دانشگاه علوم پزشکی گیلان Dosing Consideration in Pediatrics

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متخصص داروسازى بالينى

1401

Solid Dosage Forms

D



Advantage of Pill Splitting:

- Different tablet strengths often cost about the same. Patients who cannot afford their medications have received a higher strength tablet with directions to take 1/2 tablet (or even 1/4 tablet) per dose
- Some health insurers have denied payment of prescriptions for the lower strength of certain drugs, thus requiring patients to receive the higher strength tablet and split it in half for each dose
- Some healthcare organizations have not purchased all commercially available strengths of oral medications. Thus, some of the drugs may require tablet splitting for patient-specific doses in the inpatient setting.
- Patients may not be able to swallow whole tablets

Medication factors.

- Enteric-coated/extended-release tablets
- Very small tablets
- Asymmetrical tablets
- Capsules
- Teratogenic medications (e.g., bosentan).

- Hard outer coated tablet Hard outer coating will make it tough to split and it will also alter the absorption in our body.
- Extended release pill This tablet will be formulated such that it will release the medicine slowly in our body throughout the day and this property will get affected because of splitting.
- Small pills, which cannot get split.
- Capsules have to be taken as a whole always as it contains gel or powder in it.
- One should not split a vial. If medicine is exposed to oxygen it may degrade the content and affect the drugs.





- tablet splitting is preferable to dispersing or crushing tablets and giving a proportion of the tablet
- to split tablets, use a tablet splitter, which should be cleaned and replaced following manufacturer and local specifications
- tablets should be split along the scoreline
- if the tablet is not scored, consult a pharmacist prior to splitting
- tablets should not be split into less than quarter segments, unless according to manufacturer specifications
- tablets should be assessed visually to ensure segments appear equal in size
- storing tablet segments should be in accordance with local policies

- The tablet should split consistently into equal parts using either the fingers or a tablet splitting device. Use of a device is preferred.
- The medication should be of a pharmacologic and pharmacokinetic nature such that small variations in daily dose are unlikely to adversely affect patient response to therapy. For example, Narrow Therapeutic Index medications should not be included in a tablet splitting program.
- The drug selected should be supported by clinical data demonstrating desired clinical

- outcomes, data demonstrating the bioequivalence of split tablets, or meet weight variation specifications.
- The health system's Pharmacy and Therapeutics Committee or equivalent body should approve the tablets that meet the selection criteria for tablet splitting.
- Physicians, pharmacists and patients or their caregivers should be encouraged to report any problems with tablet-splitting options.
- A physician should be allowed to designate that a specific patient is not an appropriate candidate for tablet splitting.
- A patient or caregiver should have the right to request an exception to tablet splitting with appropriate justification.

Tablets That May Require Special Consideration

- Tablets with special coatings to protect the drug from moisture.
- Tablets with enteric coatings that prevent them from dissolving in the stomach.
- Time-release and extended release tablets and capsules, if the coating is an integral part of the release mechanism.
- Tablets that cannot be consistently split into equal parts, adversely affecting patient response to therapy.
- Tablets containing two medications, in which the desired dose would be obtained for only one of the two medications

Drugs Suitable for Split:

- FDA (Food and Drug Administration) has issued a list of drugs which can be split and also the warnings and risks. Most of the drugs which are prescribed for the treatment of high cholesterol (statins), high blood pressure and depression will be suitable for split.
- Medicines suitable for safe split are as follows: (a) Atorvastatin, (b) Lovastatin, (c) Rosuvastatin, (d) Pravastatin, (e) Simvastatin, (f) Amlodipine, (g) Atenolol, (h) Doxazosin, (i) Lisinopril, (j) Metoprolol, (k) Quinapril, (l) Citalopram, (m) Clonazepam, (n) Olanzapine, (o) Paroxetine, (p) Sertraline, (q) Finasteride, (r) Sildenafil, (s) Tadalafil, (t) Vardenafil, (u) Levothyroxine, (v) Metformin

Drugs Not Suitable for split

Medicines not suitable for split are Oxycodone (pain), Omeprazole (heart burn), Cetirizine (allergy), anti-seizure medications, birth control pills, blood thinners such as Warfarin and Coumadin and chemotherapy drugs.

