

# Medicines and children

## After completing this tutorial, you will be able to:

- Describe some of the most common questions about medicines that you are likely to face when your patient is a child.
- Make decisions that are clinically appropriate and practical, and mindful of relevant legislation and expert guidance.
- Summarise the most common reasons for medication errors in children.

## Why this subject matters...

Questions about medicines in children can present more of a challenge than questions about adult therapy because of the general lack of evidence in this age group. As a pharmacist you will encounter a range of questions but some of the most common include establishing safe, but effective, doses and finding suitable formulations. This tutorial is not a comprehensive overview of drug use in children, more a summary of these frequent problems and suggestions on how to resolve them.



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## Licensing of medicines

The evidence base for the use of many medicines in children is often limited. Historically, many company-sponsored drug trials have not recruited children because of ethical concerns and lack of financial return. It follows that the range of medicines that are licensed for use in children is restricted and many receive unlicensed or off-label medicines.

Endorsed by



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[The Human Medicines Regulations 2012](#) enables such use, but if you are asked about the choice of drug in a paediatric patient, always consider if there is a clinically appropriate, licensed drug first. If you can't use a licensed medicine, you should take extra steps to ensure that the use of the medicine is justified in terms of evidence, necessity, and safety. A lack of published information may sometimes make it harder to check other parameters like dose and frequency, suitability of formulation, precautions, interactions, and monitoring parameters.

The Neonatal and Paediatric Pharmacists Group (NPPG) and the Royal College of Paediatrics and Child Health (RCPCH) have produced a [position statement](#) on the use of unlicensed medicines or licensed medicines for unlicensed indications in paediatric practice.

**Practical tips**

*When advising on the use of unlicensed/off-label medicines in children it is important to protect the patient, yourself, and other healthcare professionals. These steps will help you do this:*

- *Try to gather as much evidence as is available, preferably from higher quality sources (although this is often challenging). Be thorough.*
- *Always discuss with your peers (especially when you feel rushed to give a quick answer, the intervention is critical to the patient's immediate health, or when on-call).*
- *Satisfy yourself that your advice follows that of a respectable, responsible body of professional opinion or if not, that your advice can be justified from the data you have collected and the information provided by the prescriber. It is good practice to document your reasoning carefully explaining why you gave this advice (and why other options were not suitable).*
- *Make it explicit to the prescriber that the use of the medicine is unlicensed (more accurately we should say that it is outside the terms of a 'marketing authorisation'), and highlight any limitations in the advice/ information you provide.*

## Children's ages

Several classification systems have been developed to define the age ranges in childhood. A commonly used one is as follows:

Preterm neonate - born at <37 weeks gestation

Neonate – first 28 days of life (or first 4 weeks of life)

Infant – from 1 month up to 24 months of age

Child – from 2 years up to 12 years of age

Adolescent - from 12 years up to 18 years of age

For the purpose of medicine administration, children over the age of 12 years are often considered as adults. This is not always appropriate as many 12-year-olds are not adult height and weight and have not reached puberty. Unfortunately, manufacturers of medicines and regulatory authorities have yet to standardise the age groups referred to in [Summaries of Product Characteristics](#) (SmPCs).

## Dosing

This is a common question. If the medicine is licensed for the relevant age group for the right indication then good starting points are the [BNF for Children](#), [Neonatal Formulary](#) or [SmPC](#). Sometimes SmPC advice may differ from paediatric specialist resources, so always check both.

However, the majority of questions relate to unlicensed/'off-label' use and so SmPC information is less likely to be helpful. If the medicine is frequently used in children 'off-label' (e.g. sildenafil), then try established paediatric sources first. For newer medicines or those used more rarely (e.g. clopidogrel), you may have to undertake a literature search to see if any authors have published their experience.

Failing that, contact the manufacturer to see if they have any unpublished data, or speak to experts in the field such as your hospital's paediatric pharmacist, your nearest children's hospital, or national paediatric specialist hospitals such as [Great Ormond Street](#) (London) or [Alder Hey](#) (Liverpool).

If there simply is no information, then proceed with extreme caution. Every scenario will be slightly different, and you'll need to have a frank discussion with the prescriber, exploring alternative medicines or routes, or whether the drug is needed at all.

Extrapolation from adult doses is generally not recommended due to the differences in [drug handling](#) in children, but in exceptional cases may be considered.

