Scottish Medicines Information (MI) Enquiry Answering Guidelines

These guidelines draw together current UKMi guidance and resources, have been adapted for use in NHS Scotland, and provide a guide to answering the most commonly encountered enquiries categorised by type. They can be adapted to include local resources.

The document can be used for training or as a helpful reminder for more experienced MI pharmacists. Other subjects such as drugs in psychiatry and palliative care are covered in the UKMI national enquiry answering guidelines which can be accessed via: https://www.sps.nhs.uk/articles/ukmi-enquiry-answering/?preview=true

If using this document when not working in an MI Centre, you only need to use resources which you can access – if the guideline indicates that the resource is only available in an MI Centre or with a special MI password then you would not normally be expected to use that resource.

For all enquiries you need to know:

- The enquirer
- Contact details
- Urgency of enquiry
- Purpose of enquiry e.g. patient specific, project

What sources already been used (NB. Try to assess enquirer's experience of searching more complicated resources as you may feel you need to do extra research).

Each **monograph** is divided into the following sections:

1. Background information – pointers to information that may be required.
2. Resources
    a. First-line resources, including:
        i. In-house past enquiries. Use your judgement to decide if an enquiry is too old to be relevant. Only use enquiries marked with an asterisk (*) which has been quality controlled by the MI department. For suggested keywords to search for, see the end of each monograph.
        ii. UKMi Medicines Q&As. Look for these early in your search; a relevant Q&A can save you a lot of work.
        iii. Key resources recommended for using to answer the enquiry
    b. Second-line resources which you may be able to access and could be considered if first-line resources do not provide enough information
    c. Local resources e.g. contact details of experts, relevant departments, and policies
    d. Keyword suggestions for searching Q&As and other resources
3. Answering the enquiry - useful pointers to factors that should be considered

MI resources

These guidelines should be used alongside the UKMi Essential Resources list. This lists resources for purchase and resources with free access for NHS Medicines Information Services and is accessed via: https://www.sps.nhs.uk/articles/ukmi-recommended-information-lists-and-tools/

MI Resource Guides are also available for a number of the resources mentioned in this document and should be used for advice on how to use the resource.

Risk Management

No single source is totally comprehensive or completely up-to-date in all respects. Information about Limitations of Common Information Resources used by UKMi can be accessed via: https://www.sps.nhs.uk/articles/ukmi-recommended-information-lists-and-tools/

Approved by ASMIP April 2019

Click on the hyperlinks below to access topic.

Administration of medicines

Background information

These guidelines are for situations where patients are unable to tolerate oral medicines and other options need to be considered e.g. swallowing difficulties, patients who are nil-by-mouth (NBM) etc.

- Have any other medicines or routes of administration been considered?
- Are there any restrictions on the choice of administration route? For example, patients with diarrhoea may not be able to use rectal preparations. Patients with burns, eczema, excess hair or very sensitive skin conditions may not be able to use transdermal preparations. Patients with low muscle mass will not be able to have intramuscular injections. Patients with increased bleeding risk will not be able to have subcutaneous or intramuscular injections.
- What other routes are available? For example, does the patient have a venflon inserted; do they have an enteral feeding tube in situ? Is a subcutaneous pump being used?

Nil-by-mouth (NBM) prior to surgery:

- What medicines and doses is the patient taking?
- How long is the patient likely to be NBM?
- Have any other formulations been considered?
- What medicines and doses does the patient need? Can any be suspended temporarily?

Swallowing difficulties:

- What medicines and doses is the patient taking?
- Is their swallowing expected to improve? If so when is this likely?
- Have any other methods of administration been considered or tried? E.g. transdermal patches, sublingual tablets
- Is the patient able to swallow thin liquids or are thickened fluids or sip feeds being used?

Enteral feeding tube administration:

- What type of feeding tube does the patient have e.g.nasogastric, percutaneous endoscopic gastrostomy (PEG), jejunostomy?
- What feeding regime is being used? Which feed is being given? Consider interactions between medicines and enteral feeds.
- Have any other methods of administration been considered or tried? E.g. transdermal, rectal.
- What medicines and doses is the patient taking?

Ocular administration:

- If the question is about order or administration of eye drops - what are the names and doses of the medicines?
- If the question is about number of bottles of eye drops to dispense – how long will the patient be using the eye drops for? Are the drops to go into one or both eyes? What is the dosage frequency?

Inhaled drug administration:

- What type of inhaler device can the patient manage?
- What are the doses and frequency of administration?
- What medicines are to be e.g. nebulised?
- If nebulising, what type of nebuliser is being used?

For enquiries that relate to administration of medicines to children, please refer to the 'Paediatrics' monograph.

For enquiries that relate to parenteral administration refer to Compatibility of Intravenous Drugs' and 'Compatibility of Subcutaneous Drugs' monographs.

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As www.sps.nhs.uk	Use search term 'administration' and/or filter using the drug name, to see relevant articles
British National Formulary, www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	See 'Surgery and long-term medication' and 'Administration of drugs to the eye'.
Electronic Medicines Compendium www.medicines.org.uk/emc	
Handbook of Drug Administration via Enteral Feeding Tubes. White R and Bradnam V. Online via www.knowledge.scot.nhs.uk	Always refer to the 'suggestions/recommendations' section in each monograph
The NEWT Guidelines. Smyth J. North East Wales NHS Trust. www.newtguidelines.com (subscription required)	Useful for advice about patients with swallowing difficulties and those with feeding tubes. Electronic access is preferred as this is updated between editions.
Handbook of Peri-Operative Medicine, UKCPA (Subscription required) Copy in MI.	Information and advice on the use of a range of medicines during the peri-operative period
Additional resources (tailor to local use/availability)	
Manufacturers' Medical Information departments.	May have information 'on file' regarding off label administration e.g. crushing tablets. Contact manufacturer of originator drug if possible as are more likely to have data than generic manufacturers
Rosemont Pharmaceuticals website, www.rosemontpharma.com	Rosemont are specialists in oral liquid medicines for people who have swallowing difficulties (dysphagia). The website lists the liquid formulations they make.
www.swallowingdifficulties.com	This website has been produced by Dr David Wright at the University of East Anglia. It is funded by Rosemont Pharmaceuticals. The website contains information for patients with swallowing difficulties, guidelines for healthcare professional and a list of liquid and non-oral alternatives. Some information on crushing tablets but refer to NEWT guidelines first line.

RightBreathe website, via www.rightbreathe.com, and App	Information and training materials on inhalers and spacers as well as access to BTS/SIGN NICE and GOLD respiratory guidelines
JAC/ Ascribe	Access to determine formulations that are available locally. Will also indicate cost e.g. changing to a liquid formulation can be associated with a significant cost increase.
Local Formulary Can be entered locally	

Answering the enquiry

- Have any other methods of administration been considered or tried? E.g. transdermal, rectal.
- The BNF and SPCs are a good place to start for most straightforward administration questions.
- Crushing tablets or opening capsules renders them unlicensed. Consider if there is a licensed liquid or dispersible formulation available.
- Consider any potential interactions between medicines being administered via a feeding tube and feeds.
- Is there an alternative drug that can be used or administered more easily?

Keywords: drug name, TUBE FEEDING, DRUG ADMINISTRATION, SURGERY.

Adverse Drug Reactions

Background information

Retrospective enquiries (i.e. suspected ADR has already occurred)

- Establish patient details, including age, sex etc.
- What is the indication for the drug and any relevant medical history (e.g. renal function)?
- What is the current and previous medical history if relevant, including risk factors for the ADR?
- Is there a history of adverse drug reactions or allergies?
- List current drug therapy, including OTC, alternative therapies and drugs of abuse whenever possible, plus any medication taken within the last 3 months.
- What is the timing of the reaction in relation to start or dose increase of the suspected drug?
- Obtain a full description of the signs and symptoms of the reaction; clarify reactions such as 'rash', 'abnormal liver function tests (LFTs)', 'aching all over'
- Has the suspected drug been stopped?
- How has the patient been managed so far?
- Has re-challenge, deliberate or inadvertent, been undertaken?
- Did the suspected ADR resolve when the suspect drug was stopped?
- What are the results of any relevant biochemical tests e.g. renal function tests, liver function tests, full blood count, biopsies, relevant ultrasound or screening tests?
- Does the enquirer want to know which drug, A or B, is more likely to have caused side effect X?
- Is the enquirer involved in a legal case? Always be aware that this may be the scenario (often enquirers do not mention this).
- Has the manufacturer been informed or a Yellow Card completed?

Prospective enquiries

- Does the enquirer think that the patient may be at particular risk of an ADR e.g. a patient with a history of an ADR to the same class of drugs? If so, what were the signs and symptoms of the suspected previous reaction? N.B. caution may be required when using other drugs with similar ADR profiles.
- Does the enquirer just want general information e.g. for informing a patient of possible side effects?
- Does the enquirer want to know more information about a specific side effect e.g. because the patient has asked?
- Does the enquirer want to assess the risk/benefit comparison between two drugs e.g. which is safer, drug A or drug B (often in relation to a specific side-effect)?
- Some enquiries will involve a mixture of the two e.g. if a patient has a reaction which is subsequently thought to be an ADR then it could be anticipated that the enquirer will want suggestions for alternatives.