- Don't use scissors or kitchen knives to cut tablets—this causes uneven splitting and crumbling, which changes the correct dose.
- Don't split extended-release or time-release medication.
- Don't split very small or unevenly shaped tablets.
- Don't split the entire vial of tablets at one time—air degrades the exposed drug.
- Do split your tablets only as you need them to maintain potency.
- Do use a commercially available tablet-cutting device.
- Do talk to your pharmacist if you have any physical limitations (such as arthritis) that would keep you from splitting tablets accurately or for any other concerns about tablet-splitting.

Liquid Dosage Forms

- Storage & Stability
- Measurement





"Spoons come in many different sizes and are not precise enough to measure a child's medication. Using the wrong size spoon repeatedly, causes child drug tosicity".

Use <u>only</u> the measuring tool provided with the medication when giving your child a liquid drug. Do not hesitate to ack your pharmacist how to use the measuring device properly.









مصرف داروهای وریدی

- دارو هایی که از طریق وریدی مصرف می شوند، قدرت و سرعت اثر
 بالاتری در مقایسه با فرم خور اکی دارند
- یکی از نگرانیهای مهم در مصرف فراورده های وریدی، نحوه آماده
 سازی, ناسازگاری این فراورده ها با حاملها و دارو های دیگر و نحوه
 تزریق است





Advantages & Disadvantages of I.V. medications

Advantages

- Provide direct access to the circulatory system
- A route for drugs that do not irritate the gastric mucosa
- A route for instant drug action
- A route for delivering high drug concentrations
- Instant drug termination if sensitivity or an adverse reaction occurs
- Route of administration in patients in whom use of the GI tract is limited

Advantages & Disadvantages of I. V. administration cont

Disadvantages

- Drug interaction because of incompatibilities
- Adsorption of the drug being impaired because of leaching into the I.V. container or administration set
- Errors in compounding of medication
- Speed shock
- Extravasation of a vesicant drug
- Chemical phlebitis

Common error in Administering Medications

- Lack of knowledge about drugs
- Errors in drug identity checking
- Mistakes in calculations
- Improper use of pumps and controllers

Drug incompatibilities

Three broad categories

- Physical: occur when one drug is mixed with other drugs or solutions to produce a product that is unsafe for administration
- **Chemical:** a reaction of a drug with other drugs or solutions, which results in alterations of the integrity and potency of the active ingredient
- **Therapeutic:** an undesirable effect occurring in a patient as a result of two or more drugs being given concurrently

I. V. Medication delivery

IV medication can be delivered by

- Continuous infusion
- Intermittent infusion
- IV push

مصرف داروهای وریدی

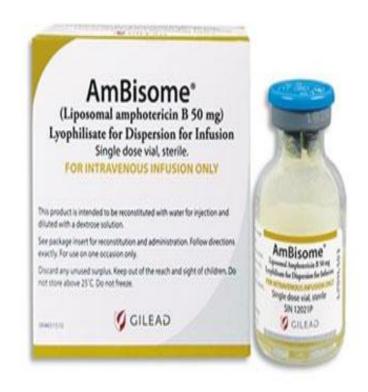
- زمانی که دارو ها به حاملی اضافه می شوند، یا چند دارو همزمان در یک
 حامل تجویز می شوند:
 - مونو گراف دارو باید چک شود تا داروها با هم ناسازگار نباشند
 - دارو ها نباید به فر اور ده های زیر اضافه شوند:
 - مانيتول
 - بیکربنات سدیم
 - فراورده های خونی
 - د تغذیه وریدی
 - امولسيونهاي دارويي نظير پروپوفول

مصرف داروهای وریدی

- فراورده های وریدی که نیاز به آماده سازی دارند نظیر آنتی بیوتیکهایی
 که به صورت پودر فرموله می شوند، بایستی بلافاصله پس از آماده
 سازی مصرف شوند
- تاخیر در مصرف ممکن است منجر به رشد میکروبی، تخریب و تجزیه دارو
 <u>گردد</u>

