or [rifampicin.mp. or Rifampin/] or [tobramycin.mp. or TOBRAMYCIN/] or [vancomycin.mp. or VANCOMYCIN/] or [nitrofurantoin.mp. or NITROFURANTOIN/] or [trimethoprim.mp. or TRIMETHOPRIM/] or [anticoagulants.mp. or \*ANTICOAGULANTS/] or [heparin.mp. or \*HEPARIN, LOW-MOLECULAR-WEIGHT/ or \*HEPARIN/] or [glucocorticoids.mp. or \*GLUCOCORTICOIDS/] or [corticosteroids.mp. or \*Adrenal Cortex Hormones/] or [\*Anti-Inflammatory Agents/] or [dexamethasone.mp. or DEXAMETHASONE/] or [hydrocortisone.mp. or HYDROCORTISONE/] or [prednisolone.mp. or PREDNISOLONE/] or [\*Proton Pump Inhibitors/ or \*Anti-Ulcer Agents/] or [omeprazole.mp. or OMEPRAZOLE/] or [lansoprazole.mp. or LANSOPRAZOLE/] or [ranitidine.mp. or RANITIDINE/] or [esomeprazole.mp.]

5. 3 and 4

Limit 5 to: Human and English Language

PubMed: (drug dosing) AND childhood obesity

MICROMEDEX: "childhood obesity".

British National Formulary for Children Online:

NHS Evidence search: ["obesity" and "drug dosing"].

Google search: "dosing in obese children", "paediatric dosing guidelines obesity".

Specialist Pharmacy Service search: obese.

In-house database / resources: "obesity", ["obesity" and "child"], ["obesity" and "paediatrics"]

Summary of Product Characteristics via emc

Clinical expert: James Stewart, Anesthetist, Cardiff and Vale University Health Board. (28<sup>th</sup> June 2018)