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	Use search terms 'adverse effect', 'side effect' and/or filter using the drug name, to see relevant articles
Electronic Medicines Compendium www.medicines.org.uk/emc/	Don't just look at undesirable effects, check precautions and contraindications for relevant information as well.
BNF www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	Don't just look at side-effects review the whole monograph, can be useful information in sections such as contraindications, cautions, monitoring requirements, allergy and cross-sensitivity.
Martindale www.knowledge.scot.nhs.uk or www.medicinescomplete.com	Often individual drug monographs link through to other monographs regarding a class effect – this should be followed as appropriate
Drugdex via www.micromedexsolutions.com or www.knowledge.scot.nhs.uk	Always look at In-Depth answers.
Meyler's Side Effects of Drugs, Dukes and Aronson. Available on The Knowledge Network via ClinicalKey www.knowledge.scot.nhs.uk Click on Meyler's Side Effects of Drugs (16th edition) in Medicines Information Resources drop-down	Presented as individual drug monographs in alphabetical order with general class monographs complemented by specific drug monographs. Also contains information on non-drugs e.g. toxins, foods.
Additional resources (tailor to local use/availability)	
Drug Safety Update via MHRA website www.mhra.gov.uk	

Drug Analysis Profiles via Yellow Card Website https://yellowcard.mhra.gov.uk/iDAP/	Complete listings of suspected ADRs reported to the MHRA through the Yellow Card Scheme by healthcare professionals and patients provided in interactive Drug Analysis Prints (iDAPs). See 'Essential Context' information at the end of the monograph to ensure data are interpreted correctly. This should also be included when sending any iDAP data to your enquirer.
EMA – European database of suspected adverse drug reaction reports http://www.adrreports.eu/	Provides public access to reports submitted electronically to EudraVigilance. EudraVigilance collects reports of suspected ADRs from European medicines regulatory authorities and pharmaceutical companies. Currently it only includes medicines licensed through the EU centralised procedure. Check 'Substances' rather than 'Products' to search by generic name
Manufacturers' Medical Information departments.	Contact manufacturer of originator drug if possible as are more likely to have data than generic manufacturers Companies are legally obliged to follow up telephone enquiries about ADRs (by sending an adverse event reporting form).
Adverse Drug Reactions, Lee A MI Centres only	Describes ADRs by organ class, lists commonly implicated drugs and gives tips on management of suspected ADRs. N.B. most recent edition is 2006.
Bibliographic databases e.g. Medline, Embase accessed via The Knowledge Network www.knowledge.scot.nhs.uk	Suggested terms: the reaction with the subheading 'chemically induced' (Medline) or 'side effect' (Embase) and/or the drug name with the subheading 'adverse effects' (Medline) or 'adverse drug reaction' (Embase).
CredibleMeds www.crediblemeds.org Free registration required for full access	Contains information on medicines that can be categorised by their potential to cause QT prolongation and/or torsades de pointes. An American resource so **note** differences between US and UK product names.
G6PD website http://www.g6pd.org/	This site should not be used in isolation for G6PD queries; no single resource is comprehensive. This site contains lists of safe and unsafe drugs and also attempts to quantify risk (low vs. high)
Natural Medicines naturalmedicines.therapeuticresearch.com/ MI Centres only	Includes adverse effects of herbal medicines.
Toxbase accessed via www.toxbase.org (password required)	May provide relevant information particularly in higher doses or if potential interactions which could elevate doses. For enquiries involving known overdose refer to Poisons Information Service.

Answering the enquiry

- For retrospective enquiries use the information you have obtained from the 'background information' questions and try to assess causality using the following criteria:
    - Nature of the reaction - certain disorders are commonly drug-induced e.g. rashes, constipation, gastrointestinal haemorrhage.
    - Previous SPC or literature reports describing the reaction.
    - The timing of the reaction can vary but most ADRs appear shortly after a drug is started or the dose is increased.
    - Outcome on drug withdrawal, if resolution occurs this is a positive dechallenge.
    - Rechallenge outcome, although positive rechallenge strongly suggests drug cause deliberate rechallenge is rarely justifiable and should not be suggested.
    - Risk factors, some patients have an increased susceptibility to ADRs (e.g. children, elderly, multiple disease states, atopic patients).
    - Laboratory and diagnostic tests should indicate if there is a non-drug cause, ADRs are often a diagnosis of exclusion.
- When interpreting ADR data for the enquirer, be clear about the limitations of the Yellow Card data. Warn that although there may be X number of reports we do not know the Y number of people who have received the drug, therefore you cannot extrapolate to predict ADR incidence. Also advise that ADR reports are based upon suspicion and other factors may have been implicated as well as the suspected drug so, especially if small numbers of reports are involved, causation may not be confirmed
- If there is a strong suspicion that an ADR has been identified complete a Yellow Card or offer to help your enquirer complete a card. Report via MiDatabankif you have access or via the MHRA's online Yellow Card http://yellowcard.mhra.gov.uk/or by using the Yellow Card App

Keywords: The drug name, disease term for the adverse effect.

Drugs in breastfeeding

Background information

Patient and infant-related:

Mother – is she breastfeeding?

- What is the condition the medicine is for? Does it need treating now or can treatment be delayed until the child is weaned?

Infant – How old is the infant, and was he/she premature or full-term?

- What is the infant's weight?
- Is the infant fed exclusively with breast milk?

  Babies are weaned onto solid foods at around six months of age. Before this age, it is recommended that children are exclusively breast fed. In practice, many children are fed by a combination of breast milk feeds and infant formula milk feeds until the age of six months when solid foods are introduced. Some infants continue to be given one or more breast milk feeds daily until they are twelve months of age or older.

  Exposure to drugs in breast milk is greatest for babies who are exclusively breastfed.
- Is the infant well? Is there anything to suggest that the infant may be at increased risk of drug harm, e.g. impaired kidney or liver function? Has the infant been prescribed any medicines?

Medicine(s)

- **Medicine** – the proposed medicine(s) and any other medicines she is taking (generic or brand name), dose, frequency, route and intended duration of treatment.
- **Indication** – The risk vs. benefit decision may differ depending on the indications e.g. an antiepileptic medicine for control of epilepsy compared to its use for neuropathic pain.
- Is the mother already taking the medicine in question?
- Is this drug therapy necessary? Have other therapies/medicines been considered or tried?
- Has the mother taken the drug during pregnancy? If so, identify whether it is appropriate to switch to an alternative if necessary. Note exposure during pregnancy does not confer safety during breastfeeding.

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
UKMi Drugs in Lactation Advisory Service (UKDILAS) www.sps.nhs.uk	UKDILAS produces concise monographs on individual drugs and also advice on drug classes. Each monograph has the date of review at the bottom. Suitable alternatives are listed where appropriate. UKDILAS has produced a guide to using the SPS website to find their information: www.sps.nhs.uk/articles/ukdilas/
LactMed https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm	Provides comprehensive monographs on individual drugs. If a drug affects the actual lactation process itself, this is also included. Note this is an American site, so care should be taken.

Source	Notes
Drugs during Pregnancy and Lactation. Schaefer et al. 3rd edition. Available via Medicines Information drop-down on The Knowledge Network www.knowledge.scot.nhs.uk	Chapter 3 includes general information about medicines use during breastfeeding. Chapter 4 provides information for individual agents and drug classes. Use the index to find the drug you want. Each monograph has a boxed 'recommendation' at the end. Can be useful to suggest safer alternatives within a drug class.
Drugs in Pregnancy and Lactation. Briggs GG et al. Available via Medicines Information drop-down via www.knowledge.scot.nhs.uk	Standard US reference text on the safety of medicines in pregnancy and breastfeeding. Each drug monograph has a section on breastfeeding at the end. Individual drug monographs are in alphabetical order. However, note that breastfeeding is not the main focus. Always ensure most update to edition is accessed, older editions are also available on The Knowledge Network
Electronic Medicines Compendium www.medicines.org.uk/emc	NB: Statements in SPCs are sometimes more cautious than current evidence requires and should not be used as the only source of information.
Medications and Mothers' Milk. Hale, T. 2019. Paper version available in MI Centres	A US reference text on the safety of medicines during breastfeeding. The preface includes key points about breastfeeding and medicines, and highlights the benefits of breastfeeding. It is particularly useful for breastfeeding related pharmacokinetics Note that brand names may differ in the UK.
Additional resources	
Maudsley Prescribing Guidelines. Taylor D et al. 13th Edition Paper copy in MI Centres	Chapter 7 contains a section on the choice of psychotropic medicines in lactation.
Psychotropic Drug Directory. Bazire S. 2018 Paper copy in MI Centres	Chapter 3 contains a section on the choice of psychotropic medicines in lactation.
The Breastfeeding Network www.breastfeedingnetwork.org.uk/	The Breastfeeding Network is a registered charity providing independent advice and support to breastfeeding women and others. They produce 'drug factsheets' on medicines in breast milk but may not be reliable and they are **not recommended for use by health professionals**. However, as patients may read them, it can be helpful to know what they say. To access them, click on 'Breastfeeding information' then 'Drugs in breast milk – is it safe?'
BNF for Children www.medicinescomplete.com	If information is lacking from other sources, BNFC can be consulted to see if the drug can be used in neonates or infants. The dose advised can be compared to the theoretical dose the infant will receive via the breast milk. It also gives an indication of paediatric experience. Information on drug safety in breastfeeding is included in drug monographs. However, this is too brief to be of real value (note—the same information is held in BNF monographs)

Source	Notes
Clinical Knowledge Summaries cks.nice.org.uk	Guidelines advise on the management of conditions in breastfeeding mothers and there is also a specific guideline on breastfeeding problems.
UKMi Drugs in Lactation Advisory Service (UKDILAS) Telephone service	UKMi Trent (0116 258 6491) and West Midlands (telephone 0121 424 7298) jointly provide support directly to healthcare professionals for complex enquiries or advice in high risk situations such as prematurity, low birth weight and multiple medications. Ensure you have adequate background information, and have checked sources available to you before contacting the specialist service.
Bibliographic databases e.g. Medline, Embase (via OVID) via www.knowledge.scot.nhs.uk	Suggested terms: BREAST FEEDING, BREAST MILK, LACTATION, MILK-HUMAN (NB: Nursing is a US term for breastfeeding).