دستور العمل آماده سازی دارو های وریدی

- دارو را با نام بیمار و دستور پزشک مطابقت دهید
 - 2. دستها را تمیز کنید
- 3. ترجيحا فراورده را در فضای مخصوص اين کار آماده کنيد
 - 4. موارد زیر را چک کنید
 - ا. تاريخ انقضا
 - 2. سالم بودن ويال دارو
 - 3. صحيح بودن نحوه نگهدارى دارو
 - بروشور دارو را به دقت مطالعه کنید



Liposomal amphotericin 3- 6 mg/kg



Conventional amphotericin 0.3-1.5 mg/kg







دستور العمل آماده سازی دارو های وریدی

- موارد زیر را کنترل کنید:
- دوز دارو، رقیق کننده، حامل و سرعت تزریق
 - 2. حساسيتهای دارويی بيمار (فرم تلفيق دارويی)
- 3. مطمئن شوید که نحوه مصرف دارو را به طور کامل متوجه شده اید
- 7. محاسبات لازم بر ای تعیین دوز و غلظت دارو ر ا انجام دهید و آن را با شخص دیگری چک کنید
 - حتما برای فراورده تهیه شده برچسب تهیه کنید

دستور العمل آماده سازی داروهای وریدی

موارد زیر در بر چسب دارو باید ذکر شود

- name of the medicine;
- strength (dose);
- route of administration;
- diluent and final volume;
- patient's name;
- date and time of preparation;
- expiry date and time;
- initials of the practitioner preparing the medicine
- initials of second checker

میزان خطاها در تجویز داروهای وریدی

Type of intravenous-related error	Number of errors (%)	Number of errors rated as serious (% of intravenous error type)
Wrong rate	266 (73.3)	95 (35.7)
Wrong volume	121 (33.3)	21 (17.4)
Wrong mix	21 (5.8)	5 (23.8)
Drug incompatibility	3 (0.8)	1 (33.3)
Total intravenous administrations with at least one clinical error	363*	99* (27.3)

*Sums exceed totals because of multiple errors within the same intravenous administration.

Errors in the administration of intravenous medications, BMJ quality & safety,

میزان خطاها در تجویز داروهای وریدی

Drug group	Number of intravenous administrations of this drug type	Number of administrations in drug group with at least one intravenous error (percentage in drug group)	Number of intravenous errors rated as serious (percentage in drug group)
Anti-infective	455	305 (67.0)	81 (26.6)
Antiemetic	24	18 (75.0)	8 (44.4)
Antiulcerant	15	14 (93.3)	3 (21.4)
Steroid	21	14 (66.7)	2 (14.3)
Diuretic	8	4 (50.0)	1 (25.0)
Anticoagulant	10	3 (30.0)	3 (100.0)
Narcotic	3	2 (66.7)	1 (50.0)
Other	7	2 (28.6)	0 (0.0)
Iron	8	1 (12.5)	0 (0.0)
Paracetamol	17	0 (0.0)	0
All drug types	568	363 (63.9)	99 (27.3)

Errors in the administration of intravenous medications, BMJ quality & safety,

Sodium Content

- Some medicines, e.g. many antibiotics, are formulated with a considerable sodium content; for example, metronidazole contains 13.15mmol/500-mg bag.
- This may be clinically significant and may need to taken into account when therapeutic choices are made.

рН

- help practitioners predict <u>possible Y-site incompatibilities</u> of medicines when no compatibility information exists
- Injections with greatly differing pH values should not be administered concurrently down the same line as this may result in either precipitation or inactivation of the medicines
 - for example, the pH of phenytoin injection is 12 and the pH of haloperidol injection is 3, making them incompatible
- The pH can also give the practitioner an indication of the irritancy of the drug.
- Medicines that are either highly acidic or alkaline may be harmful if <u>extravasation</u> into the surrounding tissue occurs, causing tissue damage.

Light-sensitive infusions

- Some drugs undergo <u>photolysis and photodegradation</u> if exposed to natural daylight (ultraviolet radiation) and <u>fluorescent light</u> during administration.
- This can result in <u>loss of therapeutic effect</u> and the <u>production of toxic products</u>.

