

Solubility Principles and Practices for Parenteral Drug Dosage Form Development

Stephanie Sweetana and Michael J. Akers

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STEPHANIE SWEETANA and MICHAEL J. AKERS*

Pharmaceutical Sciences, Lilly Research Laboratories, Indianapolis, Indiana

Introduction

A common problem experienced in the early development of drugs intended for parenteral, especially intravenous, administration is the solubilization of a slightly soluble or water insoluble active ingredient. Drug solubilization has been the subject of many scientific articles and textbooks (referenced throughout this article); yet despite this attention and available literature, product development scientists still encounter significant difficulties in solving their solubility problems.

Theories of solute solubilization are not easy to understand. Solubilization processes are amazingly complex and require a fair amount of expertise in physical chemistry to interpret and apply current theoretical models. Much of the literature deals with solubilization theory and does not offer much practical help to the inexperienced scientist under a lot of pressure to find a solution to his/her solubility problem.

This article intends to help the scientist in early drug formulation design for parenterally administered drug products by reviewing pertinent literature on solubilization and reducing it to simple approaches one can use to solve solubility problems. The classical theories of solubility, and how they relate to pharmaceutical systems of interest will be reviewed and practical applications discussed. Because of the common concerns regarding cosolvent toxicity and acceptability by medical and regulatory bodies, we also will treat this topic in some detail.

I. Pertinent Theory of Solubilization of Drugs

Solubility theories deal with conversion of a substance from one state to another, and the equilibrium phenomena that are involved. Through pioneering work of Henry, Raoult and van't Hoff in the late 1800's, the properties of various solutions have been defined in theories. These early theories form the basis by which more complex systems, such as those encountered in the biological sciences, are compared and understood.

No single theory can adequately explain solubility behavior of uncharged molecules in a variety of solvent systems. Each theory is suited for select combinations of solutes and solvents where certain intermolecular forces are assumed to predominate, or conversely, be absent. The classical theories of solubility have been explained most simply in terms of intermolecular interactions. Ideal solution theory assumes solute-solute, solventsolvent and solute-solvent interactions are completely uniform in strength and nature. An example of a solution behaving ideally is a non-polar solute in a non-polar solvent such as naphthalene in benzene. Regular solution theory evolved to account for the imbalance of intermolecular interactions that often occur between dissimilar systems of a solute and solvent. The focus of this theory are systems of low polarity such as steroids in hydrocarbon solvents. Extended regular solution theory incorporated additional parameters such as dispersion, polar and hydrogen-bonding interactions into regular solution theory. Various approaches have been used to represent these molecular interactions, leading to a variety of models to predict and explain solubility behavior of polar solutes in polar systems, each with different approximations and assumptions (1-4).

In most pharmaceutical systems, the routine application of these models to predict solubility and simplify formulation development is complex. Most drugs of interest are ionizable, contain polar polyfunctional groups, and are capable of forming multiple hydrogen bonds. The majority of parenterally acceptable cosolvents-such as propylene glycol, polyethylene glycol, ethanol and water-are capable of self association through hydrogen bond formation. Such interactions may alter solvent structure and, as a result, influence solubility in an unpredictable manner (1). Examples of this phenomena are deviations from log-linear solublization of nonpolar solutes in a polar cosolvent system (5). For the models to adequately describe solubility behavior, proper weighting must be assigned to the relative importance of competing self-associations and strong intermolecular interactions. Currently this is being modeled by various computer intensive group-contribution approaches, some of which allow for the mutual interactions of various functional groups (1).

In the biological sciences, many solutes of interest are capable of acting as acids or bases. In an ionizing media such as water, they may dissociate into ions which are usually highly water soluble. To what extent a molecule is ionized in an aqueous solution is largely dependent on its pKa and the pH of the media. The Henderson-

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rate Center, Indianapolis, IN 46285.

Hasselbalch equation is a mathematical expression of this relationship (3). In formulation development, consideration of the amount of un-ionized drug in solution is helpful to avoid unexpected precipitation of this form. As the pH of a drug solution is changed, the amount of free acid or base may increase and eventually exceed the limited solubility of this form. It is possible to calculate the pH of precipitation and of maximum solubility, if the pKa of the molecule and the solubility of the un-ionized and ionized forms are known (3, 6). Generally, two pH units above or below the pH_{max} value establishes the desired pH for formulation. For drug molecules with multiple ionizable groups these equations are more complicated to apply and so experimentally generated solubility data are usually collected.

Through our own experience, we find that theory gives us some direction with respect to experimental approaches, but we still need to rely on the empirical experimentation to screen for systems which offer the most promise in solubilizing water-insoluble drugs.

II. Formulation Design

Usually, the first approach used to increase the solubility of an insoluble drug in water is to form more water soluble salts. Berge and co-workers (7) wrote what is now a near classic review of salt form strategies acceptable for pharmaceuticals. If salt formation is not possible, e.g. too unstable, or does not render the molecule sufficiently water soluble, a series of formulation approaches may be investigated. Table I summarizes these general strategies. Often a useful approach to increase the aqueous solubility of an ionizable drug is pH adjustment. The next approach most frequently tried is the use of water-miscible cosolvents. Other approaches to be discussed briefly include the use of surface active agents and complexing agents. Development of emulsified and colloidal drug delivery systems for intravenous administration are becoming more widely and successfully applied. They may confer to the entrapped or associated drug significantly different proper-

Approach	Examples	Important Formula Considerations	Useful Tests	
pH adjustment pH 2 to 12		Drug stability pH ions to buffer or adjust pH Drug precipitation upon infusion drug concentration use of buffer/buffer capacity infusion rate Formula irritation isotonicity infusion rate & duration drug vs vchicle drug precipitation	pH rate profile pH solubility profile Freezing point depression In vitro precipitation model In vivo phlebitis model In vitro cell lysis studies	
Cosolvent	Polyethylene glycol Propylene glycol Ethanol Dimethylacetamide	Systemic toxicity total cosolvent administered Drug precipitation upon infusion drug concentration infusion rate Formula irritation isotonicity infusion rate & duration drug vs vehicle drug precipitation	Mixture studies for maximum solubility In vitro precipitation model In vivo phlebitis model In vitro cell lysis studies	
Surface Active Agents	Polysorbates Poloxamers Cremophor EL Lecithin Bile salts	Hypersensitivity in animals Formula irritation isotonicity infusion rate & duration drug vs vehicle	<i>In vivo</i> phlebitis model <i>In vitro</i> cell lysis studies	
Complexing Agents	Cyclodextrans Water-soluble vitamins	Purity of excipients and drugs Formula irritation isotonicity infusion rate & duration drug vs vehicle	Phase solubility diagrams In vivo phlebitis model In vitro cell lysis studies	
Dispersed Systems	Emulsions Liposomes Nanoparticles	Sterility Particle size Pharmacokinetics Stability	Particle size	