In most cases you'll need to obtain the child's actual weight to ensure an accurate dose calculation, but the [BNF for Children](#) does include average values if required.

Remember that for most drugs the adult maximum dose should not be exceeded. For example, an older child weighing 70kg prescribed cefotaxime 50mg/kg every 6 hours for

meningitis should be given the maximum adult dose of 12 grams per day, rather than 14 grams that the calculation would predict.



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Calculating drug doses for children who are obese is a separate consideration, and you'll need to go back to first principles as you would in an obese adult. For example:

- What is the volume of distribution of the drug? Does it stay in the vascular compartment or distribute into fat?
- What is the therapeutic range of the drug? The more narrow, the more cautious you will need to be.
- What is the side effect profile of the drug? The greater the risk of serious toxicity, the more careful you'll need to be.

SPS has produced guidance on [dosing in children who are obese](#).

### ***Practical tip***

*When advising on a dose, also think about the practicalities of how the medicine will be given: can your dose be measured accurately? Consider whether the dose can be rounded up or down to make administration easier (and safer) depending upon the therapeutic range.*

*For example a 20-month-old child weighing 14.2 kg starting omeprazole at 700 micrograms/kg once daily would require a dose of 9.94 mg. Because the drug does not reliably suspend in water and omeprazole has a wide therapeutic range, it is safer to round up to the nearest whole tablet (10mg).*

## Administration to children

Questions around the practical administration of medicines to children present similar problems to those described for [doses](#) because good quality data and appropriate formulations are often lacking. Below, we look only at enteral administration as an example; for information on other routes refer to the [Information sources](#).

### Enteral administration

Some children may be able to [swallow tablets](#) but younger children or patients with a feeding tube often require a liquid formulation, and this forms the basis of many clinical problems that pharmacists deal with. If the medicine is licensed in children, and the manufacturer produces a liquid/dispersible preparation then this is often the preferred option. However there are some exceptions such as with very viscous liquids which may be difficult to administer through more narrow feeding tubes, or liquids containing unsuitable [excipients](#).

If a suitable licensed liquid is not available, then consider:

- A **different route** of administration.



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- Changing to a **different drug** that is available as a licensed liquid or dispersible tablet.
- Sourcing the medicine from an NHS or industry '**specials**' **manufacturer**, which in the absence of a licensed product, is usually the next best (safest) longer-term solution. However, do check the cost as some of these are disproportionately expensive. In addition, remember that special products can take some time to arrive from the manufacturer so you may need to investigate other options to resolve the problem in

the short term. Finally they may have a short expiry date which may have an impact upon further supplies.

- **Importing a licensed liquid** from outside the UK. The EU and US are preferred as they have similar licensing standards to the UK but note that there may not be an English patient information leaflet. Again, advise the enquirer of costs as importing medicines can be expensive and that there may be delay while the medicine is ordered. It is also important to think about the long-term implications of importing – does it mean the patient must rely solely on the hospital for future supplies?



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- Establishing whether a tablet or the contents of a capsule could be **dissolved or dispersed in water** and an appropriate volume withdrawn. This isn't without risk because parents/carers must perform some careful measurement, particularly for less soluble drugs when the concentration may vary throughout the mixture. Remember that the drug should be mixed with water immediately prior to administration and shaken well. It must never be stored in the aqueous state. Some tablets may also be **crushed** and mixed with a small amount of food. However the taste of crushed tablets can sometimes be unpalatable.
- Using a **tablet cutter** to divide tablets into halves or quarters. This will never give an exact dose and so is not suitable for drugs with a narrow therapeutic range, cytotoxic agents, or very small tablets.



- Giving an **injection orally**. Remember to establish whether any excipients are suitable for administration by mouth and/or to be given to children (see [Medication choice](#), below). Think about the practical aspects if the injection ampoule is made of glass: generally this is not a desirable option for children treated at home. If it is essential, you may need to think about the supply and disposal of sharps bins, using a filter needle to remove any shards of glass from the injection and education of the carers to ensure safe administration etc.
- **Extemporaneous dispensing** of the medicine is seen as a last resort by some specialist paediatric bodies: the variability in standards of manufacture increases the risk of errors.

