Use of the Injectable Medicines Guide website in clinical areas - IntraVENOUS medicine monographs (January 2013)

Introduction

The ‘IntraVENOUS medicines’ section of the Injectable Medicines Guide website contains monographs which give information on the recommended method(s) of preparing and administering intraVENOUS injections and infusions. Monographs include links to:

- The British National Formulary’s (BNF and BNFc)
- The manufacturer’s Summary of Product Characteristics (SPC) and the manufacturer’s Patient Information Leaflet (PIL), which are produced by the supplier, can be found in the ‘Current Supplier’ section of the monograph.
- The Medicine Compendium UK (emc)
- Other relevant publications

The monographs must be used in conjunction with best practice detailed in injectable medicine guidelines in use locally. In addition the user should be aware of the content of the following documents (which can be found on the ‘Documents and Links’ page of the website):

- The Royal College of Nursing - Standards for Infusion Therapy.

Finding a monograph on the website

- Log-in to the website (some organisations have the Guide on the local intranet and log-in is not required)
- Select the ‘Inj Med Guide’ (or ‘local guide’ if available) tab on the menu bar on the top right hand side of the home page or use the quick link ‘Injectable Medicines Guide’ on the left hand side of the website home page.
- Select ‘IntraVENOUS drugs’ THEN EITHER:
  - Type in the first few letters of the medicine into the search box and click ‘Go’
  - Click on the down arrow on the ‘Medicine index’ box below to see all the preparations with names beginning with those letters
  - Select the relevant monograph from the list displayed
- OR
  - Click on the down arrow in the ‘Medicine index’ box
  - Type in the first letter of the medicine name and scroll through the list of monographs
  - Select the relevant monograph from the list displayed

Viewing a monograph

- When the relevant monograph is selected in the ‘Medicine index’ box (see above), click on the ‘Show monograph’ button.
- When the monograph is displayed use the blue buttons at the top left hand side of the monograph to switch between the detailed monograph ‘Display Full Monograph’ and the short monograph ‘Display Short Monograph’. The short monograph is designed to show only information absolutely essential for the safe preparation and administration of the medicines.

Once in the monograph, clicking on any of the blue ‘underlined’ monograph headings opens a new window which gives an explanation of the terms used and some general background information. The content of each of these windows is reproduced in the following pages.
Printing a monograph
Printing can be done when the monograph is open for viewing:

- Click on the orange ‘Print Monograph’ button at the top left hand side of the monograph.
- Then use the browser print function from the tool bar.

Printing can also be done as follows:

- When the relevant monograph is selected in the ‘Drug name’ search box (see above), click on the ‘Print monograph’ button.
- Then use the browser print function from the tool bar.

N.B. Do not use the print option from the browser tool bar without first selecting the ‘Print monograph’ button as pages may not display correctly and information may be missed off the right hand side of the printed page.

Printing other pages from the website:
For printing items from the ‘documents and links’ page of the website first set the printing options to ‘Landscape’. This will enable the correct display and avoid unintentional loss of information at the right hand margin of the printed page.

Important: printed copies of monographs may not be up-to-date. If possible always check with the electronic version of the Injectable Medicines Guide.

Comments on the Injectable Medicines Guide website
If you have any comments on the Injectable Medicines Guide, or have any suggestions for improvement please contact: Gill Bullock, Pharmacy, Charing Cross Hospital, Tel: 020 331 11142 gill.bullock@imperial.nhs.uk

Disclaimer
The information in the Injectable Medicines Guide has been carefully checked. No responsibility can be accepted for any errors or omissions. The reader is assumed to possess the necessary knowledge to interpret the information that this document provides.

Headings used in the Injectable Medicines Guide monographs for intravenous medicines

METHOD OF ADMINISTRATION:

- All medicines can be administered via the central route. For some medicines this is the preferred or essential route, for example, vasoconstrictor medicines (e.g. adrenaline and noradrenaline).
- Medicines of extreme pH (<5 or >9) or osmolarity (>600mOsmol/L) should preferably be administered centrally rather than peripherally due to their potential to cause vein injury (RCN 2010 Standards for Infusion Therapy)
- Central venous administration provides rapid dilution and distribution of the medicine, avoiding local toxicity to the vein wall.
- The concentration and rate of administration of a medicine administered centrally is important. Central administration via a neck vein delivers medication close to the heart where some may have a toxic effect. For example, potassium and calcium must be administered slowly when given via the central route to allow for dilution within the circulation, as high concentrations can be toxic to the heart causing asystole.