Answering the enquiry

The following principles should be followed when prescribing for breastfeeding mothers:

- It is seldom required that a breastfeeding mother stop breastfeeding in order to take a medication.
- The benefits of breastfeeding must be recognised; a recommendation to stop breastfeeding must not be made lightly. If the mother must withhold breastfeeding, think of the practicalities for both her and the infant. The mother will need to express the milk and discard it; the infant may need to take formula milk. In households where the infant is exclusively breastfed, there may not be bottles/teats readily available.
- The benefit and risk to both mother and infant must be considered.
- Neonates and premature infants are at greater risk from exposure to drugs via breast milk, because of immature excretory functions and the consequent risk of drug accumulation.
- Infants exposed to drugs via breast milk should be monitored for unusual signs or symptoms.
- Avoid unnecessary drug use and limit use of over-the-counter (OTC) products.
- Avoid use of drugs known to cause serious toxicity in adults or children.
- Drugs licensed for use in infants do not generally pose a hazard to full-term, healthy infants.
- Choose a regimen and route of administration which presents the minimum amount of drug to the infant.
- Be more cautious about recommending long-acting preparations, since these are more likely to cause adverse effects.
- Multiple drug regimens may pose an increased risk especially when adverse effects such as drowsiness are additive.
- Avoid new drugs if a therapeutically equivalent alternative with more safety data is available.

Keywords

BREAST FEEDING, LACTATION, MILK-HUMAN, MILK, PREMATURITY INFANT PREMATURE, drug name, and disease name (if appropriate).

Compatibility of intravenous drugs

Background information

- How many intravenous lines are available, what type of lines are they (central or peripheral), how many lumens does each line have? Can other lines be inserted if necessary?
- What is the patient receiving through the lines at the moment? Ask about blood products, TPN, etc. as well as drugs. For current drugs:
  - Check dose and administration schedule - are they being given continuously, or by short infusion or as a bolus? If continuous infusion, can they be given intermittently?
  - What diluents and concentrations are being used?
  - Are filters being used? If yes, where are they placed and what size are they, e.g. 0.2 micron?
  - Can any drugs be discontinued?
- Which drugs are to be added and why? Which brand(s) will you be using?
- How will the drugs be mixed, e.g. in the same bag, the same intravenous line (Y site), same syringe or the same venflon?
- Is there a choice of drugs that could be used?
- Are there any limitations on choice, e.g. fluid and electrolyte restrictions, renal or hepatic dysfunction?
- Can the patient tolerate administration by another route, e.g. nasogastric tube, oral, rectal, intramuscular, subcutaneous, topical?

N.B. If the enquiry concerns the compatibility of drugs in a syringe driver for subcutaneous administration please refer to the 'Compatibility of subcutaneous drugs' monograph.

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
BNF www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	
Electronic Medicines Compendium www.medicines.org.uk/emc	
The Injectable Medicines Guide 'Medusa' www.injguide.nhs.uk (subscription required)	Pharmacy password required for compatibility information
Handbook on Injectable Drugs AHSP, paper/ online (subscription only) MI centres will have a copy/	This is a US resource. Consider concentrations and diluents used

Source	Notes
online access.	
IV Compatibility database via Micromedex in The Knowledge Network www.knowledge.scot.nhs.uk Choose IV Compatibility tab	This is a US resource, but it does include UK drug monographs. Be aware that as well as compatibility data, further information about giving set compatibility etc is available via hyperlink. Contains different/additional data to the Handbook on Injectable Drugs. Consider concentrations and diluents used
Additional resources	
Pharmaceutical manufacturer.	Contact manufacturer of originator drug if possible as are more likely to have data than generic manufacturers They may have unpublished data, although many generics manufacturers have little or no information.
Bibliographic databases e.g. Medline, Embase. via www.knowledge.scot.nhs.uk	Suggested terms: ADMINISTRATION-INTRAVENOUS and DRUG INCOMPATIBILITIES
Stabilis www.stabilis.org/	Compatibility and stability data to supplement other resources. Compiled by hospital pharmacists in France. Free access. Click arrow next to French flag to view in English language.
Add local IV monographs (if differs from Medusa)	

Answering the enquiry

When checking compatibilities, consider alternative ways of solving the problem, e.g. by using other routes of drug administration. You must consider problems associated with other routes and whether they would be appropriate for that particular patient.

When answering this type of enquiry consider:

- Are all drugs essential?
- What are the possible mechanisms of interactions/incompatibility – chemistry i.e. pH, adsorption?
- Is it possible to administer drugs by an alternative route?
- Could another line be inserted?
- Is there more than one option available, i.e. could a different drug be used to avoid a compatibility problem?
- Could the timing of administration be altered to avoid the need for mixing?

Keywords: drug names, ADMINISTRATION-INTRAVENOUS, DRUG INCOMPATIBILITIES

Compatibility of subcutaneous drugs

Background information

- Which other medicines is the patient receiving, what are they for and by what routes are they being given?
- Which drugs need to be mixed, what are they for and what is the dose?
- What is the diluent to be used and the concentration required or the preferred total volume?
- Over what time period is the infusion to be given?
- What other routes of administration are available, e.g. intravenous lines?
- Establish how the patient is fed – an enteral feed tube offers a potential alternative route.

N.B. If the enquiry concerns the compatibility of drugs for intravenous administration please refer to the 'Compatibility of intravenous drugs' monograph.

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
BNF www.medicinescomplete.com	Section on prescribing in palliative care includes information about drug administration via syringe drivers.
Palliative Care Formulary (PCF). Twycross et al. Available via www.knowledge.scot.nhs.uk	Website for healthcare professionals working in palliative care. Includes a syringe driver compatibility database. You will need to register separately with www.palliativedrugs.com to access Syringe Driver Survey Database.
Scottish Palliative Care Guidelines www.palliativecareguidelines.scot.nhs.uk	A subcutaneous medication section has compatibility charts www.palliativecareguidelines.scot.nhs.uk/guidelines/end-of-life-care/syringe-pumps.aspx
Palliative Care Matters website www.pallcare.info (may be updated)	Website for healthcare professionals working in palliative care. Includes a syringe driver compatibility database www.pallcare.info/mod.php?mod=sdrivers&menu=14 http://bo Use in preference to PANG for syringe driver compatibilities. ok.pallcare.info/index.php?op=plugin&src=sdrivers Consider concentrations and diluents used
Palliative Care Adult Network Guidelines (PANG) http://book.pallcare.info/(as above)	Website aiming to offer up-to-date, evidence based information and guidance on professional aspects of palliative care. Developed by a collaboration of UK cancer networks, Royal College of GPs and the Welsh Palliative Care Implementation Board. Includes: • an interactive opioid dose calculatorbook.pallcare.info/index.php?op=plugin&src=opiconv • syringe driver compatibility database book.pallcare.info/index.php?op=plugin&src=sdrivers

Source	Notes
	Should be used in preference to the PCF book, but not electronic version of PCF (www.palliativedrugs.com).
The Syringe Driver: Continuous Subcutaneous Infusions in Palliative Care. Dickman and Schneider. Available in MI Centres	Contains comprehensive information about two or more admixtures of commonly used combinations. Consider concentrations and diluents used
Additional resources	
Electronic Medicines Compendium www.medicines.org.uk	However, very few injectable drugs are licensed for subcutaneous injection or infusion.
A Guide to Symptom Relief in Palliative Care. Regnard and Dean. Paper copy may be available in MI Centre	The chapter on 'Problems with syringe pump infusions' (within Drug Information) contains useful trouble shooting advice.
Oxford Handbook of Palliative Care. Watson M et al. E-book available via The Knowledge Network www.knowledge.scot.nhs.uk	Chapter 4 contains general information on the principles of drug use in palliative care, including syringe drivers.
Bibliographic databases e.g. Medline, Embase. via www.knowledge.scot.nhs.uk	Suggested terms: SUBCUTANEOUS-DRUG-ADMINISTRATION, INJECTIONS-SUBCUTANEOUS, ADMINISTRATION-SUBCUTANEOUS

Answering the enquiry

- GPs and hospital doctors are able to refer patients to a Macmillan nurse or an alternative specialist. Find out if this has been done. For enquiries about managing a specific patient (other than straightforward medicines information queries), advise the enquirer to contact this nurse.
- Mixing two or more licensed drugs for administration via a syringe driver, where one is not a vehicle for administering the other, falls within the definition of manufacture and results in a new, unlicensed product. The person undertaking this preparation, unless an exemption applies (doctors, dentists, nurse and pharmacist independent prescribers, and supplementary prescribers), must hold a manufacturer's licence. The exemption allows these prescribers to mix medicines themselves or direct others to mix. Directions must be in writing.
- Some drugs are too irritant to be given subcutaneously, e.g. prochlorperazine, diazepam and chlorpromazine.
- Phenobarbital is incompatible with most drugs given by continuous subcutaneous infusion and it is generally advisable to give via a separate syringe driver. If dexamethasone is to be mixed with other drugs, use as much diluent as possible before adding dexamethasone.
- Using more than one syringe driver may be an option if there are compatibility problems and alternative routes are unsuitable.
- Using a larger total volume will improve stability of many drug combinations and may be an option for some patients.

- Confirm maximum volume of the syringe driver. There may be limitations on concentrations that mean more than one daily syringe driver change is needed. Check whether this is going to be practical.

Keywords: Drug names, ADMINISTRATION-SUBCUTANEOUS, DRUG INCOMPATIBILITIES

Drugs in hepatic impairment

Background information

- Clinical condition of the patient, age, sex, presumed diagnosis and previous medical history if relevant?
- Type of liver disease and cause (e.g. acute, chronic, cirrhosis, etc).
- Results of immunological/virological screens (e.g. hepatitis) and other diagnostic tests (e.g. biopsies).
- Symptoms (e.g. ascites, jaundice, varices, encephalopathy), extent and severity.
- Liver function tests (bilirubin, alkaline phosphatase, ALT, AST, GGT) – most recent ones if possible. Are they stable or changing?
- What are the most recent albumin levels?
- What is the most recent INR/prothrombin time for clotting?
- What is the current medication including doses and any changes/short courses in last 2-3 months (e.g. antibiotics)?
- Ask about renal function. Multi-organ failure often co-exists but enquirers often forget to mention this.
- If requesting advice on dosage or suitability of a drug in hepatic dysfunction, what is the indication for the drug and have alternatives been considered? What agent would normally be used if the patient did not have liver dysfunction?
- Is it suspected that the hepatic impairment is drug induced? Include questions about duration and dose of suspected drug, timescales, type of liver injury, how patient has been managed, what other drugs are being taken or were taken recently, and could there be another cause?