TABLE I Summary of Parenteral Formulation Approaches

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ties from the free form, providing the opportunity to prolong drug presence in the bloodstream or to alter disposition in the body. "Heroic" methods, reported in the literature for various cancer drugs, will also be reviewed although these methods use types and amounts of excipients that probably would not commonly be considered approvable for intravenous administration.

The basis for reliable formulation development is accurate determination of solubility. Traditional methodology is the "equilibrium method" (8) where excess drug is added to the solvent system, and some means of agitation is employed under constant temperature. Samples are withdrawn, filtered, and analyzed for drug concentration over a period of time and equilibration is demonstrated by uniformity of the data over the time interval. For sparingly soluble drugs where equilibria are slow, accurate determinations of solubility may be difficult. Useful techniques in these instances include using highly specific analytical methods to detect parent compounds, minimizing the amount of excess solid added, and assuring sufficient equilibration time (1). Solid state factors and batch-to-batch variation (different polymorphs, hydration state, crystallinity, crystal homogeneity, and impurities) may affect reproducibility of drug solubility determinations.

A. pH Adjustment

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Current FDA approved marketed parenteral products range in pH from 2 to 11. A comprehensive listing of these products may be found in Table II. For biocompatability reasons, formulation of injectables within the pH ranges of 4 to 8 is most common. However, to achieve sufficient drug solubility, a pH outside this range may be necessary.

The pH at which a product is formulated is usually determined from the pH solubility and pH rate profiles of the drug (9). A recent example of their application to aid parenteral formulation development is CI-988, a cholecystokinin-B receptor antagonist (10).

Additional formulation variables to be considered are the necessity of a buffer, buffer capacity, and drug concentration. These can influence supersaturated drug concentrations in the bloodstream, a condition that may lead to in vivo drug precipitation. The blood is very efficient at pH neutralization and normally maintains a narrow pH range of 7.38 to 7.42. For example, a low incidence of phlebitis was observed in the rabbit ear vein model when solutions over the pH range of 3 to 11, with buffer concentrations of approximately 0.3 M, were administered in a single small volume (1 mL) bolus dose (11). Simple screening tests consisting of a computational model where drug solubility is plotted as a function of dilution, and in vitro dilution experiments were shown to be effective tools in evaluating the ability of the pH-solubilized drug to remain in solution dilution (12, 13). Davio et al. (14) showed that in vivo precipitation of the pH-solubilized drug ditekiren was dependent upon drug concentration and infusion rate. Low concentration drug solutions, which are rapidly diluted below

saturation solubility, and rapid infusions were preferred to minimize precipitation.

The most commonly used buffer components in parenteral products and their pKa's are; citric acid (3.13, 4.76, 6.40), acetic acid (4.76) and phosphoric acid (2.15, 7.20, 12.33). When buffers are employed, the stability of the molecule must also be considered, since it may be influenced by the ions in solution (9). Examples of buffer catalyzed solution degradation include famotidine, a histamine H2 receptor inhibitor (15) and loracarbef, a zwitterionic cephalosporin (16).

B. Use of Cosolvents

Investigation of the solubilizing potential of various cosolvents may be approached empirically by determining the compounds solubility in cosolvent compositions similar to marketed products (21–23), or by one of several systematic approaches, such as log-linear solubility relationships or statistical experimental design.

In the study of log-linear solubility relationships, Yalkowsky and Roseman (20) investigated a range of solutes in binary cosolvent mixtures of ethanol, propylene glycol, and glycerin in water and discussed the closeness of fit of apparent solubility to a log-linear solubility equation. Briefly, this technique involves experimentally determining the solubility of a compound in increasing percentages of a cosolvent and generating a semi-logarithmic plot of the apparent solubility of the drug as a function of the volume-fraction of the cosolvent. Using the slope and the solubility of the compound in pure water, an equation may be written to describe the solubility in a binary system.

Assuming that the log-linear increases in solubility of individual cosolvents are additive, equations may also be written for ternary and quaternary mixed cosolvent systems (24). Mathematically, these relationships are described by the following equations:

> Binary cosolvent system $\log C_x = \log C_w + \alpha_x f_x$ Ternary cosolvent system $\log C_x = \log C_w + \alpha_x f_x + \alpha_a f_a$ Quaternary cosolvent system

$$\log C_x = \log C_w + \alpha_x f_x + \alpha_a f_a + \alpha_b f_t$$

where C_W is the drug solubility in water; α 's are the slopes of the semi logarithmic plots; C_r is the drug solubility; f is the volume fraction of the cosolvent; and the subscripts a, b, x denote the cosolvents A, B, and X

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 TABLE II

 Examples of Marketed Parenteral Products with Solution pH Outside Range of 4 to 8 (18, 19)