Light-sensitive infusions

- To reduce these reactions, the products must be protected from light not only during storage but <u>also once</u> <u>diluted and ready for use</u>.
- Periodic visual inspection of the diluted solution for the occurrence of discoloration and/or precipitation is recommended during its infusion.

Visual inspection of prepared product

- <u>All products</u> prepared for intravenous use make reference to this requirement as part of the preparation procedure.
- Hold the syringe or infusion container up to a light source and, while looking straight through the solution, invert the product. Usually all that is seen are air bubbles
- Observe for a few seconds for anything (particles) moving downwards and any untoward color changes as described in the specific monograph.

Displacement value

- Injection products formulated as dry powders or lyophilised cakes must be reconstituted with a suitable diluent before administration.
- Sometimes the final volume of the injection is greater than the volume of liquid added to the powder.
- This volume difference is called the displacement value

Displacement value

• Example:

- The displacement value of amoxicillin injection
 250mg is 0.2 mL.
- If 4.8mL of diluent is added to a 250-mg vial, the resulting volume is 5mL, i.e. 250mg in 5 mL.
- If 5mL of diluent is added, the resulting volume is
 5.2 mL, i.e. 250mg in 5.2mLor 240.38mg in 5mL.

Displacement value

This must be taken into account when reconstituting the drug if only part of the vial is to be used.

Cefotaxime:

- Reconstitute each 500-mg vial with 2mLWFI (use 4mL for each I-g vial; I0mL for each 2-g vial)
- Displacement value 0.2mL/500mg; 0.5mL/1 g; 1.2 mL/2 g

Flushing intravenous lines and cannulas

- Flushing between the administration of different medicines
 - To avoid any problems with incompatibilities.
 - Ensures the total drug dose is presented for systemic effect
 - Prolongs the viability of the cannula or line
- If two drugs being administered one after the other are known to be compatible, then flushing the line or cannula need only be done before and after administration of the medicines.

Flushing intravenous lines and cannulas

- Commonly 5-10mL of NaCl 0.9% or Gluc 5% is used to flush the dead space of a cannula, whereas 20mL is usually needed for an administration set.
- The practitioner must check each monograph before deciding which flush to use, to ensure that both drugs are compatible with the chosen flush.

Flushing intravenous lines and cannulas

Frequent flushing of unused lines is also necessary in order to maintain patency of the line or cannula.

Safe admixture

• A safe admixture is one that is:

- > Free from microorganisms
- > Free from particulate matter ,undecomposed and clinically compatible

Incompatibility

- Reaction between two or more drugs are be administration through single IV line or given in a single solution are no longer <u>safe</u> or <u>effective</u> for patients
- Characteristics:
- Color Change
- Hazy Appearance
- Precipitation

Not all Incompatibility are dangerous

Some are just normal

Color Change:

 Cefazolin or Dobutamin may show some color change but not a sign of incompatibility

* Hazy Appearance:

 When Ceftazidime is reconstituted, CO2 gas is released and cause a Hazy Appearance

* Precipitation:

✓ When Paclitaxel is refrigerated , dissolve again at room temperature

Contributing Factors

Light:

> Amphotericin, Cisplatin, Metronidazole must be protected from light

Temperature:

 Cefazolin is stable at room temperature for 24 hours but under refrigeration for 14 days

Consentration dependent:

Co-trimoxazole 5 ml/ml D5W stable for 2 hours, where as 5ml/125 ml is stable for 6 hours

Length of time in solution:

Meropenem is stable when diluated in NS at room temperature for≤ 4 hours and under refrigeration≤ 24 hours

Difference in pH

Types of Incompatibilities

- Therapeutic Incompatibility
- Physical Incompatibility
- Chemical Incompatibility
- Drug IV Container Incompatibility

Physical Incompatibility

- The incompatibility that is mainly on solubility changes and container interactions
- Insolubility
- Sorption Phenomena
- Gas formation
- Change of pH of solution

Prevention

- i. Do not administer a precipitate forming drug
- ii. Avoid mixing drugs prepared in special diluents with other drugs
- iii. In administration of multiple intravenous medications, prepare each drug in a separate syringe

Chemical Incompatibility

- Results from the molecular changes or rearrangement and leads to chemical decomposition
- > Hydrolysis
- > Oxidation reaction
- Reduction reaction
- Photolysis