Advice on selecting an appropriate vascular access device for administration of intravenous fluids and medication can be found in the following flow chart which has been adapted from BJJN 2010, Vol 19, No 2 Central venous access devices Part 1: Devices for acute care.
Selecting an appropriate vascular access device for administration of intravenous fluids and medication

**Infusate criteria for use in peripheral infusions:**
- Should be administered at a concentration and rate appropriate for peripheral administration.
- Osmolarity should be 600mOsm/L or less.
- pH should be between 5 and 9.
- Should not be a vasoconstrictor.
- Medication should not be a vesicant or irritant.

**Catheter lumens:**
- Consider the need for single or multi-lumen catheter to deliver the prescribed therapy.
- Select the least number of lumens to deliver the required therapy.

**Considerations for subcutaneous infusion (S/C) include:**
- Hydration, intermittent infusions, and continuous infusions of isotonic fluids and a few selected medications.
- S/C route is not appropriate for administration of fluids in an emergency.
- Patient assessed appropriately for this mode of therapy.
INSTRUCTIONS FOR RECONSTITUTION:
Some medicines are presented as dry powders and must be reconstituted before use. The volume of diluent required for reconstitution and the recommended diluent to use is described.

DISPLACEMENT VALUE:
Where reconstitution is necessary and the dose of the medicine required is less than a complete vial it may be necessary to calculate the displacement value of the medicine. Displacement values are usually only applicable to paediatrics.

e.g. 
To give a dose of 125mg amoxicillin from a 250mg vial
The displacement value of amoxicillin 250mg is 0.2mL
If 4.8ml of diluent is added to a 250mg vial, the volume of the resulting solution is 5mL (i.e. 4.8mL plus 0.2mL)
Therefore 125mg will be contained in 2.5mL of the solution.

INSTRUCTIONS FOR DILUTION AND SUITABLE DILUENT:
Many medicines require further dilution before they can be given by injection or infusion. This section indicates if the medicine can be diluted in sodium chloride 0.9% or glucose 5% (the most common diluents) before use. Information on other suitable diluents (infusion fluids) can be found in the ‘compatibility information useful in clinical practice’ section of the monograph.
Details of the volume of diluent to be used are given where this is important.
When preparing an intravenous medicine for administration, do not mix vials/ampoules from more than one manufacturer to make up the required dose.

EXPIRY TIME TO BE WRITTEN ON THE ‘MEDICINE ADDED’ LABEL
Unless otherwise stated in the monograph, infusions should be given an expiry time of 24 hours if prepared in a clinical area. Be aware that local policies may differ.
N.B. The use of a different diluent or concentration to that recommended in the ‘instructions for dilution and suitable diluent’ section may affect the stability of the solution and reduce the expiry time.
Administration of a dose prepared in a clinical area should be started immediately (exceptions; see NPSA Patient Safety Alert 20: Promoting safer use of injectable medicines. March 2007).

EXAMPLE CALCULATION:
In a number of monographs, example calculations are given.

• The information provided does not replace the need to accurately calculate the correct infusion rate for a particular patient and the example calculation should only be used to check that the infusion rate calculated for a specific patient is in the correct range. Doses given in this section are just an example, and should not be used as a reference for prescribing or checking the prescription.
• For adult patients if a calculated infusion rate gives a figure to two decimal places, round to one decimal place when setting the infusion pump e.g. 5.24mL/hour (and below) is rounded down to 5.2mL/hour and 5.25mL/hour (and above) is rounded up to 5.3mL/hour.
• Always check that the units in the example calculation match those for the infusion device you are using.