$\mathbf{PH} < 4$ Antrinone LactateInocor (Sanofi Winthrop)SolutionE. 3.24 Schurdoni E., IFAntracurium BesplateInocor (Sanofi Winthrop)SolutionIE, IF $3-4$ Chiofalizapovide HCIIbirina (Rocite)PowderIEIE $3-4$ Chiric acid, HCICiproBoxacinCiproBoxacinCiproBoxacinPowderIE $2.5-4.5$ NaOH, HCIDopamine HCIIbirina (Marion MerreliaSolutionIFIF $3.7-4.1$ Citric acid, Na citrateDiszer HCIConcernateIFIFIE $3.7-3.5$ Lactic acid, ethylDopyenitic HelateCardizen (Marion Merrelia)SolutionIF, IE $3.7-3.5$ Lactic acidPentapi Citrate and DroperidolDroperidolDow)SolutionIM, IF, IE $3.2-3.8$ Lactic acidPentapi Citrate and DroperidolInovar (Janssen)SolutionIM, IF, IE $3.4.2$ NaOH, HCIGlycopyrrolate Haloperiol Lactate Haloperiol Lactate Haloperiol Lactate Haloperiol Lactate Haloperiol Lactate Haloperiol Lactate Haloperiol Lactate Haloperiol Lactate Haloperiol Cachario NaOh, HCIMethylopate HCI Nabaroperine HCI Nabarone HCINabaroperine HCI Nabaroperine HCI Nabaroperine HCI Nabaroperine HCI Nabaroperine HCI Nabarone HCI Nabaro HCI (Carbar)SolutionIM, IF H,	pH (constituted)	pH Adjustment	Generic Name	Trade Name	Marketed Form	Routes
3.24 Lactic acid, NaOH Anninone Lactate Proceer (Sanof) Winthrop) Solution IB, IF 3.25-3.65 Benzensulfonic acid Anninone Lactate Proceer (Sanof) Winthrop) Solution IB, IF 3.4 Chlordiazepoxide HCI Benzensulfonic acid, HCI Benzensulfonic acid, HCI Dosynchrony Powder IB, IF 3.4-4 Chirdiazepoxide HCI Dasarbazine Difficace Powder IB, IF 3.4-3 Chirdiazepoxide HCI Dosyncycline Hyclate Difficace Powder IF 3.4-4 Chirdiazem HCI Dosyncycline Hyclate Dosyncycline Hyclate Dosyncycline Hyclate Binsmer HCI Doweder IF 3.4-5 Lactic acid Perntaryl Cirtare and Dower (Shering) Solution IM, IF, IB 34.2 NaOH, HCI Holperidol Lactine Beinerido (Horsin) Solution IM, IB, IF 3.4-4 Lactic acid Fentaryl Cirtare and Dower (Glasc) Solution IM, IB, IF 34 NaOH, Cirtic acid Methyldopate HCI Modemet (Glasc) Solution IM, IB, IF 34 NaOH, Cirtic acid Methyldopate HCI <td>pH < 4</td> <td></td> <td></td> <td></td> <td></td> <td></td>	pH < 4					
3Chiordiazepoxide HCI Bernzymanuffe HCI 23-3.5Lactic acid, HCI Ciprofloxacin Direct-Dorie (Mies) Concentrate Direct-Dorie (Mies) Concentrate Direct-Dorie (Mies) Concentrate Direct-Dorie (Mies) Concentrate Direct-Dorie (Mies) 	3.2-4 3.25-3.65	Lactic acid, NaOH Benzenesulfonic acid	Amrinone Lactate Atracurium Besylate	Inocor (Sanofi Winthrop) Tracrium (Burroughs Wellcome)	Solution Solution	IB, IF IB, IF
3-4 Benzquinamide HCI Emeit-Can (Rorrig) Powder IM, IF 3-4-3 Grife scid Dacabazine DTIC-Dome (Miles) Concentrate IF 3-4-4 Grife scid Dacabazine DTIC-Dome (Miles) Powder IB, IF 3-4-3 Chrie scid, Na citrate Diffazern HCI Cardizern (Marion Merrell Solution IF 3-3.8 Lactic acid Droperidol Inapsine (Lanssen) Solution IM, IF, IB 2-7.3.5 Lactic acid Fentanyl Citrate and Innovar (Janssen) Solution IM, IF, IB 3-4.1 Lactic acid Fentanyl Citrate and Innovar (Janssen) Solution IM, IB, IF 3-4.2 NaOH/HCI Gipcopyrotale Robinul (Robins) Solution IM, IB 3-4.2 NaOH, HCI Methylogate HCI Aldone (East HCI (Merek) Solution IM, IF 3-4.2 NaOH, HCI Methylogate HCI Aldone (Sanoh) Solution IM, IF 3-4.4 Lactic acid Haloperidol Lactate NaOH, IF Maloperide (Maxo) S	3		Chlordiazepoxide HCl	Librium (Roche)	Powder	IB
3.3-3.9 Lactic acid, HCL Ciprofloxacin Ciprofloxacin Ciprofloxacin Ciprofloxacin Dirtcopin (DuPont) Powder IF, IB 2.5-4.5 NaOH, HCL Dogamine HCL Dotycycline Hyclate Dirtcopin (DuPont) Solution IF, IB 1.8-3.3 Dotycycline Hyclate Dirtoperidol Inapsine (Canssen) Solution IM, IF, IB 23.8 Lactic acid, ethyl Ergonovine Maleate Innovar (Lanssen) Solution IM, IB, IF 33.6 Lactic acid Porperidol Innovar (Lanssen) Solution IM, IB, IF 33.8 Lactic acid Fertanyl Cirrate and Innovar (Lanssen) Solution IM, IB, IF 33.4 Lactic acid Holger/dol Lactate Holder (MeNeil) Solution IM, IB 34 Tartaria caid Methyleopate HCl NaOH, HCl Micasone Maleate Mulacate Solution IM, IF 34 NaOH, HCl Micasone HCl Nacarate, cirris acid Nabupkine HCl Nubain (DuPont) Solution IM, IB 34 Cirrate, cirris acid Nabupkine HCl Nabosone HCl Naconte HCl	3-4		Benzquinamide HCl	Emete-Con (Roerig)	Powder	IM, IF