Prevention

- i. Store drugs in relatively water-proof containers
- ii. Minimize the exposure time of the drug
- iii. Keep away from suspected reducing agents
- iv. Storing drugs in lightproof containers can usually prevent photolysis

Drug IV Container Incompatibility

 Incompatibility that arise from the chemical reaction of the drug and the Intravenous container

Adsorption:

The property of a solid/liquid to attract and hold to its surface a gas, liquid, solute or suspension e.g: propofol

General Ways Of Prevention/ Minimization Of Incompatibilities

Mix thoroughly when a drug is added to the preparation

Minimize the number of drugs mixed together in an IV solution

Separation of drug doses by time and place

Solutions should be administered promptly after mixing so that occurrence potential reactions can be minimized

Usage of multi-lumen catheters

Use in-line filters

Always refer to compatibility references (Check for compatibility)

One cannot easily remember all these incompatibilities, but the reference should be available for ready consultation when intravenous therapy is being used



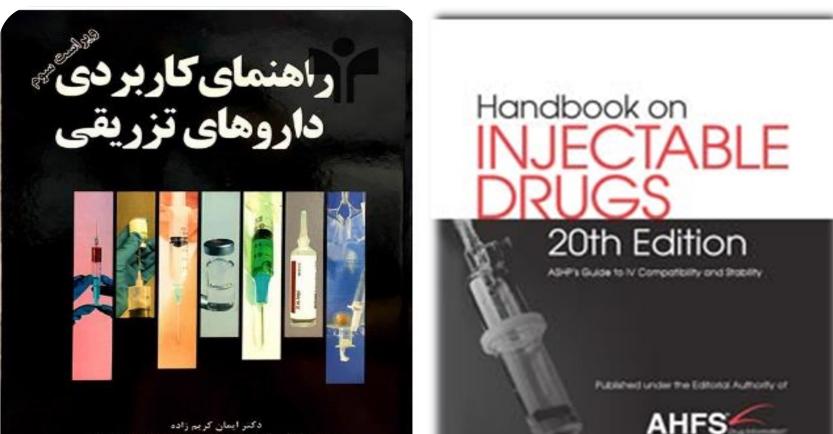
AmBisome – technical information	
Incompatible with	Amphotericin is incompatible with NaCl 0.9% and all electrolyte solutions. Amphotericin is incompatible with most drugs; care must be taken to avoid inadvertent contact in infusion lines.
Compatible with	Flush: Gluc 5% Solutions: Gluc 5% Y-site: Not recommended
рН	5-6
Sodium content	< 0.5 mmol/vial
Storage	Store below 25°C in original packaging. Do not freeze.
Displacement value	0.5 mL/vial but this is already accounted for in the initial reconstitution of the vial
Stability after preparation	 From a microbiological point of view, should be used immediately; however: Reconstituted vials are single use only but may be stored at 2-8°C for 24 hours. Prepared infusions may be stored at 2-8°C and infused (at room temperature) within 24 hours.
Pharmacokinetics	Elimination half-life: 7-10 hours after first dose; 100-153 hours after several doses.

 Risk rating: RED
 Score = 8

 High-risk product: Risk-reduction strategies are required to minimise these risks.

 Image: Rec rec reduction reduction strategies are required to minimise these risks.