Electronic calculator
An electronic calculator is included in a number of monographs. All results obtained using the electronic calculator must be cross-checked against the relevant ‘example infusion rate table’ (provided as a link) to ensure the answer obtained is in the appropriate range.
FLUSHING:
- Sodium chloride 0.9% is recommended as a flush for most drugs. In a very few circumstances sodium chloride 0.9% should not be used and glucose 5% is recommended as an alternative.
- Water for injections should not be used as a flush because water haemolyses red blood cells (leading to hyperkalaemia).
- Do not flush at a rate which exceeds the rate of administration of the IV injection or infusion to be flushed.
- For some infusions, e.g. those containing a vasoactive medicine (e.g. inotropes, antihypertensive agents, vasodilators, anti-arrhythmic agents), the central venous access device should not be flushed when the infusion is discontinued. For these preparations, when the infusion is discontinued, disconnect the giving set, aspirate the cannula contents and discard it, then flush with sodium chloride 0.9%.

ADVERSE EFFECTS WHICH MAY BE CAUSED BY IV ADMINISTRATION AND SUGGESTED MONITORING:
This section includes details of adverse effects that may occur acutely, either during or very shortly after, administration of a medicine by the intravenous route and suggested appropriate monitoring. Use this information carefully as it is not intended to be an exhaustive list of all possible adverse effects resulting from administration of the medicine, or all required monitoring. A full list of possible adverse effects can be found in the medicine’s ‘Summary of Product Characteristics’ (SPC) available as a ‘link’ in the ‘Current Suppliers’ section of the monograph. Be aware that the monitoring suggested may not be possible in all clinical areas.

EXTRAVASATION:
Extravasation is the inadvertent administration of a vesicant or irritant medicine into the tissues. Administration of a non-irritant or non-vesicant solution into the tissues is classified as infiltration. The following have the potential to cause tissue injury if extravasation occurs and should, if possible, be administered via a central venous access device:-
- medicines that have an extreme pH (less than 5 and greater than 9)
- medicines with high osmolarity (greater than 600mOsmol/L)
- cytotoxic medicines
- calcium preparations
- glucose preparations ≥ 20%
- medicines liable to precipitate e.g. diazepam
- vasoconstrictors e.g. noradrenaline and adrenaline
- preparations which contain alcohol, polyethylene glycol and certain other injection excipients.
The ‘National Extravasation Information Service’ provides information on factors which may result in tissue damage if a medicine is accidentally extravasated and suggested treatment. It can be accessed via the ‘documents and links’ page of the website.
COMPATIBILITY INFORMATION USEFUL IN ROUTINE CLINICAL PRACTICE:
Compatibility charts in common use can be found on the ‘documents and links’ page of the website.

General principles:
1) It should **NEVER** be necessary to administer an IV injection via a running infusion that also contains a medicine additive. Any infusion containing a medicine should be stopped temporarily and the line should be flushed both before and after the injection is given. If an IV injection is administered via a line which is being used to administer a compatible crystalloid (e.g. sodium chloride 0.9% infusion) this can be used as the flushing solution.

2) Infusions containing a medicine should ideally be infused separately. If it is absolutely necessary to administer two infusions via the same vascular access device, mixing should occur as close to the vascular access device as possible.

3) A medicine should not be added to any infusion which already contains a medicine additive unless the addition is one of a very few exceptions which are identified in the appropriate monographs.

4) All medicine mixtures should be checked for signs of incompatibility, for example cloudiness, change in colour, haze or formation of precipitate.

5) The cannula insertion site should be regularly checked for signs of local inflammation. Chemical phlebitis may be attributable to a medicine incompatibility.

6) Additions should never be made to the following infusions and these infusions should always be infused separately
   - Parenteral nutrition solutions (except glutamine)
   - Sodium bicarbonate infusions
   - Phosphate preparations
   - Blood components
   - Plasma substitutes e.g. artificial volume expanders such as starches and gelatins

7) Try to avoid infusing a medicine which is being administered at a very low infusion rate in conjunction with another infusion containing a medicine additive because the ‘dead-space’ volume of the vascular access device may result in prolonged contact of the two medicines.

8) If it is necessary to infuse **more than** two medicines via the same delivery route ensure that all medicines are compatible with each other and with the diluents used.

9) It is good practice to infuse inotropes and vasopressors via a dedicated infusion lumen of a central venous access device. Different inotropes and vasopressors may be infused in combination via the same lumen provided they are compatible.