3-4 Christ acid Dacktbazne D1C-Dome (Miles) Solution IF 3.7-4.1 Christ acid, Na cirrate Diffiazem HCl Cardizem (Marion Merrell Solution IF 3.7-3.1 Christ acid, Superine Hyclate Droperidol Inarapine (Lanssen) Solution IM, IF, IB 3.7-3.5 Lactic acid, ethyl Ergenowine Maleate Inapsine (Lanssen) Solution IM, IF, IB 2.7-3.5 Lactic acid Fentanyl Cirrate and Imovar (fanssen) Solution IM, IB, IF 3.2-3.8 Lactic acid Fentanyl Cirrate and Droperidol Imovar (fanssen) Solution IM, IB, IF 3.2-3.5 Lactic acid Fentanyl Cirrate and Imovar (fanssen) Solution IM, IB, IF 3.4 Lactic acid Haloperidol Lactete Robinul (Robins) Solution IM, IB 3.4 NaOH, HCl Microperidol Normadyne (Schering) Solution IM, IF 3.4 NaOH, Alctric acid Methylegoneric Primaco (Sandoz) Solution IM, IF 3.4 NaOH, HCl Microperidol Natent (Durbont) Solution IM, IF 3.4 NaOH, HCl Microperidol Natent (Marchell (Merck)) Solution IM, IF 3.4	3.3-3.9	Lactic acid, HCl	Ciprofloxacin	Cipro I.V. (Miles)	Concentrate	IF
23-4-3. NaCH, HCL Dispanner HCL Dirdipii (DUPORI) Solution IF, IB 1.8-3.3 Doxycycline Hyclate Dirdipii (DUPORI) Solution IF, IB 3-3.8 Lactic acid, ethyl Ergonovine Maleate Ergotrate Maleate (Lilly) Solution IM, IB, IF 3-3.8 Lactic acid, ethyl Ergonovine Maleate Ergotrate Maleate (Lilly) Solution IM, IB, IF 3-3.4 Lactic acid Properidol Innovar (Janssen) Solution IM, IB, IF 3-3.5 Lactic acid Properidol Innovar (Janssen) Solution IM, IB, IF 3-3.4 Lactic acid Haloperidol Lactate Holdel (McNeil) Solution IM, IB, IF 3-4.2 NaOH, chric acid Methylopate HCl Morrodyne (Schoring) Solution IM, IF 3-4.1 Maleate Maleate Maleate Solution IM, IF 3-4 NaOH, HCl Milazolan HCl Versod (Roche) Solution IM, IF 3-4 Nacitrate, citric acid Maleate Maleate Maleate Solution IM, IB 3-4 Citric acid, Na citrate Ordansetron HCl Nacitrate, Citric acid Nacitrate, Citric acid Solution IM, IB 3-4 Tartarie acid	3-4	Citric acid	Dacarbazine	DTIC-Dome (Miles)	Powder	IB, IF
1.8-3.3 Doxycycline Hyclate Vibrany in IV (Roerig, Powder IF 3-3.8 Lactic acid, ethylacte Droperidol Inapsine (Lanssen) Solution IM, IF, IB 3-3.8 Lactic acid, ethylacte Ergonovine Maleate Ergonovine Maleate Ergonovine Maleate Ergonovine Maleate Solution IM, IF, IB 3-3.6 Lactic acid Fentanyl Citrate and Innovar (Janssen) Solution IM, IB, IF 3-3.6 Lactic acid Haloperidol Lactate Haldol (McNeil) Solution IM, IB 3-3.4 Lactic acid Methyldopate HCI Normodyne (Schering) Solution IF 3-4.2 NaOH, HCI Milazolam, HCI Versed (Roche) Solution IM, IF 3-2.4 Milrinone Lactate Primacor (Sanof Winthrop) Solution IM, IF 3-4 Retrate, citric acid Malbuphine HCI Nubain (DuPont) Solution IM, IB, JF 3-4 Citric acid, Na citrate Ondansetron HCI Narcence Powder IF 3-4 NaOH Papaverine HCI Narcence Powder IF 3-4 Solution <t< td=""><td>2.5-4.5 3.7-4.1</td><td>NaOH, HCI Citric acid, Na citrate</td><td>Diltiazem HCl</td><td>Cardizem (Marion Merrell</td><td>Solution</td><td>IF IF, IB</td></t<>	2.5-4.5 3.7-4.1	NaOH, HCI Citric acid, Na citrate	Diltiazem HCl	Cardizem (Marion Merrell	Solution	IF IF, IB
3-3.8 Lactic acid Droperidol Inapisite (Iansken) Solution IM, IF, IE 2.7-3.5 Lactic acid Fentanyl Citzate and Innovar (Janssen) Solution IM, IB, IE 3.2-3.8 Lactic acid Fentanyl Citzate and Innovar (Janssen) Solution IM, IB, IE 3-3.6 NaOH/HCI Glycopyrrolate Robins) Solution IM, IB, IE 3-3.4 Lastic acid Halpperidol Lactate Haidel (McNeil) Solution IM, IE, IE 3-4.2 NaOH, citric acid Methyleopate HCI Trandate (Glaxo) Solution IM, IF, IE 3-4.2 Tartaric acid Methyleopate HCI Matate Matade (Glaxo) Solution IM, IF, IE 3-4 Solution IM, IE Image (Schering) Solution IM, IE 3-4 Cartra cid Methyleopate HCI Versed (Roche) Solution IM, IE, IE 3-4 Citra acid, Na sittate Ondansetron HCI Natate (Classone HCI Solution IM, IB, IE 3-4 Tartaric acid, Na Talaxone HCI Natoschite HCI Solution IF 3-4	1.8-3.3		Doxycycline Hyclate	Vibramycin IV (Roerig, Elkins-Sinn)	Powder	IF