If the hepatic impairment is suspected to be drug-related refer to the monograph 'Adverse drug reactions'.

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	Try keywords such as LIVER FUNCTION-IMPAIRED or LIVER DISEASES
Relevant Medicines Q&As via www.sps.nhs.uk	**The following Medicines Q&As give further guidance on approach to answering liver-related enquiries:** • What pharmacokinetic and pharmacodynamic factors need to be considered when prescribing drugs for patients with liver disease? • Why is the adverse effect profile of a drug relevant when prescribing for patients with liver disease? • What is the Child-Pugh score?
BNF & BNF-C www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	

Source	Notes
Electronic Medicines Compendium www.medicines.org.uk/emc	The 'pharmacokinetics' and 'undesirable effects' sections may also be useful.
Martindale via www.medicinescomplete.com or www.knowledge.scot.nhs.uk	Often individual drug monographs link through to other monographs regarding a class effect – this should be followed as appropriate
Drugdex via www.micromedexsolutions.com or www.knowledge.scot.nhs.uk	In-Depth Answers provide information on dosage adjustment in hepatic insufficiency.
LiverTox https://livertox.nih.gov/	This joint venture between the Liver Disease Research Branch of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Library of Medicine's (NLM) National Institutes of Health provides up-to-date information on diagnosis, cause, frequency patterns and management of liver injury attributable to prescription and non-prescription medications, herbal and dietary supplements.
Pharmaceutical manufacturers	Contact manufacturer of originator drug if possible as are more likely to have data than generic manufacturers May have information about any reduction of doses which may be necessary in hepatic impairment. May have relevant pharmacokinetic details if working from first principles.
Medicines Learning Portal liver section	Useful information on drugs in liver
Bibliographic databases e.g. Medline, Embase.via www.knowledge.scot.nhs.uk	If no information can be found in standard resources on use of a specific drug in a specific type of liver disease, consider conducting a literature search for relevant papers. This should be done before using pharmacokinetic/pharmacodynamic data to predict drug handling from first principles. Suggested terms: LIVER DISEASES, BILIARY TRACT DISEASES, LIVER-TOXICITY, HEPATITIS-TOXIC, CHOLESTASIS, HEPATITIS, LIVER FUNCTION-IMPAIRED, (NB: take care if using "LIVER DISEASES" - may not include some cholestatic conditions)
Meyler's Side Effects of Drugs, Dukes and Aronson. Available on The Knowledge Network via ClinicalKey www.knowledge.scot.nhs.uk Click on Meyler's Side Effects of Drugs (16th edition) in Medicines Information Resources drop-down	

Additional resources (tailor to local use/ availability)	
Therapeutic Drugs. Dollery Paper copy in some MI Centres	Although this resource is very old (2nd edition 1999) monographs have information about drug use in high-risk groups and are useful for basic pharmacokinetic data for older drugs.
Applied Therapeutics: The Clinical Use of Drugs. Koda-Kimble. Paper copy in some MI Centres	There is a section listing drugs reported to cause clinically significant hepatotoxicity and the likely mechanism.
Goodman & Gilman's Pharmacological Basis of Therapeutics. Paper copy in some MI Centres	Has information about drug metabolism and hepatic effects
Drugs and the Liver. A guide to drug handling in liver dysfunction. North-Lewis P. Paper copy in some MI Centre	Covers background information on liver function, principles of drug use in liver disease and includes a section of worked examples of commonly asked questions. Includes an'*aide memoire'* section for collecting background data. N.B. Published in 2008

Answering the enquiry

- The following factors should be considered when deciding an optimum drug treatment for a patient with liver disease:
    - Type, extent and severity of liver disease
    - Pharmacokinetics and pharmacodynamics of the drug
    - Adverse reactions of the drug
    - Patient specific factors e.g. age, comorbidities, severity of the condition being treated, concomitant medications
- In patients with hepatic dysfunction, avoid hepatotoxic drugs where possible. Patients with existing hepatic disease are not more prone to hepatotoxicity (unless it is dose-related), but they have diminished reserve hepatic function and may suffer disproportionately if hepatotoxicity does occur. Drug hepatotoxicity on top of existing liver disease will also confuse the diagnostic picture. Even clinically insignificant and/or transient changes in LFTs may confuse the diagnostic picture.
- For drugs metabolised by the liver, be alert to signs of drug side effects, know what they are and monitor for them. Monitor drug levels where appropriate.
- Non-systemic treatments should be chosen where possible. Renally excreted drugs are also preferred as long as renal function is normal. Monitor for any changes in renal function.
- Drugs that increase the risk of bleeding should be avoided or used with extreme caution, depending on the severity of liver disease.
- Drugs that are highly dependent on the liver for deactivation or clearance are likely to need dose reduction in moderate to severe liver disease.
- Avoid sedating drugs in patients at risk of developing encephalopathy. Many of these drugs have long half-lives and are metabolised by the liver so their duration and intensity of action may be prolonged. The brain also becomes more sensitive to sedating effects in liver disease. A sedative drug may precipitate or mask encephalopathy.
- The doses of highly protein-bound drugs may need reducing in patients with low albumin levels due to chronic liver disease.
- Drug prescribing should be kept to a minimum – use the smallest effective doses at the greatest interval, and titrate according to clinical response.

Keywords: Include drug names and LIVER FUNCTION-IMPAIRED or LIVER DISEASES

Interactions

Background information

- Establish patient details, including age, sex etc.
- Consider whether the interaction is drug-drug, drug-food, drug-test or drug-disease.
- Which drugs are being taken by the patient already? How long have they been taken and what are the indications?
- Has the enquirer read about the interaction or has it been flagged by a prescribing or dispensing system? If so where/which system?
- If the patient is already taking both drugs, have any problems been identified or investigated? Ask for details of any suspected interaction (e.g. symptoms, lack of effect, timescales of starting drugs, any action already taken).
- If there is an interaction, is there any reason why alternatives can't be used?
- What is the patient's liver and renal function?
- Is the patient taking any other medicines, including complementary, OTC and illicit medicines?
- If any ongoing or future monitoring is required, who would do this?

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
BNF via www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	
Electronic Medicines Compendium www.medicines.org.uk/emc	Check contraindications and precautions and special warnings as well. Pharmacokinetics section 5.2 may also advise on biotransformation which can affect drug interactions.
Stockley's Drug Interactions via www.medicinescomplete.com	Check full monographs and not just summaries.
Stockley's Interactions Checker (Stockley's Interactions Alerts) via www.medicinescomplete.com	Use in conjunction with Stockley's Drug Interactions
Medscape Drug Interactions Checker http://reference.medscape.com/drug-interactionchecker Free registration required	Some of the interactions can be very theoretical but useful for cross checking with Stockley

Source	Notes
Credible Meds (QT prolongation) www.crediblemeds.org/ (previously www.azcert.org) Free registration required	Contains information on medicines that can be categorised by their potential to cause QT prolongation and/or torsades de pointes. An American resource so **note** differences between US and UK product names.
Drugdex via www.micromedexsolutions.com or www.knowledge.scot.nhs.uk	
Antiviral drugs: www.hiv-druginteractions.org/	University of Liverpool resource freely available to healthcare workers, patients and researchers offering comprehensive evidence-based tables of drug interactions between the HIV drugs or key interactions between Protease Inhibitors, NNRTIs, NRTIs, or Entry/Integrase Inhibitors and other drugs that may be prescribed to the HIV+ patient.
Hepatitis antiviral medicines www.hep-druginteractions.org/	University of Liverpool resource offering a comprehensive drug-drug interaction resource for antiviral drugs used for hepatitis and other medicines which is freely available to healthcare workers, patients and researchers.
Cancer drug interactions via: http://www.cancer-druinteractions.org/checkerhttp://www.cancer-druginteractions.org.	University of Liverpool resource offering a comprehensive drug-drug interaction resource for anticancer drugs and other medicines which is freely available to healthcare workers, patients and researchers.
Natural Medicines Comprehensive Database naturalmedicines.therapeuticresearch.com/ MI Centres only	For complementary drug-drug, drug-food, and drug-disease interactions.
Additional resources	
Meyler's Side Effects of Drugs, Dukes and Aronson. Available on The Knowledge Network via ClinicalKey www.knowledge.scot.nhs.uk Click on Meyler's Side Effects of Drugs (16th edition) in Medicines Information Resources drop-down	Covers some drug-drug interactions

Source	Notes
Bibliographic databases e.g. Medline, Embase via www.knowledge.scot.nhs.uk	Suggested terms: DRUG INTERACTION, FOOD-DRUG-INTERACTIONS, HERB-DRUG-INTERACTIONS
Transformer Website http://bioinformatics.charite.de/transformer/	To be used only as a supplementary resource. Provides theoretical data on Cytochrome P450 and Transporters for individual drugs and combinations – Although this is referenced, it provides little or no information on significance of each pathway to a particular drug
Cytochrome p450 website: http://medicine.iupui.edu/flockhart/	A table containing drugs listed in columns under specific cytochrome P450 isoforms. Drugs are included if there is published evidence that they are metabolised, at least in part, via the specific CYP isoform. The clinical table highlights clinically relevant drugs. These tables have not been updated for several years so do not include new drugs or more up-to-date information. Use with caution and cross-check with SPCs
Stockley's Herbal Medicines Interactions Paper edition available in some MI centres.	