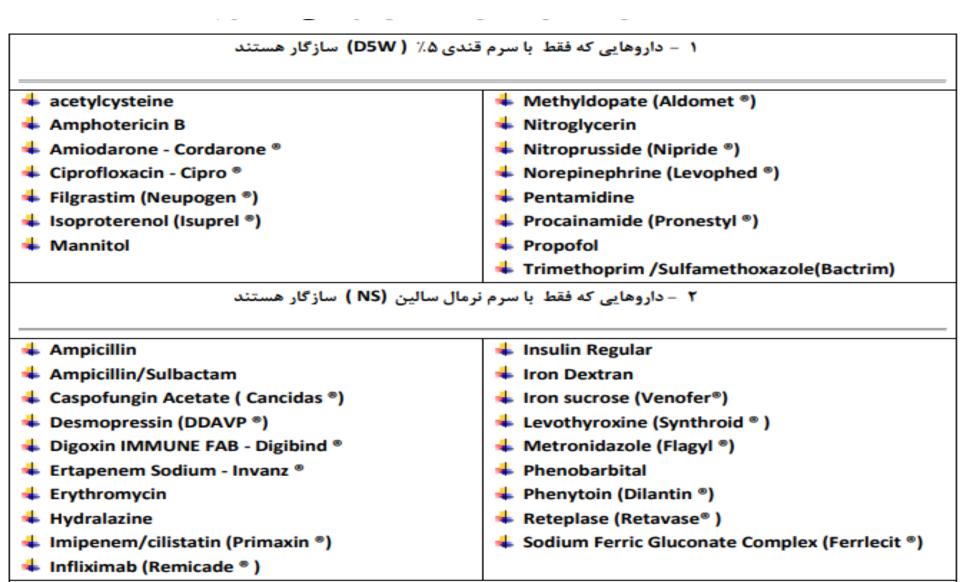
This assessment is based on the full range of preparation and administration options described in the monograph. These may not all be applicable in some clinical situations.



دکتر ایمان کریم زاده بعبو فببنت غلمي كرود ناروت

دکتر سها نمازی علمى الرود باروسارى بالمنى بالممكمة فاروسان

D



- A multi-dose vial is a vial of liquid medication intended for parenteral administration (injection or infusion) that contains more than one dose of medication.
- Multi-dose vials are labeled as such by the manufacturer and typically contain an antimicrobial preservative to help prevent the growth of bacteria.
- The preservative has no effect on viruses and does not protect against contamination when healthcare personnel fail to follow safe injection practices.

- Multi-dose vials should be dedicated to a single patient whenever possible.
- multi-dose vials must be used for more than one patient, they should only be kept and accessed in a dedicated clean medication preparation area (e.g., nurses station), away from immediate patient treatment areas.
- This is to prevent inadvertent contamination of the vial through direct or indirect contact with potentially contaminated surfaces or equipment that could then lead to infections in subsequent patients.
- If a multi-dose vial enters an immediate patient treatment area, it should be dedicated for single-patient use only.

- If a multi-dose has been opened or accessed (e.g., needle-punctured) the vial should be dated and discarded within 28 days unless the manufacturer specifies a different (shorter or longer) date for that opened vial.
- If a multi-dose vial has not been opened or accessed (e.g., needle-punctured), it should be discarded according to the manufacturer's expiration date.

- If using a multi-dose vial with a rubber stopper and a sharp safe needle system:
- I. Remove the thin seal cap from the top of the vial without touching the rubber stopper.
- > 2. Clean the rubber stopper with antiseptic.
- 3. Using the appropriate sharp safe needle for medication withdrawal and injection, inject a volume of air into the vial equivalent to the amount of solution to be withdrawn.
- 4. Insert the spike of the sharp safe needle into the vial until the "wing" of the pin touches the vial's rubber stopper.
- 5. Hold the vial with the non-dominant hand and turn it up and pull the sharp safe needle back to where the bevel is beneath the fluid level.

- If using an ampoule:
- I. Lightly tap, shake or swirl the ampoule to dislodge any solution from the neck of the container.
- 2. Ensure the glass ampoule is appropriately wrap/covered for your protection i.e. by an ampoule cracker, antiseptic swab, gauze, etc.
- 3. Grasp the ampoule, snap off the top away from you and others, and discard the top in an appropriate sharps disposable container.
- 4. Insert the appropriate sized sharp safe needle into ampoule and draw up the appropriate amount of solution, and then remove the needle from the ampoule.
- 5. Do not allow the needle to touch edges of ampoule
- 6. Gently advance the plunger of the syringe to expel air from the solution.

- Remove the filled syringe with the drawing up needle attached. Do not leave the drawing up needle in the vial.
 Avoid touching the top of the vial.
- Detach the filled syringe and attach a new sterile injection needle.
- Hold the vial on a fat surface. Pierce the self-sealing stopper in the center with the needle tip and inject the measured air into the space above the solution. Do not inject air into the solution. If the vial in use is a single-use vial, there is no need to inject air into the vial.