2.7-3.5.Lactic acid, ethyl lactateErgonovine MaleateErgotrate MaleateErgotrate MaleateErgotrate MaleateIM, IB3.2-3.8Lactic acidFentaryl Citrate and Droperiod I. Lactate Haloperiod I. Lactate Labetald HCIInnovar (Janssen)SolutionIM, IB, IF3-3.6Lactic acidGlycopyrolate Haloperiod I. Lactate Methyldopate HCIRobinal (Robins) Normodyne (Schering) Trandate (Glaxo)SolutionIM, IB3-4.2NaOH, citric acid MaleateMethyldopate HCI Milrinone Lactate Milrinone Lactate Milrinone Lactate Minocycline HCI Nabania (DuPont)SolutionIM, IF3.2-4Milrinone Lactate Milrinone Lactate PlasMilozolam HCI Minocycline HCI Nabania (DuPont)Solution Mile IM Monto IDUPont)IM, IB3.4HCI HCI Nabuphine HCI Nabania (DuPont)Nabuphine HCI Nabania (DuPont)Solution SolutionIM, IB3.4Tartaric acid, Na citrateTolazoline HCI Pyridoxine HCI Pyridoxine HCI Pyridoxine HCI Pyridoxine HCI Pyridoxine HCI (Steris)Solution Pyridoxine HCI (Steris) SolutionIB, IF9.1 > 8Diamox (Lactele) 	3-3.8	Lactic acid	Droperidol	Inapsine (Janssen)	Solution	IM, IF, IB
3.2-3.8 Lactic acid Fentanyl Citrate and Droperiod Innovar (Janssen) Solution IM, IB, IF 2-3 NaOH/HCI Glycopyrrolate Haloperiod Lactate Labetalol HCI Robinul (Robins) Solution IM, IB 3-3.6 Lactic acid Haloperiod Lactate Labetalol HCI Robinul (Robins) Solution IM, IB 3-4 NaOH, citric acid Methyldopate HCI Aldomet Ester HCI (Merck) Solution IM, IF 3-4 Maleate Maleate Versed (Roche) Solution IM, IF 3-4 Malozalan HCI Wethyldopate HCI Michaete Solution IM, IF 3-2.4 Milrinone Lactate Pimacor (Sanoft Winthrop) Solution IM, IB, IF 3-2.4 Milrinone Lactate Minocin (Ledrel) Solution IM, IB, IF 3-3.4 HCI Nalbuphine HCI Nabin (DuPont) Solution IM, IB, IF 3-3.4 Citric acid Nalouchine HCI Narcan (DuPont) Solution IM, IB, IF 3-3.4 NaOH Papaverine HCI Papaverine HCI Napaverine HCI Nabuphine 3-4 NaOH Papaverine HCI Papaverine HCI Papaverine HCI Solution IB, IF 2-3.5 A Citrac Pridoxine HCI <td>2.7-3.5</td> <td>Lactic acid, ethyl lactate</td> <td>Ergonovine Maleate</td> <td>Ergotrate Maleate (Lilly)</td> <td>Solution</td> <td>IM, IB</td>	2.7-3.5	Lactic acid, ethyl lactate	Ergonovine Maleate	Ergotrate Maleate (Lilly)	Solution	IM, IB
2-3 NaOH/HCI Glycopyrolate Robinul (Robins) Solution IM, IB 3-3.6 Lactic acid Haloperido Lactate Normodyne (Schering) Solution IB, IF 3-4 Jabetalol HCI Normodyne (Schering) Solution IM 3-4.2 NaOH, citric acid Methyldopate HCI Aldomet Ester HCI (Merck) Solution IM, IF 3-4 Maloutia Malacate Methylopate HCI Aldomet Ester HCI (Merck) Solution IM, IF 3-2.4 Milrinone Lactate Minocyclin HCI Naon (Lactate, Citric acid and Million) Solution IM, IB, IF 3-5.4 Na citrate, citric acid and scitate Ondonsetron HCI Naton (Lactate, Citric acid, Na citrate, citric acid, Na citrate, citric acid, Na citrate, Citric acid, Na citrate, Citric acid, Na citrate Ondonsetron HCI Papaverine HCI Papaverine HCI (Citris) Solution IF 3-4 Tattaric acid, Na Tolazoline HCI Papaverine HCI (Stirs) Solution IB, IF 3-4 Tattaric acid, Na Tolazoline HCI Pridoxine HCI (Stirs) Solution IB, IF 9.2 HCI/NaOH Acctazolamide Na Diamox (Laderle) Powder IM, IB, IF 9.2 HCI/NaOH Acctazolamide Na Aminophylline (Abbutt, Solution IB, IF <td>3.2-3.8</td> <td>Lactic acid</td> <td>Fentanyl Citrate and Droperidol</td> <td>Innovar (Janssen)</td> <td>Solution</td> <td>IM, IB, IF</td>	3.2-3.8	Lactic acid	Fentanyl Citrate and Droperidol	Innovar (Janssen)	Solution	IM, IB, IF
3-3-6 Latter acid Halded Latetale Halded (McNeil) Solution IM 3-4 Labetalol HCI Normodyne (Schering) Solution IB, IF 3-4.2 NaOH, eitric acid Methyldopate HCI Aldomet Ester HCI (Merck) Solution IF 3-3 NaOH, HCI Midazolam HCI Methylergonovine Methergine (Sendoz) Solution IF 3-2-2.8 Macrete, citric acid Minocyclinch HCI Nuboxine HCI Nubarce (Sandof Winthrop) Solution IM, IF 3-3.4 Cltric acid, Na citrate Naloxone HCI Naracan (DuPont) Solution IM, IB, IF 3-4 Cltric acid, Na citrate Ondansetron HCI Solution IF Payaverine HCI (LiByly) Solution IF, IF 3-4 NaOH Papaverine HCI Prizoxine HCI (LiByly) Solution IB, IF 3-4 Tartaric acid, Na Tolazoline HCI Prizoxine HCI (Steris) Solution IB, IF 3-4 Tartaric acid, Na Tolazoline HCI Prizoxine HCI (Steris) Solution IB, IF 2-3.8 Tartaric acid, Na Cltricacid Na Diamox (Lederle)	2-3	NaOH/HCl	Glycopyrrolate	Robinul (Robins)	Solution	IM, IB