Answering the enquiry

- If the enquiry is prospective, reference to BNF, eMC and Stockley may be all that is required. Note that that SPC warnings are often extrapolated from other drugs in the same class and an assessment should be made as to how relevant this is to the individual drug.
- If there is likely to be little experience with the two drugs used together e.g. new drug or rarely used, review interactions with drugs from the same class and consider the pharmacology and pharmacokinetics.
- Consider whether an interaction is likely, on what basis and the limitations of information (e.g. if new drug/not widely used/ previous experience with combination unlikely).
- Can the two drugs be given together with appropriate monitoring? If so what should be monitored and who should monitor?
- Could a safer alternative be used?
- Could a different route of administration overcome the problem?
- If an interaction is suspected and either the outcome is serious or it is not already well documented e.g. for a new drug, then this should be reported via the Yellow Card Scheme. See www.yccscotland.scot.nhs.uk

Keywords: DRUG INTERACTIONS and drug names.

Paediatrics

Background information

These points are in addition to those required for enquiries related to other categories e.g. ADR, compatibility, etc.

- Establish patient details, including age and sex.
- What is the weight (Kg) of the child? Confirm any discrepancy between age and weight.
- If weight is not known, try to find out whether the child is considered under or overweight for their age. For some drugs (e.g. cytotoxic agents) a more accurate dose is obtained by calculating body surface area, therefore you will need height as well as weight measurements.
- If the patient is a young infant (less than 3 months old), were they premature? If so, what is their gestational age?
- What is the intended route of administration? If the route is oral, is the child able to swallow tablets?
- Are there any problems that may affect drug or formulation choice e.g. renal failure, cystic fibrosis, fluid requirements?

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
BNF for Children www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	
Electronic Medicines Compendium www.medicines.org.uk/emc	
Medicines for Children www.medicinesforchildren.org.uk/	Extensive range of patient information leaflets about medicines for children to view or print. Also leaflets and videos about how to give medicines to children and information on missed doses. Written in plain English and contains practical advice. Produced by the Royal College of Paediatrics and Child Health (RCPCH), Neonatal and Paediatric Pharmacists Group (NPPG), and national child health charity, WellChild.
Paediatric Formulary http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80 App also available http://www.ubqo.com/paediatricformulary	Previously known as Guy's St Thomas' and Lewisham hospitals paediatric Paediatric Formulary.

Source	Notes
Martindale via www.medicinescomplete.com or www.knowledge.scot.nhs.uk *Athens login*	
Drugdex www.micromedexsolutions.com	Look at In-Depth Answers
Neonatal Formulary: Drug Use in Pregnancy & the First Year of Life. Northern Neonatal Network. Book available in MI	A companion website to the book at www.neonatalformulary.com provides free updates and additional information for readers (the text of the book itself is not available online).
ADD local guidelines	
Additional resource	
Pharmaceutical manufacturer	Contact manufacturer of originator drug if possible as are more likely to have data than generic manufacturers May have unpublished data.
Paediatric Care online. RCPCH Partnership Group. www.pcouk.org May be available in some MI centres.	
Pediatric & Neonatal Dosage Handbook. (Paediatric Lexicomp). May be available in some MI centres.	
Neonatal and Paediatric Pharmacists Group www.nppg.org.uk	Contains links to useful documents, relevant guidelines and advice, but membership of NPPG is required for access to the full website.
Great Ormond Street Hospital www.gosh.nhs.uk/medical-conditions/medicines-information/	Useful medicines information leaflets. Other sections of the website describe procedures and treatments and list GOSH clinical guidelines.
NICE Evidence www.evidence.nhs.uk	NICE Evidence includes a number of paediatric and child sources.Try searching for your search term and 'paediatric' Difficult to identify useful resources as there is no filter for age; use the Source filter to narrow down to paediatric organisations
The Knowledge Network www.knowledge.scot.nhs.uk	There is an extensive collection of specialist paediatric e-books as well as Dynamed, BMJ Best Practice etc. Some books are superseded – check for most up to date version

Source	Notes
Bibliographic databases e.g. Medline, Embase.via www.knowledge.scot.nhs.uk	Suggested terms: CHILD (explode term), restrict search to documents relating to specific age ranges, INFANT-NEWBORN, INFANT-PREMATURE, NEONATAL DISEASES.

Answering the enquiry

- Consider whether recommendations are within the drug's licensed indications or whether you are advising off-label use. Prescribing unlicensed medicines, or medicines outside the terms of their licence (off-label), alters the prescriber's professional responsibility and liability. The prescriber and pharmacist should have sufficient information to support using the medicine. Be aware that the manufacturer's patient information leaflet may not be relevant to the child and the parents should be warned of this and appropriately reassured.

- When calculating a dose on a mg/kg basis never exceed the maximum recommended dose (usually the adult dose). If the child is obese consider calculating using ideal body weight.

- When assessing the appropriate dose (making reference to available paediatric dosage formularies) take account of available formulations and their suitability.

- If doses require calculation based on surface area, use recognised reference tables (see back pages of BNF for Children) or a recognised formula to calculate surface area.

- With smaller doses used in paediatrics it is much easier to make ten-fold errors in calculations. Be especially vigilant with decimal points or avoid using them (and quote appropriate units in full), e.g. 100 micrograms NOT 0.1mg. Do not use trailing zeros, e.g. 5mg NOT 5.0mg.

- Always have calculations checked.

- Always quote dose to be given rather than volume of liquid to avoid potential for errors, as multiple strengths of medicines (and manufactured specials) are common in paediatric practice.

- Consider timing of administration to avoid giving during school time if possible. Consider the hours the child will be awake to avoid interrupting sleep to give medicines. Opt for once or twice daily dosing where appropriate.

- Consider formulation and appropriateness for the child's age. As a general rule, liquid formulations are preferable for children aged less than 5 years. Choose sugar-free formulations where available. If a sugar containing preparation has to be used, provide advice on teeth cleaning after administration to reduce the risk of dental caries.

- The availability of a formulation in an apparently suitable form does not ensure its suitability for use in children. Consider excipients, e.g. alcohol, sorbitol. For premature or low birth weight infants with very low total fluid requirements, concentrated preparations may be more appropriate than dilute ones.

- Consider how the dose will be given:
  - Will an oral syringe be necessary or is it better to provide a formulation where the dose is contained in 5mL? Round the dose up or down if it makes administration easier (and safer) if the medicine has a wide therapeutic range.
  - If the parents are considering mixing the medicine with a drink to mask the taste check the potential for drug-drink interaction and advise that they should mix with a small volume of drink. The whole drink must be consumed to ensure the intended dose is given.
  - Avoid mixing the dose in a baby's feeding bottle.

- If no suitable liquid formulation is available, consider crushing tablets or opening capsules and mixing with a small amount of soft food, again ensuring the whole dose is consumed. Always consider potential for drug-food or drug-drink interaction. Remember this renders the product unlicensed.
- Avoid intramuscular injections where possible. The exception to this may be for one off doses where there is no other suitable formulation, e.g. vaccines.

- If you are considering recommending an extemporaneous preparation, consider how supply will be continued in the longer term. The local community pharmacist may require details of special-order manufacturers to obtain the product; these can be very expensive. Also think about whether the preparation needs to be stored in a fridge or has a short expiry, and what implications this has

Keywords: CHILD, INFANT, INFANT-NEWBORN INFANT-PREMATURE NEONATAL DISEASES, PAEDIATRICS and relevant drug names.

Pharmaceutical *NOTE: there are four sections to this document.*

NOTE: If the enquiry concerns the advisability of crushing tablets, opening capsules, mixing medicines with food or drink, please refer to the 'Administration of medicines' monograph. See also the 'Interactions' monograph. If the enquiry concerns the advisability of mixing injectable products in syringes or fluid bags, please refer to the 'Compatibility of Intravenous Drugs' and 'Compatibility of Subcutaneous Drugs' monographs.

Enquiries about pharmaceutical excipients

Background information

- What is the reason for asking about excipients? Does the patient have a known problem, or is one suspected?
- What is the nature of any known or suspected reactions to excipients?
- For patients experiencing intolerance to a product, how long has the patient been taking the medicine that might be causing the problem? What is its brand name and manufacturer?
- Is the patient taking other medicines? Has the patient had a similar reaction with another medicine, food or drink? It may be possible to rule out suspected problems with excipients if the patient has no problems already taking medicines, foods or drinks that contain these excipients.
- For enquiries about lactose or sodium content, an assessment of the total quantity provided by all of the patient's medicines can indicate the likelihood of a significant problem occurring.
- *For enquiries about **natural rubber latex allergy**:*
  - Obtain a full description of what happens when the patient is exposed to natural rubber latex.
  - Which products do they intend to use, including the brand name if possible, and why?
- *For enquiries about **products of animal origin** or **suitability for patients with religious beliefs:***
  - Establish clearly which substances the patient objects to and the reason why. For example, the enquirer may ask for a gelatin-free product – gelatin usually comes from animals and so is unsuitable for vegetarians; gelatin in a non-edible form (e.g. tasteless capsule shell) is suitable for Jewish patients if no alternative is easily available; all gelatin in medicinal products is deemed suitable for Muslim patients.
  - What is the drug to be prescribed and why?
  - Which other medicines is the patient taking?

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	Includes numerous documents on gluten, lactose and sodium content of medicines. Also information on kosher and halal medicines, E-numbers, excipients in toothpastes and natural rubber latex in dental local anaesthetics.
BNF & BNF-C via www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	The presence of selected excipients is noted. See General guidance section for details.
Electronic Medicines Compendium www.medicines.org.uk/emc	All excipients need to be declared on the labeling and in the SPC/PIL of injectable, topical or eye preparations. Excipients known to have a recognised action or effect must be declared on the labeling of all other medicinal products. See EMA Guideline. Use Advanced search – 'Search by section' can be used to find SmPCs that contain, or do not contain, an excipient.
MIMS www.mims.co.uk Access available within MI centres	Useful tables comparing sensitising excipients in eye preparations, emollients and topical steroids.
Manufacturers' Medical Information departments.	
Handbook of Pharmaceutical Excipients. Rowe, Sheskey, Cook and Fenton. Paper copy may be available in MI centre.	Comprehensive guide to the uses, properties and safety of pharmaceutical excipients.
Martindale www.medicinescomplete.com or www.knowledge.scot.nhs.uk	
Injectable Medicines Guide (Medusa) www.injguide.nhs.uk Password required	Monographs include information on latex content. Website also has links to other locally produced documents listing latex status (see Documents and Links Library).