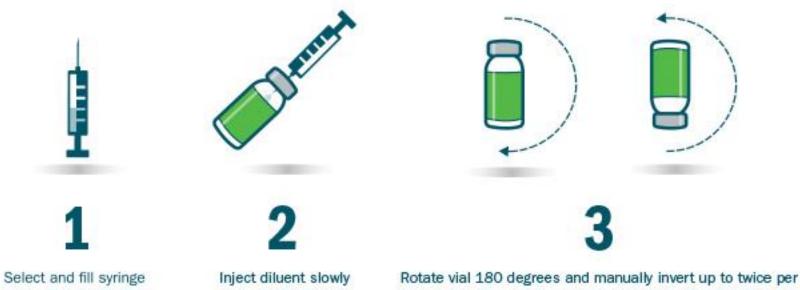


Sterile for 96h Not suitable for suspensions: NPH









with 18 mL of 0.9% sodium chloride

into CroFab® vial

second until no solid material remains in the vial. Do not shake. The entire dose should then be further diluted in normal saline to a final total volume of 250 mL for infusion

- A drug in powdered form is necessary when a medication is unstable as a liquid form for a long period
- Flush IV line before and after administration. The most common fluid administered as an IV flush is sodium chloride 0.9%. In some instances, glucose 5% may be used if it is more suitable for use due to compatibility with the IV medicine being administered.
- Insert the diluent syringe into the vial, via the rubber cap at a 45 degs angle, with needle bevel uppermost. Changing the angle to 90 degs as the needle pushes through is considered to minimise coring, in which rubber is forced into the lumen of the needle with the resultant risk that it may then be injected into the patient (Dougherty and Lister, 2004);

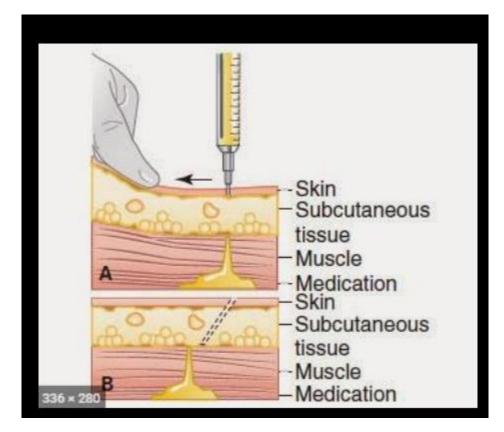
Before reconstitution: Store at 20^o to 25^oC. After reconstitution: Stable for 24 hours at room temperature or 10 days if refrigerated 36^o to 46^oF.
Reconstitution: For I.M. Use: Add 2 mL of Sterile Water for Injection. SHAKE WELL. Withdraw entire contents. Provides an approximate volume of 2.2 mL (225 mg per mL). For I.V. Use: See insert.

INTRAMUSCULAR INJECTION SITES

- Deltoid Used for smaller volumes Typically no more than 1 mL • Some sources state 2 mLs can be given here, but this is painful for the patient
- Ventrogluteal and Dorsogluteal Used for larger volumes
 Typically less than 3 mLs Some resources state up to
 5mLs but this is very painful for the patient •
- Ventrogluteal The safest site for adults and children older than 7 months • Deep and not close to any major blood vessels

Z TRACK METHOD

• Pulling the skin downwards or sideways at the site before injection. Must remove needle from injection site prior to releasing the skin because the needle could snap off and remain in the muscle • After removing the needle the track is closed when the skin is released, preventing leakage of medication into the subQ tissue or even out of the injection site itself • Can be utilized with all IM injections but must be utilized with caustic medications or medications that will stain the skin • Caustic – Rocephin and Phenergan • Discoloration – Vit BI2 and Iron



There are two main reasons for diluting medicines within neonatology and paediatrics. Firstly the dosages required are usually very small. Sometimes the volume required is so small that it is not straightforward to measure it accurately. See BOX 6 for a worked example. Secondly some drugs require further dilution for reasons such as viscosity and/or irritation of veins, e.g., phenobarbitone should be diluted by 10 times the volume of drug drawn up