3-4Labelator FCINormodyne (Seneing)SolutionIB, IP $3-4.2$ NaOH, citric acidMethyldopate HCIAldomet Ester HCI (Merck)SolutionIF $27-3.5$ Tartaric acidMethyldopate HCIAldomet Ester HCI (Merck)SolutionIM, IF $3-4$ NaOH, HCIMidazolam HCIWersed (Roche)SolutionIM, IF $2-2.8$ Mihrinone LactatePrimacor (Sanofi Winthrop)SolutionIM, IB, IF $2-3.6$ Na citrate, citric acidNalbughine HCINubain (DuPont)SolutionIM, IB, IF $3-4$ HCINalavanie HCINatoxine HCINarean (DuPont)SolutionIF $2-3.4$ Acetic acidOxytocinPiridoxine HCIPapaverine HCI (Cilay)SolutionIF, IF $2-3.4$ Tartaric acid, NaTolazoline HCIPapaverine HCI (Cilay)SolutionIB, IF $2-3.4$ Tartaric acid, NaTolazoline HCIPriscoline HCI (Steris)SolutionIB, IF $2-3.4$ Tartaric acid, NaTolazoline HCIPriscoline HCI (Steris)SolutionIB, IF 9.2 HCI/NaOHAcetazolamide NaDiamox (Lederle)PowderIM, IB, IF 9.4 Amobarbital NaAminophyllineAminophylline (Abbott, SolutionIB, IF $9.6-10.4$ NaOHAcetazolamide NaCaricat (BerroughsPowderIM, IB, IF $9.6-10.4$ NaOHAcetazolamide NaAminophylline (Abbott, SolutionIB, IF $9.6-10.4$ NaOHAcetazolamide NaPowderIB, IF <td>3-3.6</td> <td>Lactic acid</td> <td>Haloperido] Lactate</td> <td>Haldol (McNeil)</td> <td>Solution</td> <td>IM TD TP</td>	3-3.6	Lactic acid	Haloperido] Lactate	Haldol (McNeil)	Solution	IM TD TP
3-4.2 NaOH, eitric acid Methyldopate HCl Midome Ester HCl (Merck) Solution IF 2.7-3.5 Tartaric acid Methylgopate HCl Midome Ester HCl (Merck) Solution IM, IF 3 NaOH, HCl Midazolam HCl Versed (Roche) Solution IM, IF 3.2-4 Minropetine Lactate Minropetine HCl Minocycline HCl Nator (Raofi Winthrop) Solution IM, IB, B 3.4 HCl Natorat (Careas) Solution IM, IB, B Solution IM, IB, B 3.4 HCl Natorne HCl Natoran (DuPont) Solution IM, IB, IB 3.4 Citric acid, Na citrate Ordansetron HCl Zofran (Cereas) Solution IB, IF 2.5-4.5 Acetic acid Ordansetron HCl Pridoxine HCl Prineson (Parke-Davis) Solution IB, IF 3-4 Tartaric acid, Na Totazoline HCl Prinoscin (Parke-Davis) Solution IB, IF 2-3.8 - Tartaric acid, Na Cetezolamide Na Diamos (Lederle) Powder IM, IB, IF 9.2 HCl/NaOH Acectazolamide Na Diamos (Lederle) Pow	5-4		Labelator FICI	Trandate (Glavo)	Solution	1D, 1F
2.7-3.5 Tartaric acid Methylergonovine Maleate Methergine (Sandoz) Solution IM, IF 3.2 NaOH, HCI Midazolam HCI Versed (Roche) Solution IM, IF 3.2-4 Minoxetine HCI Minoxetine HCI Nubain (DuPont) Solution IM, IF 2-2.8 Minoxetine HCI Nubain (DuPont) Solution IM, IB, IF 3.4 HCI Naloxone HCI Narcan (DuPont) Solution IF 2-5.4.5 Acetic acid Oxytocin Pitocin (Parke-Davis) Solution IF, IF 3-4 Tartaric acid, Na Tolazoline HCI Papaverine HCI Papaverine HCI (Lilly) Solution IB, IF 2-3.8 Tartaric acid, Na Tolazoline HCI Pridoxine HCI (Steris) Solution IB, IF 9.2 HCI/NaOH Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 9.4 NaOH Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 9.4 Tartaric acid, Na Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 9.4 NaOH Acetazolamide Na	3-4.2	NaOH, citric acid	Methyldonate HCl	Aldomet Ester HCl (Merck)	Solution	IF
3 NaOH, HCl Midazolam HCl Milrinone Lactate Versed (Roche) Solution IM, JF 3.2-4 Minocycline HCl Minocycline HCl Primacor (Sanofi Winthrop) Solution IF 3.5 Na citrate, citric acid Nalbuphine HCl Nubain (DuPont) Solution IM, IB 3.4 HCl Naloxene HCl Nuran (DuPont) Solution IF 3.4 Citric acid, Na citrate Ondansetron HCl Zofran (Cerenex) Solution IF 3.4 NaOH Papaverine HCl Purpicoxine HCl (Lilly) Solution IB, IF 2.5-4.5 Acetic acid Oxytocin Piridoxine HCl Pricoin (Parke-Davis) Solution IB, IF 2-3.8 Pyridoxine HCl Priscoline HCl (Ciba) Solution IB, IF 2-3.8 Pyridoxine HCl Priscoline HCl (Ciba) Solution IB, IF 9.2 HCl/NaOH Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 9.6-10.4 Amiophylline Aminophylline (Abbott, Wellow) Solution IB, IF 9.6-10.4 Aazthioprine Na Imuran (Burroughs Powder IM, IE, IF	2.7-3.5	Tartaric acid	Methylergonovine Malcate	Methergine (Sandoz)	Solution	IM, IF
3.2-4 Milrinone Lactate Primacor (Sanofi Winthrop) Solution IF 2-2.8 Minocycline HCI Muotan (Laderle) Powder IF 3.5 Na citrate, citric acid Nalbuphine HCI Nubain (DuPont) Solution IM, IB 3.4 HCI Naloxone HCI Narcan (DuPont) Solution IF 3.3-4 Citric acid, Na citrate Ondansetron HCI Paraverine HCI Papaverine HCI Solution IF 2-3.8 Pridoxine HCI Papaverine HCI Papaverine HCI (Lilly) Solution IB, IF 2-3.8 Pridoxine HCI Priscoline HCI (Ciba) Solution IB, IF 2-3.8 Pridoxine HCI Priscoline HCI (Ciba) Solution IB, IF 9.2 HCI/NaOH Acctazolamide Na Zovirax (Burroughs Powder IM, IB, IF 9.6 NaOH Acctazolamide Na Zovirax (Burroughs Powder IM, IE, IF 9.6 NaOH Azathioprine Na Imura (Burroughs Powder IM, IE, IF 9.6 NaOH Amoharbital Na Amyiellin-N (Apothecon) Powder IM, IE, IF	3	NaOH, HCl	Midazolam HCl	Versed (Roche)	Solution	IM, IF