Additional resources	
Food Additives and Ingredients Association www.faia.org.uk/	Includes information on E numbers, including a full list of E numbers, a description of the main additive categories and an explanation of why additives are needed.
Coeliac UK www.coeliac.org.uk	Includes advice on what gluten is and how to achieve a gluten-free diet and a list of prescribable gluten-free foods. Also a section for healthcare professionals with links to coeliac disease management guidelines.
Medicines and Healthcare products Regulatory Agency	Staff at the MHRA Information Centre can search the licensing database to identify products that do not contain specific excipients. Email info@mhra.gsi.gov.uk – enquiries are answered within 20 working days.
Muslim Council of Britain (MCB) www.mcb.org.uk,	Can also be contacted on 0845 26 26 786. Advice on medicines suitable for someone on a Halal diet can also be sought from a recognised local Imam
Religious leaders' approval for consumption of gelatin in medicinal products by Muslims www.immunize.org/concerns/porcine.pdf	Guidance from the World Health Organisation & the Islamic Organisation for Medical Sciences stating 'The gelatin formed as a result of the transformation of the bones, skin & tendons of a judicially impure animal is pure and it is judicially permissible to eat it'.

Answering the enquiry

- The individual product's Summaries of Product Characteristics should always be checked as formulations may change and quantities of excipients used may vary by manufacturer, product, formulation and strength.
- It is our duty as a health professional to abide by the wishes of a patient, regardless of the reason why a person objects to products of a certain animal origin. Therefore, for example, if a Muslim patient refuses products containing gelatin, it is our responsibility to help them to find a suitable alternative product, if possible.
- The MHRA recommends that an unlicensed medicine should only be used when a patient has special requirements that cannot be met by use of a licensed medicine.

Keywords: Name of the excipient (e.g. LACTOSE, GLUTEN, ALCOHOL, SODIUM CHLORIDE), RUBBER or LATEX and relevant drug names.

Enquiries about stability of refrigerated products out with the recommended storage temperature

Background information

For products that have been stored at temperatures outside the manufacturer's recommended limits:

- What was the highest (or lowest) temperature?
- How long were the products exposed to this temperature?
- What are the brand names of the products?
- Where are they stored now?

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
Electronic Medicines Compendium www.medicines.org.uk/emc	Some products licensed to be stored in a refrigerator have additional licensed storage data at higher temperatures
Manufacturers' Medical Information departments	May be able to provide additional off-label extended stability data.
Specialist Pharmacy Services Fridge Database via www.sps.nhs.uk	Provides stability information for medicines, intended for storage in the fridge, inadvertently stored outside recommended storage temperatures
Additional resources (tailor to local availability)	
Add any local health board policies on vaccines storage	

Answering the enquiry

- The individual product's Summaries of Product Characteristics should always be checked as formulations may change.

Keywords: ROOM TEMPERATURE/FREEZING and relevant drug names.

Enquiries about products in multi-compartment compliance aids (MCA), also known as monitored dosage systems (MDS)

Background information

The MCA

- What type of device is being used?
- How long will the product be stored in the device?
- Is the medicine being repackaged within a single MCA compartment?
- Does the device provide protection from water vapour and/or atmospheric gases i.e. sealed "blister" type or unsealed?
- Does the device provide protection from light?

The medicine(s)

- Brand name(s) of medicine(s) to be stored in the MCA.
- Solid dose formulation:
  - film coated or sugar coated (sugar coating provides a better barrier to moisture and light),

- hard or soft gelatin capsule shells (both have a high water content. Do not put with tablets, or put hard and soft gelatin capsules in the same compartment),
- effervescent/dispersible or hygroscopic (are sensitive to moisture),
- buccal/sublingual (may be swallowed by mistake).

- Cytotoxic medicines should not be put in an MCA.
- Type of packaging:
  - foil packaging/desiccant (usually indicates moisture sensitivity),
  - glass container (usually provided for a reason, so do not put in an MCA),
  - dark coloured blister pack (indicates light sensitivity).
- Do (es) the medicine(s) have additional/complex instructions (some MCAs cannot accommodate additional instructions)?
- Does the patient take other medicines not in an MCA (PRN medicines and/or multiple methods can cause confusion for patients and/or carers)?
- Chemical structure:
  - hydrolysis is most likely to occur in ester-containing drugs (RCOOR').

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&Asvia www.sps.nhs.uk	
BNF & BNF-C via www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	Can check for special instructions
Electronic Medicines Compendium www.medicines.org.uk/emc	Check for special storage instructions, formulation or complex dosage instructions
Specialist Pharmacy Services website www.sps.nhs.uk	Provides stability information for branded and some generic medicines in medicines compliance aids - MCAs. Guidance on how to use the information is at www.sps.nhs.uk/articles/usage-of-medicines-in-compliance-aids/
Manufacturers' Medical Information departments.	May be able to provide additional off-label extended stability data.
Additional resources	

PSNC Special Container Database (SCD) http://psnc.org.uk/	For MCA questions: a medicinal product is granted special container status in cases where it is not practical to split an original pack, for example where the product is sterile or hygroscopic. The SCD is under construction and an archived database is available. Special container details for specific products can also be identified using the Dictionary of Medicines and Devices. This resource applies to NHS England but identification of products requiring special container may be relevant to stability issues.
Improving patient outcomes - the better use of multi-compartment compliance aids (July 2013) Membership required	RPS recommendations on the use of MCAs

Answering the enquiry

- The individual product's Summaries of Product Characteristics should always be checked.
- There are many ways patients can be helped to take their medicines safely; MCAs may not be the only option. Ask if a patient assessment has been done and other options considered.

Keywords: COMPLIANCE AIDS and relevant drug names.

Enquiries about extemporaneous preparations

Background information

- Establish clearly what product has been prescribed including all ingredients, strengths and vehicles.
- What condition is it being used to treat? What else has been tried?

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
BNF & BNF via www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	:
Special-order manufacturers. Details via BNF or BNF-C www.medicinescomplete.com	

NHS Pharmacy Production Units, e.g. Tayside	
JAC/ Ascribe	
Scottish Drug Tariff http://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Scottish-Drug-Tariff/	Parts 7S and 7U list special formulations and unlicensed products which have approved tariff prices
List of preferred unlicensed dermatological preparations (specials). British Association of Dermatologists. www.bad.org.uk/healthcare-professionals/clinical-standards/specials	A list of unlicensed dermatological preparations recommended for manufacture and supply in NHS hospitals (includes drug, vehicles and strength).
Pro-file Database www.pro-file.nhs.uk Registration required	Produced by Guy's and St Thomas' Hospital NHS Trust. Useful for sourcing unlicensed 'special' medicinal products.
Pharmaceutical importers	
Association of Pharmaceutical Specials Manufacturers http://www.apsm-uk.com/	Includes a list of specials manufacturers who are members of APSM and a link to their websites. Includes information about specials and links to relevant guidance in the resources section, including documents on medicines manipulation – crushing, opening or splitting tablets, and a patient information leaflet about specials.

Answering the enquiry

- Approximately a third of 'Specials' produced within the NHS are for Dermatology; clinicians are encouraged to prescribe from the list of preferred specials prepared by the British Association of Dermatologists. The aim of the list is to ensure quality, safety and availability of extemporaneously manufactured products.
- If no information is available on the stability of the requested product, it may be possible to substitute the requested product with one that has been made previously or one that is from an approved list.
- Is there a licensed alternative available? The MHRA recommends that an unlicensed medicine should only be used when a patient has special requirements that cannot be met by use of a licensed medicine.
- If the patient is a hospital inpatient, consider what arrangements need to be made to continue supply of the product after the patient is discharged. Will a special-order manufacturer be able to supply the product? Can the community pharmacist easily obtain supplies?

Keywords: DISPENSING-EXTEMPORANEOUS and relevant drug names.

Pharmacokinetics

Background information

- What is the drug, dose, frequency, indication, route and duration of therapy?
- What is the patient's age, gender and weight?
- What is their renal and hepatic function? (For background information required and relevant calculations please see the enquiry answering guidelines 'Drug use in hepatic impairment' and 'Renal impairment').
- Does the patient have any other disease states or conditions e.g. hypothyroidism, hyperthyroidism, hypoalbuminaemia?
- Is there concurrent medication?
- Have any previous drug levels been taken? If so, check the exact time they were taken in relation to drug administration and confirm the units of measurement.

Pharmacokinetic definitions and calculations

Bioavailability (F): the fraction of the dose that reaches the systemic circulation as intact drug.

$$\text{Bioavailability} = \text{Bioavailability factor (F)} \times \text{dose}$$

Volume of distribution (Vd): a hypothetical volume that relates the concentration of drug in the plasma to the total amount of drug in the body.

$$\text{Vd (L)} = \frac{\text{Total amount of drug in the body (mg)}}{\text{Plasma drug concentration (mg/L)}}$$

Clearance (Cl): the volume of blood cleared of drug per unit time and the units are normally litres per hour or ml per minute.

$$\text{Cl} = \frac{\text{F x (Dose/Dose interval)}}{\text{Average steady state plasma drug concentration } (C_{ss})}$$

Loading dose: the dose required to rapidly achieve the desired plasma drug concentration (C)

$$\text{Loading dose} = \frac{\text{Vd x C}}{\text{F}}$$

Maintenance dose: the regular dose required to maintain the desired plasma drug concentration.

$$\text{Maintenance dose} = \frac{\text{Cl x } C_{ss} \text{ x dose interval}}{\text{F}}$$

Steady-state: the equilibrium achieved after multiple dosing when the rate of drug administration equals the rate of drug elimination. At steady-state the amount of drug in the body, and the plasma concentration, are constant.