### **Practical tip**

*Medicines should almost never be added to an infant's feeding bottle (a notable exception is Gaviscon Infant sachets) or added to large quantities of food (another exception here is pancreatin). This is because if the child does not consume the entire bottle or all the food, then an unknown proportion of the dose may have been taken. Occasionally it may be acceptable to use a small amount of food or juice to disguise the medicine (e.g. on a teaspoon) but take care to ensure the child receives the full dose.*

## Medication choice

Besides the normal factors you should consider when choosing a medicine for any patient, there are some extra considerations for children. We have already looked at the problem of [dosage](#), and the practical aspects of [administration of oral medicines](#), but here are two other considerations:

### Excipients

Some excipients can cause problems in both adults and children, such as sorbitol which is commonly found in liquid medicines. However there are some excipients that present special problems in children such as those in the table below. Exposure to these agents should be minimised as far as possible but occasionally a medicine containing a problem excipient may be indicated after a careful risk-benefit assessment (e.g. amiodarone containing benzyl alcohol).

Excipient	Linked with
Glucose and sucrose	Obesity, and tooth decay if taken orally
Benzyl alcohol	A gasping syndrome in neonates
Ethanol	CNS effects
Aspartame	A source of phenylalanine in patients with phenylketonuria
Polyoxyl castor oils	Severe anaphylactoid reactions
Propylene glycol	CNS effects especially in neonates and children under 4 years
Colourants (e.g. tartrazine)	Hypersensitivity and behavioural disturbances

This table is not a comprehensive list and exclusion does not indicate safety

NPPG have produced a position statement on [how to choose an oral medicine](#) for a child taking into account its excipient content.

### ‘Alarm bell’ drugs

There are some medicines that are not generally used in children, if possible, because of specific safety concerns. Examples include:

- Tetracyclines due to their deposition in growing teeth and bones
- Systemic chloramphenicol because of ‘grey baby’ syndrome in newborns
- Aspirin because of an association with Reye’s syndrome

How you proceed with clinical problems involving these medicines depends upon the exact scenario, but usually you should explore with medical colleagues whether a safer alternative would be suitable and undertake a risk-benefit assessment. There will be some special situations when it is not appropriate to suggest an alternative such as aspirin for heart disease (e.g. Kawasaki disease).



## Reducing risk

Reports of **medication errors** are more common in infants and children. In general the same types of medication errors occur as in adults such as the wrong doses or frequencies being used, doses being missed etc. However, the consequences of such errors are likely to be more severe. Factors that contribute to medication errors are numerous but the panel below highlights some of the more common pitfalls.



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### Common reasons for medication errors in children

- Incorrect use of information resources (e.g. doses described in terms of total daily dose [t.d.d] being prescribed three times a day)
- Lack of familiarity with drug (e.g. in hospitals, errors are more likely to occur in clinical areas where children are treated alongside adults such as in emergency departments or theatres)
- Use of unlicensed/off-label drugs due to lack of clinical information/experience
- Lack of licensed paediatric dose units and/or the need to use adult formulations
- Complex calculations and dilutions
- Displacement volumes
- Extemporaneous preparation of oral liquids

To try to reduce the risk associated with different concentrations of medicines being available, and patients unknowingly being switched between different strengths resulting in under- or overdosing, the NPPG and RCPCH recommend use of a [standard concentration liquid](#), where one exists. The BNF for Children includes this information in the relevant drug monographs in the 'Prescribing and dispensing information' section.



If you want to learn more about this important area of risk and have an hour to spare, [listen](#) to expert paediatric pharmacists discuss the challenges of ensuring safe use of medicines in children across the primary and secondary care interface in an SPS webinar. You can come back to this exercise later if you prefer but we strongly recommend it.

Almost all prescribing and administration of medicines to children requires a **calculation** at some point. Calculations involving infusions can be particularly complex, especially where doses are expressed in terms of mg/kg/minute, for example.

It goes without saying that correct calculations are vital. Clues that would normally point to you having made an error in an adult, such as needing multiple injection ampoules, are not always present when prescribing or administering medicines for children. In a child it is quite possible to obtain a dose that is ten times too high from a single ampoule or tablet which has been marketed for adult use. You may like to refresh your calculation skills [here](#).

### ***Practical tip***

*Do not be afraid to get someone to check your calculations. This is particularly important if you are less familiar with prescribing in children.*

## Suggested questions

If you're dealing with a clinical problem concerned with the use of a medicine in a child, then the questions you'll need to ask will depend upon the nature of the problem you're faced with, so you'll need to revisit many of the other tutorials including [administering medicines](#), [injection compatibility](#), [interactions](#), and [adverse reactions](#).