2-2.8Minocycline HCIMinocicl (Lederle)PowderIF3.5Na citrate, citric acidNaloxone HCINutain (DuPont)SolutionIM, IB, IF3.4HCINatione HCINarcan (DuPont)SolutionIF3.4HCINatoxone HCIZofran (Cernenx)SolutionIF2.5-4.5Acetic acidOxytocinPitocin (Parke-Davis)SolutionIF3-4NaOHPapaverine HCIPapaverine HCI (Cluly)SolutionIB, IF2-3.8Pyridoxine HCIPyridoxine HCI (Steris)SolutionIM, IB, IF2-3.8Pyridoxine HCIPyricoline HCI (Steris)SolutionIM, IB, IF2-3.8Tartaric acid, Na citrateTolazoline HCIPriscoline HCI (Ciba)SolutionIM, IB, IF9.2HCI/NaOHAcctazolamide Na Acyclovir NaZovirax (Burroughs Wellcome)PowderIM, IB, IF9.6-10.4AminophyllineAminophyllineAminophylline (Abbott, Uellowne)SolutionIB, IF9.6-10.4Anobarbital Na Anapicillin NaAnytal Na (Lilly) PowderPowderIM, IB, IF9.6-10.4Anobarbital Na Polycillin-N (Apothecon) PowderPowderIM, IB, IF9.6-10.4Anobarbital Na Polycillin-N (Apothecon) PowderPowderIM, IB, IF9.6-10.4Anobarbital Na Polycillin-N (Apothecon) PowderPowderIM, IB, IF9.6-10.5NaOHBetamethasone Na Polycillin-N (Apothecon) (Schering)PowderIM, IB, IF9.10	3.2-4		Milrinone Lactate	Primacor (Sanofi Winthrop)	Solution	IF
3.5Na cirrate, cirre acidNatoppine PC1Nutbain (DuPont)SolutionIM, IB3.4Cirric acid, Na citrateOndansetron HC1Zofran (Cernex)SolutionIF3.4Natoppine PC1Papaverine HC1Papaverine HC1Papaverine HC1Papaverine HC12.5-4.5Acetic acidOxytocinPitocin (Parke-Davis)SolutionIF3-4Natoppine PC1Papaverine HC1Papaverine HC1Papaverine HC1SolutionIB, IF2-3.8Pyridoxine HC1Pyricoxine HC1Pyricoxine HC1 (Ciba)SolutionIM, IBIF2-3.8Tartaric acid, NaTolazoline HC1Priscoline HC1 (Ciba)SolutionIB, IF2-3.8CitrateTolazoline HC1Priscoline HC1 (Ciba)SolutionIB, IF9.1SolutionAninophyllineDiamox (Lederle)PowderIM, IB, IF9.2HC1/NaOHAcetazolamide Na Acyclovir NaDiamox (Lederle)PowderIM, IB, IF9.6-10.4AminophyllineAminophyllineAminophyllineSolutionIB, IF9.6-10.4Amobarbital Na August Na (Lilly)PowderIM, IB, IFFotacillin-N (Apothecon) Totacillin-N (Apothecon)PowderIM, IB, IF9.6-10.4Anobarbital Na PO4PO4Celestone PhosphateSolutionIB, IF9.10NaOHBetamethasone Na PO4Celestone PhosphateSolutionIB, IF9.2-10NaOHDiazoxideHyperstat (Schering) SolutionSolutionIB9.10.	2-2.8	Net o rota coa o cotación contrátio	Minocycline HCl	Minocin (Lederle)	Powder	IF D/ m
3.3-4 Clitric acid, Na citrate Nation PLC Nation PLC Nation PLC 3.3-4 Clitric acid, Na citrate Ondiansetron HCI Zofran (Cerenex) Solution IF 3.4 NaOH Papaverine HCI Pitocin (Parke-Davis) Solution IF 3-4 NaOH Papaverine HCI Papaverine HCI (Lilly) Solution IB, IF 2-3.8 Tartaric acid, Na Tolazoline HCI Pyridoxine HCI (Steris) Solution IB, IF 2-3.8 Tartaric acid, Na Tolazoline HCI Priscoline HCI (Steris) Solution IB, IF 2-3.8 Tartaric acid, Na Tolazoline HCI Priscoline HCI (Steris) Solution IB, IF 9.2 HCI/NaOH Acctazolamide Na Diamox (Lederle) Powder IM, IB, IF 10.5-11.6 Accyclovir Na Zovirax (Burroughs Powder IF 8.6-9 Aminophylline Aminophylline (Abbott, Solution IB, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IM, IB, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 9.10 Anapicillin	3.5	Na citrate, citric acio	Nalouphine HCl	Nubain (DuPont)	Solution	IM, IB
2.5-4.5 Acetic acid Oxytocin Pitocin (Parke-Davis) Solution IF 3-4 NaOH Papaverine HCI Papaverine HCI (Lilly) Solution IB, IF 2-3.8 Pyridoxine HCI Pyridoxine HCI (Steris) Solution IB, IM 3-4 Tartaric acid, Na Toiazoline HCI Priscoline HCI (Steris) Solution IB, IM 3-4 Tartaric acid, Na Toiazoline HCI Priscoline HCI (Ciba) Solution IB, IM 9.2 HCI/NaOH Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 9.2 HCI/NaOH Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 8.6-9 Aminophylline Aminophylline (Abbott, Solution IB, IF IK 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IB, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IB, IF 9.6 NaOH Azathioprine Na Clelome) Powder IM, IB, IF 9.6 NaOH Betamethasone Na Celestone Phosphate Solution IB, IM 9.2-10 </td <td>33-4</td> <td>Citric acid Na citrate</td> <td>Ondansetron HCl</td> <td>Zofran (Cerenex)</td> <td>Solution</td> <td>IF</td>	33-4	Citric acid Na citrate	Ondansetron HCl	Zofran (Cerenex)	Solution	IF