Half-life: is the time taken for the amount of drug in the body (or the plasma concentration) to fall by half.

Half-life is used to determine both time to reach steady-state conditions with chronic dosing and time for elimination. As a rule of thumb it takes approximately 3 to 5 half-lives to achieve steady-state conditions or for a drug to be completely eliminated from the plasma.

Half-life is proportional to Vd and inversely proportional to clearance:

$$\text{Half-life (hrs)} = \frac{\text{0.693 x Volume of distribution (L)}}{\text{Clearance (L/hr)}}$$

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDatabank, or MiDB sharer (subscription required).	
Relevant Medicines Q&Asvia www.sps.nhs.uk	
BNF & BNF-C via www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	Provides details of recognised therapeutic ranges for drugs that require monitoring e.g. digoxin, phenytoin, theophylline, gentamicin.
Electronic Medicines Compendium www.medicines.org.uk/emc	Section 5.2 'Pharmacokinetic properties' provides pharmacokinetic information including absorption, distribution, metabolism, elimination and half-life.
Local guidance on Gentamicin and Vancomycin dosing, calculators for adult patients Via add links	
Basic Clinical Pharmacokinetics. Winter ME. Paper copy in MI centre	Easy to understand explanations of the basic principles of pharmacokinetics in the clinical setting. Part One explains basic principles; Part Two illustrates, with worked examples, the clinical application of pharmacokinetics.
Bibliographic databases e.g. Medline, Embase via www.knowledge.scot.nhs.uk	Terms include PHARMACOKINETICS, ABSORPTION, INTESTINAL ABSORPTION, BIOLOGICAL TRANSPORT, TISSUE DISTRIBUTION, BIOTRANSFORMATION, DRUG ABSORPTION, DRUG ACCUMULATION, DRUG ACTIVATION, DRUG ADSORPTION, DRUG BIOAVAILABILITY, DRUG CLEARANCE, DRUG DIFFUSION, DRUG DISPOSITION, DRUG DISTRIBUTION, DRUG ELIMINATION, DRUG EXCRETION, DRUG HALF LIFE, DRUG PENETRATION, MAXIMUM PLASMA CONCENTRATION, PLASMACONCENTRATION-TIME CURVE, TIME TO MAXIMUM PLASMA CONCENTRATION, DRUG METABOLISM, DRUG RELEASE.
Drugdex www.micromedexsolutions.com	
Additional resources	
Goodman and Gilman's Manual of Pharmacology and Therapeutics. May be available in MI Centre	Chapter One provides a general overview of pharmacokinetics.
Pharmacokinetics Made Easy, Birkett DJ. May be available in MI Centre	An easy to understand explanation of pharmacokinetics with a practical approach.

Answering the enquiry

- Always have calculations checked.
- Pharmacokinetic parameters in elderly and paediatric patients may not be the same as in adult patients and may alter drug response.
- For highly protein bound drugs consider checking albumin levels.
- If therapeutic drug level monitoring (TDM) is recommended ensure that levels are not taken before steady state is reached.

Keywords: PHARMACOKINETICS, ABSORPTION, BIOLOGICAL AVAILABILITY, CLEARANCE-DRUG, VOLUME OF DISTRIBUTION, EXCRETION, EXCRETION-DRUG, HALF LIFE, METABOLISM, METABOLISM-DRUG, METABOLITES-ACTIVE, FIRST-PASS PHENOMENON.

Pregnancy

Background information

The key information required before answering an enquiry about drug use in pregnancy is:

Medicine(s)

- Has the patient taken the medicine already? Or is this a prospective enquiry? The ideal is to consider medicines before exposure. While you may be in a position to simply advise against exposure if it has not already been taken. More detailed scans, reduced doses, additional drug monitoring etc may be necessary if exposure has occurred.
- **Medicine** – the proposed medicine(s) and any other medicines the patient is taking or wants to take (generic or brand name, dose, frequency, route)
- **Indication** – it is helpful to know the indication in order to be able to advise best about risk/benefit (and necessity of drug) and to suggest alternatives if necessary**.**
- Is drug therapy necessary? Have other therapies/medicines been tried?
- Has the patient been on this or alternative medicine(s) during previous pregnancies and were symptoms controlled?

Pregnancy

- Is the patient already pregnant? Is she trying to conceive?
- Stage of pregnancy in weeks – at the time of the enquiry and at the time of the exposure. Be as accurate as possible as developmental sensitivities to teratogens may be dependent on stage of pregnancy.
- Have any investigations been performed?
- Previous pregnancies or miscarriages?

Referral to UKTIS – Document the GP or Consultant contact details and a patient identifier in case the UK Teratology Information Service (UKTIS) want to follow up the exposure.

Resources

Source	Notes
First-line resources	N.B. At least two resources should be used for all pregnancy enquiries.
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	
Relevant Medicines Q&As via www.sps.nhs.uk	
Toxbase www.toxbase.org	Monographs from UKTIS are available on this website. Click on 'Exposure in pregnancy'.

Source	Notes
BUMPS – Best use of medicines in pregnancy www.medicinesinpregnancy.org	This website provides information leaflets produced by UKTIS (see Toxbase above) for pregnant women and their partners. Monographs cover a variety of medicines, drug classes, recreational drugs and products such as face cream and hair dye. There are fewer monographs than on Toxbase. The site also has an 'online reporting' facility for women to record their drug exposure during a current or previous pregnancy in order to help UKTIS understand how medicines, lifestyles or illnesses may affect foetal development.
Drugs during Pregnancy and Lactation. Schaefer. Available via Medicines Information drop-down on The Knowledge Network www.knowledge.scot.nhs.uk	Chapter 1 provides a useful overview of the risks of drug use in pregnancy. Chapter 2 contains information on drugs in pregnancy by therapeutic class. Each monograph has a boxed 'recommendation' at the end that may suggest suitable alternatives.
Drugs in Pregnancy and Lactation. Briggs et al. Available via Medicines Information drop-down on The Knowledge Network Via www.knowledge.scot.nhs.uk	US resource, some drug names may be different. Drug monographs are listed in alphabetical order and provide in-depth data. Each monograph is assigned a risk category. Do not rely solely on these; always read the full monograph.
Electronic Medicines Compendium www.medicines.org.uk/emc	
Drugdex and Reproductive Risk Information via www.micromedexsolutions.com	The Reproductive risk information can be found from the drug monograph- click on "Toxicology" link on right hand side (under Related Results).
BNF & BNF-C via www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	Pregnancy advice is based on manufacturer's information which is available in the SPC and tends to be more cautious than the specialist pregnancy information resources.
Local Obstetric Guidelines Add link locally	
Clinical Knowledge Summaries cks.nice.org.uk/	Many guidelines include information on the management of that condition during pregnancy. There are specific guidelines on some common medical conditions in pregnancy.
Additional resources	

Source	Notes
UK Teratology Information Service (UKTIS); specialist centre for drugs in pregnancy.	UKTIS (Telephone 0844 892 0909) provides information to medicines information centres on safety of medicines in pregnancy. Before contacting UKTIS ensure you have checked available resources and have obtained all the background information.
Prescribing in Pregnancy. Rubin D. 4th Edition on www.knowledge.scot.nhs.uk	Chapter 1 of this UK reference includes a table showing the time and stages of embryo and foetal development. Chapter 2 discusses management of common, minor and self-limiting conditions. Other chapters cover management of chronic conditions and drug abuse during pregnancy.
Handbook of Obstetric Medicine. Nelson-Piercy C. 5th Edition in GRI MI Centre 4th Edition on www.knowledge.scot.nhs.uk	Early chapters cover the management different disease areas during pregnancy. Later chapters consider the differential diagnosis of medical problems in pregnancy.
Royal College of Obstetrics and Gynaecologywww.rcog.org.uk/en/guidelines-research-services/guidelines/	A range of guidelines on women's health are available.
Maudsley Prescribing Guidelines. Taylor D et al. 12th Edition available on Royal Pharmaceutical Society website (membership required) Paper copy in MI Centres	Chapter 7 contains a section on the choice of medicines for psychiatric conditions in pregnancy.
Psychotropic Drug Directory. Bazire S. Paper copies in MI Centres	Chapter 3 contains a section on the choice of medicines for psychiatric conditions in pregnancy.
The Knowledge Network *www*.knowledge.scot.nhs.uk	A number of resources including, BMJ Best Practice, Dynamed, Maternal Health Portal with numerous links
Bibliographic databases e.g. Medline, Embase. And MIDIRS via www.knowledge.scot.nhs.uk	Suggested terms: PREGNANCY, PREGNANCY-COMPLICATIONS, ABNORMALITIES-DRUG INDUCED, CONGENITAL MALFORMATIONS plus individual drug name

Answering the enquiry

- Consider benefits and risks of medication to both the expectant mother and developing baby.
- Consider the implications of unmanaged acute and chronic conditions on the expectant mother's and developing baby's health.
- Consider the period of gestation and, if possible, avoid all drugs during the first trimester.
- Where appropriate, use the lowest effective dose for as short a period as possible.
- Older drugs are often preferred to newer drugs as there is more information about their safety.
- Avoid polypharmacy where possible.
- Remember to consider maternal contraindications and precautions.
- Reassure the patient/enquirer if the drug has already been taken and if there is no indication from the literature that the drug poses significant harm.
- Detailed scans during pregnancy may be appropriate if a medicine has been taken.
- Remember there is a background risk of major congenital malformations of 2-3% in the population and 10-20% for miscarriage for a relatively young, healthy mother. This risk is higher for older mothers irrespective of their health or medicines they may be taking.