The following summarises specific points to be considered when interpreting the compatibility information provided:-

1) The information is provided as a guide only and is not exhaustive.

2) Published compatibility information is usually based on specific medicine infusion concentrations and requires careful interpretation if different concentrations are used.

3) Compatibility information supplied is relevant to the standard infusion concentrations recommended for use in this website but may not apply to other concentrations such as off-license concentrations used in fluid restricted patients. Check with a pharmacist if different concentrations are used.

4) Medicine compatibility information is mainly based on physical compatibility i.e. there are no visible sign of incompatibility. However, clinical efficacy is not implied as this may not have been demonstrated.

5) **When stated as compatible in the Injectable Medicines Guide it is assumed that medicines meet close to the vascular access device and not in an infusion bag, burette or syringe.**

6) When using the compatibility information, check that the medicines are compatible with the infusion fluids in use. For example if dopamine in sodium chloride 0.9% is to be infused through a line containing dobutamine in glucose 5%, check that both dopamine and dobutamine are compatible with both sodium chloride 0.9% and glucose 5%.

7) pH values have been included in the Injectable Medicines Guide. Medicines with widely differing pH values are usually incompatible.
SPECIAL HANDLING PRECAUTIONS:
This section details any special handling precautions described in the manufacturer’s COSHH data sheet which should be used in addition to wearing gloves and an apron when preparing and administering an intravenous medicine.

SODIUM CONTENT (mmol):
The sodium content stated is of the product as it is supplied by the manufacturer. It is stated in mmol throughout. The sodium content will alter if sodium chloride 0.9% is used to reconstitute or dilute the medicine.

OSMOLARITY:
1) The majority of intravenous medicines are formulated to have an osmotic pressure similar to that of plasma. This minimises disturbance to the tissues when administered.
2) Infiltration into tissues of solutions with an osmolarity greater than that of plasma (>290 mOsmol/l) may cause tissue damage. It is recommended that if the osmolarity is greater than 600mOsmol/L the medicine should be infused via a central venous access device, unless there is a clinical emergency in which case a large peripheral vein can be used.
3) The following is a selection of medicines that have high osmolarity and may potentially cause a problem if extravasated.

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Osmolarity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium gluconate 10%</td>
<td>670mOsmol/L</td>
</tr>
<tr>
<td>Calcium chloride 5mmol/10ml</td>
<td>1,500mOsmol/L</td>
</tr>
<tr>
<td>Glucose 20%</td>
<td>1,110mOsmol/L</td>
</tr>
<tr>
<td>Glucose 50%</td>
<td>2,775mOsmol/L</td>
</tr>
<tr>
<td>Magnesium sulphate 10%</td>
<td>933mOsmol/L</td>
</tr>
<tr>
<td>Mannitol 20%</td>
<td>1,100mOsmol/L</td>
</tr>
<tr>
<td>Parenteral nutrition bags</td>
<td>(variable with bag contents)</td>
</tr>
<tr>
<td>Potassium chloride 20mmol/10ml</td>
<td>4,000mOsmol/L</td>
</tr>
<tr>
<td>Sodium bicarbonate 4.2%</td>
<td>1,004mOsmol/L</td>
</tr>
<tr>
<td>Sodium bicarbonate 8.4%</td>
<td>2,008mOsmol/L</td>
</tr>
<tr>
<td>Sodium chloride hypertonic solutions (concentrations exceeding 1.8%)</td>
<td></td>
</tr>
<tr>
<td>X-ray contrast media</td>
<td></td>
</tr>
</tbody>
</table>

pH:
Medicines with a high or low pH, i.e. greater than 9 or less than 5 (e.g. aciclovir, amphotericin, ganciclovir, methylthioninium chloride, phenytoin, phenobarbital) are likely to cause tissue damage if extravasation occurs. It is recommended that these products are administered via a central venous access device unless in a clinical emergency in which case a large peripheral vein can be used. The pH stated is usually that of the undiluted reconstituted medicine but in most circumstances dilution does not significantly alter the pH.