There are also some more [general questions to ask](#) when problem solving.

However, as a minimum, you'll normally ask about:

- Patient's age and weight.
- For neonates and infants whether they were born prematurely, and if so, by how long.
- Relevant medical and drug history.



## Information sources

Your choice of information source depends upon the type of clinical problem you're dealing with, so you may need to refer to other tutorials on this site. Note also that, as with other questions, the advice may differ from source to source, so always check more than one place and discuss with a senior colleague if you are unsure what to advise.

The [BNF for Children](#) should usually be at the top of your search strategy for most questions. The NPPG and RPS have produced a [quick reference guide to the BNF for Children](#) which is highly recommended.



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The [Evelina London Paediatric Formulary](#) is a valuable free online resource that often gives practical advice on common issues that affect children.

For neonates, the [Neonatal Formulary](#) should be amongst your first choices. Its [companion website](#) does not include the text of the book, but provides access to supplementary information, and archived content about medicines that have been discontinued.

Resources that have performed the searching and evaluation for you, such as **Martindale**, **AHFS Drug Information**, **Lexicomp** and **Micromedex** can sometimes be helpful for questions involving children. If you search the primary literature using **Medline** or **Embase** then learn to use the limit function to confine your search to the age group that you are interested in.

If you think you might need to recommend the use of a '**special**' medicine, then the RPS have produced guidance on the [prescribing of specials](#) which can help you through your decision-making.

Don't forget **local experts** such as your hospital's own paediatric pharmacist (who should have access to the members-only [NPPG](#) message board), or your nearest paediatric

specialist centre such as [Great Ormond Street](#) (London) or [Alder Hey Children's Hospital](#) (Liverpool).

In the south of England the [Paediatric Innovation, Education and Research](#) (PIER) network and the [Healthier Together](#) initiative have developed guidance including clinical pathways for the management of a range of childhood conditions. The West of Scotland Managed Knowledge Network have also developed a [drug formulary](#) for neonates. When using other hospitals' guidelines, remember to check whether you have any local guidelines too.

The [NICE Clinical Knowledge Summaries](#) allow you to browse by clinical speciality and there are many on child health.

For questions about intravenous medicines, the [NHS Injectable Medicines Guide](#) has a series of monographs specific to children.

Remember that adult resources can still sometimes be helpful for certain clinical problems affecting children (e.g. the [Renal Drug Database](#) for questions about prescribing in kidney disease).



The RCPCH and the NPPG have produced a range of really helpful support materials for parents, carers and patients on the [Medicines for Children](#) website that you can download or signpost for patients and carers. There are information leaflets, videos, and other materials to show what medicines are for, their side effects and how to administer them.

Be careful about conducting a general internet search on this subject. If you do, you may like to look at our brief guide to [evaluating websites about medicines](#).

## Presenting your answer

Once you've asked sufficient questions, gathered the information required and assessed it, you'll need to provide an **answer**. We can offer you some [general guidance on answering clinical problems](#).

## Next steps in learning...



If you are a pharmacist with an interest in the use of medicines in children, then you may like to join the [Neonatal and Paediatric Pharmacists Group](#) (NPPG).

The Group aims to improve the care of neonates, infants and children by advancing all aspects of the development of pharmacists and pharmacy services involved in caring for children. Their website contains a wealth of information. There is also an NPPG conference every autumn, which is an excellent way to learn, keep up-to-date, and to meet colleagues with similar interests.



As a pharmacist you need to be able to explain what an **unlicensed medicine** is, in a clear and accurate way. There is a valuable [guide for patients and carers](#) about the use of unlicensed medicines in children on the Medicines for Children website. This is an excellent basis on which to build your own explanation when talking to patients.





CPPE has a [child health gateway](#) page that links to several learning programmes including [Consulting with children and young people](#). This e-learning package focuses on the key skills and behaviours you can adopt to make sure you communicate effectively with children and young people.

There is some good advice on working with children to help them take their medicines on the [NetDoctor](#) website. The advice is aimed at the parents of children with attention deficit hyperactivity disorder, but many of the ideas suggested could apply to other children and other medicines. There are some helpful lessons here for pharmacists.



The taste of a medicine is an important factor that may influence adherence in children. Read more about the specific impact of using unpalatable antibiotics such as flucloxacillin and erythromycin in children [here](#).