Keywords: PREGNANCY plus drug name and disease name (if appropriate)

Renal impairment

Background information

- Diagnosis and previous medical history if relevant.
- Establish patient details, including age, sex, ethnic origin, height, weight etc.
- U&Es and serum creatinine, eGFR - most recent if possible. Are they stable or changing? Is the renal impairment acute or chronic?
- Calculate the patient's estimated creatinine clearance (CrCl). Use ideal body weight if obese*. See notes below.
- Current medication - include all drugs (prescription and OTC) currently taken by the patient including doses.
- Is the renal impairment suspected to be drug-induced? Which drug(s) are suspected?**

> ** *If the renal failure is suspected to be drug related please refer to the monograph on 'Adverse drug reactions'*

- Is the patient receiving renal replacement therapy (RRT), if so how often and what type?
  - Haemodialysis (HD)
  - Haemodiafiltration (HDF)
  - Peritoneal Dialysis (PD) [automated peritoneal dialysis (APD) and continuous ambulatory peritoneal dialysis (CAPD)]
  - Continuous arteriovenous haemofiltration (CAVHF)/continuous venovenous haemofiltration(CVVHF)
  - Continuous arteriovenous haemodialysis (CAVHD)/continuous venovenous haemodialysis(CVVHD)
  - Continuous arteriovenous haemodiafiltration (CAVHDF)/continuous venovenoushaemodiafiltration (CVVHDF)
- For enquiries about dosage or suitability of a drug in renal impairment, ask:
  - What is the indication for the drug and have alternatives been considered?
  - What agent would normally be used if the patient did not have renal impairment?
  - Is the patient currently taking the drug in question?
  - For most drugs and for most patients (over 18 years and of average build and height) dosage adjustment based on eGFR is acceptable. However, calculate the patient's estimated creatinine clearance (CrCl) using the Cockcroft & Gault equation (see below), and monitor plasma-drug concentrations and clinical response:
    - For potentially toxic drugs with a narrow therapeutic index
    - For adults at extremes of body weight (BMI <18.5kg/m^2 or >30kg/m^2) and use ideal body weight or adjusted body weight.
  - For children, serum-creatinine concentration is sometimes used as a measure of renal function but is only a rough guide even when corrected for age, weight, and sex. Base dose recommendations on severity of renal impairment expressed in terms of GFR (mL/minute/1.73 m2) (see below).
  - Where an accurate GFR is considered necessary e.g. in chemotherapy dosing, an isotope GFR determination should be performed.

Cockcroft and Gault equation

$$\text{CrCl mL/minute (male)} = \frac{1.23 \times (140 - \text{age in years}) \times \text{weight in kg}}{\text{serum creatinine (micromol/l)}}$$

$$\text{CrCl mL/minute (female)} = \frac{1.04 \times (140 - \text{age in years}) \times \text{weight in kg}}{\text{serum creatinine (micromol/l)}}$$

Calculation of estimated GFR (mL/minute/1.73 m^2) in children
Child over 1 year: eGFR = 40 x height (cm)/serum creatinine (micromol/ litre) Neonate: eGFR = 30 x height (cm)/serum creatinine (micromol/ litre)

Resources

Source	Notes
First-line resources	
In-house past enquiries on MiDB, or MiDB sharer (subscription required).	Try keywords such as KIDNEY FAILURE, KIDNEY FAILURE-ACUTE, KIDNEY FAILURE-CHRONIC, KIDNEY FUNCTION-IMPAIRED, KIDNEY DISEASES.
Relevant Medicines Q&As via www.sps.nhs.uk	The following Medicines Q&As give further guidance on approach to answering renal impairment-related enquiries: • What factors need to be considered when dosing patients with renal impairment? • What factors need to be considered when dosing patients on renal replacement therapies?
Local Guidance/ Calculators for creatinine clearance, Add link locally	
BNF & BNF-C via www.medicinescomplete.com or via www.knowledge.scot.nhs.uk or App	
Electronic Medicines Compendium www.medicines.org.uk/emc	SPCs should always be checked as they may give advice on the need to reduce doses and a suitable regimen in renal impairment.
The Renal Drug Database www.renaldrugdatabase.com/ or via www.knowledge.scot.nhs.uk Registration required – contact ann.lees@nes.scot.nhs.uk	Doses reflect specialist practice and may differ from the licensed dose. Uses calculated GFR (Cockroft & Gault) and not eGFR
Introduction to Renal Therapeutics. Ashley C & Morlidge C. 2008 edition available via www.knowledge.scot.nhs.uk	This discusses diseases affecting the kidney and their management rather than providing dosing guidance. Useful for background information and general principles of dose adjustment in renal impairment and renal replacement therapies
eGFR calculator. The Renal Association About eGFR - The Renal Association	Online calculator for eGFR. Has link to UKeCKD guide plus other useful background information.

Source	Notes
Martindale via www.medicinescomplete.com or www.knowledge.scot.nhs.uk	
Drugdex via www.micromedexsolutions.com	Where relevant, in-depth monographs have a 'dosage in renal failure' section with links to more general drug consults e.g. ACE inhibitor-induced acute renal failure.
NICE guidance on chronic kidney disease in adults www.nice.org.uk/guidance/cg182	Recommends the use of the CKD-EPI creatinine equation to calculate eGFR, in preference to the MDRD equation
Additional resources	
Department of Health guidance on eGFR	**Notes** Has a link to eGFR Frequently asked questions and information on how to calculate eGFR. Last modified 2010
Pharmaceutical manufacturers.	Contact manufacturer of originator drug if possible as are more likely to have data than generic manufacturers Manufacturers may have information about any necessary reduction of doses in renal impairment.
Renal association Home - The Renal Association	Includes guidelines
Meyler's Side Effects of Drugs, Dukes and Aronson. Available on The Knowledge Network via ClinicalKey www.knowledge.scot.nhs.uk Click on Meyler's Side Effects of Drugs (16th edition) in Medicines Information Resources drop-down	For information on drug-induced renal impairment.
The Knowledge Network www.knowledge.scot.nhs.uk For Dynamed Plus, BMJ Best Practice, a range of textbooks and guidelines etc	Some books are superseded – check for most up to date version
Bibliographic databases e.g. Medline, Embase accessed via The Knowledge Network www.knowledge.scot.nhs.uk	If no information can be found in standard resources on using a drug in a specific type of renal disease, consider conducting a literature search for relevant papers. This should be done before using pharmacokinetic/pharmacodynamic data to predict drug handling from first principles. Suggested terms: KIDNEY FAILURE, ACUTE KIDNEY FAILURE, CHRONIC KIDNEY FAILURE, KIDNEY INJURY (Embase); ACUTE KIDNEY INJURY, RENAL INSUFFICIENCY, RENAL INSUFFICIENCY,CHRONIC (Medline)

Answering the enquiry

Patients not on renal replacement therapies (RRT) – for more in-depth guidance see Medicines Q&A What factors need to be considered when dosing patients with renal impairment?

- There are three approaches to altering drug maintenance doses in patients with renal impairment:
  - Give the standard dose at extended intervals.
  - Give a reduced dose at usual intervals.
  - Give a combination of reduced dose and extended interval.

  Drugs that require maintenance of a serum concentration over the dosing interval should be administered at usual intervals, but with reduced doses. Drugs for which specific peak serum concentrations must be achieved should be dosed with the standard dose at extended intervals.
- For most drugs loading doses or single doses will be the same as for those with normal renal function.
- When choosing a drug for patients with renal impairment:
  - Only use drugs where there is a definite indication for prescribing.
  - Choose a drug that has minimal or no nephrotoxicity.
  - Use recommended dosage regimens for renal impairment.
  - Use plasma concentration measurements to adjust dose if possible and clinically relevant.
  - Monitor for evidence of clinical efficacy and toxicity

Patients on renal replacement therapies (RRT) – for more in-depth guidance see Medicines Q&A What factors need to be considered when dosing patients on renal replacement therapies?:

- There are a number of inter-dependent factors that need to be considered when dosing patients on RRT. Consider the drug, the patient and type of RRT.
- Alteration of drug dosage is only necessary if renal clearance exceeds 25% of total body clearance.
- Drugs which are cleared by the kidneys are usually dialysed, and vice versa, although there are some anomalies.
- Dose adjustment for RRT is only necessary for drugs that require dose adjustment because of the presence of renal failure. No RRT is as effective as the normal kidney – so for most drugs doses used will never be larger than those recommended in normal renal function.
- Physicochemical drug characteristics affecting drug removal include protein binding, volume of distribution, water/lipid solubility, and molecular weight. Drugs that are highly protein bound (>80%) and/or have a large Vd (>1L/kg), are unlikely to be removed to a significant degree. In general, very large molecules are less likely to be removed than smaller ones.
- Pharmacokinetic studies that formed the basis for many of the drug dosing recommendations used today were performed in the 1980s and 1990s using less efficient techniques of RRT than those employed currently. These studies varied in design, used different haemofilters, blood, dialysate and ultrafiltration rates and calculated drug clearance by different methods. Advice on drug dosage in continuous RRT from the literature should therefore be applied cautiously to individual patients. Dosing recommendations based on this older data may result in underdosing of drugs e.g. antibiotics.
- In patients on HD, dose after the dialysis session otherwise a proportion of the drug may be removed during the HD session and its duration of action reduced. For CRRT and CAPD, since these are continuous processes, there is no need to schedule doses around RRT sessions.
- For toxic drugs, and for drugs with a narrow therapeutic index, drug monitoring with measurements of plasma concentrations, where available, and monitoring of the patient for therapeutic response and adverse effects, are essential.
- Information from specialist sources may provide dosing information outside the product licence.
- The omission of a drug from reference sources does not imply that the drug is safe for use in patients with impaired renal function.
- You should consider other therapeutic options that don't require adjustment in renal failure e.g. drugs that are primarily metabolised by the liver.

Keywords: KIDNEY, KIDNEY FUNCTION-IMPAIRED, KIDNEY FAILURE, drug name

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