OTHER COMMENTS:
This section:
- States if a product requires protection from light whilst it is being administered.
- Gives details of any required pre-medication.
- Highlights any SPC changes or a significant NPSA/MHRA alert which has become available since a monograph was last published.
INFUSION PUMP TO USE ACCORDING TO THERAPY CATEGORY:
The following information is taken from the Medical Devices Agency Device Bulletin: ‘Infusion systems MDA DB2003(02) v2.0 Nov 2010’
Infusion pumps are designed for a variety of clinical applications and their performance characteristics vary. The same level of technical performance of infusion pumps is not necessary for every clinical therapy. There are three therapy categories (A, B and C) and they determine the performance and safety parameters of the infusion pump required to deliver a particular medicine.

**Therapy categories and critical performance parameters for an infusion pump**

<table>
<thead>
<tr>
<th>Therapy Category</th>
<th>Therapy description</th>
<th>Patient group</th>
<th>Critical performance parameters for infusion pump</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Medicines with narrow therapeutic margin</td>
<td>Any patient</td>
<td>Good long term accuracy</td>
</tr>
<tr>
<td></td>
<td>Medicines with short half-life¹</td>
<td>Any patient</td>
<td>Good short term accuracy</td>
</tr>
<tr>
<td></td>
<td>Any infusion given to neonates</td>
<td>Neonates</td>
<td>Rapid alarm after occlusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Small occlusion bolus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Able to detect very small air embolus (volumetric pumps only)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Small flow rate increments</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Good bolus accuracy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rapid start-up time (syringe pumps only)</td>
</tr>
<tr>
<td>B</td>
<td>Medicines, other than those with a short half-life¹</td>
<td>Any patient except neonates</td>
<td>Good long-term accuracy</td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>Fluid maintenance Transfusions</td>
<td>All volume sensitive patients except neonates</td>
<td>Alarm after occlusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Small occlusion bolus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Able to detect small air embolus (volumetric pumps only)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Small flow rate increments</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bolus accuracy</td>
</tr>
<tr>
<td>Diamorphine²</td>
<td></td>
<td>Any patient except neonates</td>
<td></td>
</tr>
<tr>
<td>C³</td>
<td>Parenteral nutrition Fluid maintenance Transfusions</td>
<td>Any patient except volume sensitive patients or neonates</td>
<td>Long-term accuracy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alarm after occlusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Small occlusion bolus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Able to detect air embolus (volumetric pumps only)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Incremental flow rates</td>
</tr>
</tbody>
</table>

**Notes on Table**
1) The half-life of a medicine cannot usually be specified precisely, and may vary from patient to patient. As a rough guide, medicines with half-lives of five minutes or less might be regarded as ‘short’ half-life drugs.
2) Diamorphine is a special case. The injected agent (diamorphine) has a short half-life, whilst the active agent (the metabolite) has a very long half-life. It is safe to use a device with performance specifications appropriate to the half-life of the metabolite.
3) Not all infusions require an infusion pump. Some category C infusions can appropriately be given by gravity.
PRODUCT RISK FACTORS: This section describes the risk category that the injectable product has been allocated using the NPSA risk assessment tool described in the NPSA Patient Safety Alert 20; Promoting safer use of injectable medicines.

- This section is only accessible using a ‘pharmacy’ password.
- This section is intended to provide an example product risk assessment only and is not intended to replace a locally performed product risk assessment.

OTHER INJECTABLE ROUTES OF ADMINISTRATION:
This section is only accessible using a pharmacy password. It includes injectable routes, other than IV (both licensed and, if known, unlicensed) which may be used.

CURRENT SUPPLIERS:
This section includes electronic links to the following:
- Summary of Product Characteristics (SPC)
- Patient Information Leaflets (PILs)

PHARMACY NOTES:
This section is only accessible using a ‘pharmacy’ password. It includes:

- Notes on identified inconsistencies e.g. rate of administration of digoxin differs in BNF and SPC.
- Information on how long the reconstituted/diluted preparation can be stored before use is included if available.

LINKS TO EXTERNAL RESOURCES:
The following electronic links are included. This information can only be accessed via the internet:
- British National Formulary (BNF)
- BNF for children (BNFc)
- Electronic medicines compendium (emc)

Other useful links, can be found on the ‘Documents and Links’ page of the website.