3-4 NaOH Papaverine HCI Pyridoxine HCI Papaverine HCI (Lilý) Solution IB, IF 2-3.8 Tartaric acid, Na citrate Tolazoline HCI Pyridoxine HCI (Steris) Solution IB, IM pll > 8 Tolazoline HCI Priscoline HCI (Ciba) Solution IB, IF pl. HCI/NaOH Acetazolamide Na Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 10.5-11.6 HCI/NaOH Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 8.6-9 Aminophylline Aminophylline Aminophylline (Abbott, Begent) Solution IB, IF 9.6-10.4 Acetazolamide Na Amobarbital Na Amytal Na (Lilly) Powder IM, IB, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Welloome) Powder IB, IF 8.5 NaQHPO4, NaOH Betamethasone Na Celestone Phosphate Solution IB, IF 9.1.6 NaOH Diazoxide Hyperstal (Schering) Solution IB, IF 9.2-10 NaOH Chlorothiazide Na Solution IB, IF If 9.2. NaOH Flucrourac	2.5-4.5	Acetic acid	Oxytocin	Pitocin (Parke-Davis)	Solution	ÎF
2-3.8 Pyridoxine HCl Pyridoxine HCl (Steris) Solution IM, IB 3-4 Tartaric acid, Na citrate Tolazoline HCl Priscoline HCl (Steris) Solution IB, IM pH > 8	3-4	NaOH	Papaverine HCI	Papaverine HCl (Lilly)	Solution	IB, IF
3-4 Tartaric acid, Na citrate Tolazoline HCl Priscoline HCl (Ciba) Solution IB, IM pII > 8 9.2 HCl/NaOH Acetazolamide Na Acyclovir Na Diamox (Lederle) Powder IM, IB, IF 10.5-11.6 Acyclovir Na Zovirax (Burroughs Powder IF 8.6-9 Aminophylline Aminophylline (Abbott, Solution IB, IF 9.6-10.4 Amobarbital Na Amytal Na (Lilly) Powder IM, IF, IF 9.6 NaOH Azathioprine Na Inuran (Burroughs Powder IM, IF, IF 9.6 NaOH Azathioprine Na Inuran (Burroughs Powder IM, IF, IF 9.6 NaOH Azathioprine Na Inuran (Burroughs Powder IM, IB, IF 9.6 NaOH Betamethasone Na Celestone Phosphate Solution IB, IM 8.5 Na ₂ HPO ₄ , NAOH Betamethasone Na Celestone Phosphate Solution IB, IF 11.6 NaOH Diazoxide Hyperstat (Schering) Solution IB 9-2.10 NaOH Fluorouracil Fluorouracil (Roche) Solution IB	23.8		Pyridoxine HCl	Pyridoxine HCl (Steris)	Solution	IM, IB
citrate pH > 8 9.2 HCl/NaOH Acetazolamide Na Diamox (Lederle) Powder IM, IB, IF 10.5-11.6 Acyclovir Na Zovirax (Burroughs Powder IF 8.6-9 Aminophylline Aminophylline (Abbott, Elkins-Sinn, American Regent) Solution IB, IF 9.6-10.4 Amobarbital Na Amytal Na (Lilly) Powder IM, IF, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IB, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IB, IF 9.6 NaOH Betamethasone Na Celestone Phosphate Solution IB, IM, IB, IF 9.10 MaOH Chlorothiazide Na Sodium Diuril (Merck) Powder IB, IM 9.2-10 NaOH Betamethasone Na Celestone Phosphate Solution IB, IF 9.10.5 Diazoxide Hyperstat (Schering) Solution IB IF 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB 9.2.10.5 NaOH Elasix Fuorouracil (Roche) <	3-4	Tartaric acid, Na	Tolazoline HCl	Priscoline HCI (Ciba)	Solution	IB, IM
9.2HCI/NaOHAcetazolamide Na Acyclovir NaDiamox (Lederle) Zovirax (Burroughs Wellcome)PowderIM, IB, IF10.5-11.6Acyclovir NaZovirax (Burroughs Wellcome)PowderIF8.6-9AminophyllineAminophylline (Abbott, Elkins-Sinn, American Regent)SolutionIB, IF9.6-10.4Amobarbital Na Azathioprine NaAmytal Na (Lilly) Wellcome)PowderIM, IF, IF9.6NaOHAzathioprine Na MoHImuran (Burroughs Wellcome)PowderIB, IF8-10Ampicillin Na PO ₄ Polycillin-N (Apothecon) Totacillin-N (Beecham) Omnipen-N (Wyeth)PowderIM, IB, IF8.5Na ₂ HPO ₄ , NaOHBetamethasone Na PO ₄ Celestone Phosphate SolutionSolutionIB, IM9.2-10NaOHChlorothiazide Na Diazoxide Diethylstibestrol DiphosphateSolutionIB, IF9.2NaOHFluorouracil 	-17 - 9	citrate				
10.5-11.6Acyclovir NaZovirax (Burroughs Wellcome)PowderIF8.6-9AminophyllineAminophylline (Abbott, Elkins-Sinn, American Regent)SolutionIB, IF9.6-10.4Amobarbital Na Azathioprine NaAmytal Na (Lilly)PowderIM, IF9.6NaOHAzathioprine Na Mohar Mathematican Regent)Imuran (Burroughs Wellcome)PowderIB, IF9.6-10.4Amobarbital Na Azathioprine Na B-10Amobarbital Na Azathioprine Na Melcome)Amytal Na (Lilly)PowderIM, IF, IF9.6NaOHAnapicillin Na Polycillin-N (Apothecon) Omnipen-N (Wyeth)PowderIM, IB, IF8-10Anapicillin Na PO4Celestone Phosphate Omnipen-N (Wyeth)SolutionIB, IM8.5Na2HPO4, NaOH PO4Betamethasone Na PO4 (Schering)SolutionIB, IM9.2-10NaOHChlorothiazide Na DiazoxideSodium Diuril (Merck) Fluorouracil (Schering)PowderIB, IF9.2NaOHFluorouracil FluorouracilFluorouracil (Roche) Fluorouracil (Roche)SolutionIB9.2NaOHElsisk FluorouracilFluorouracil (Roche) Fluorouracil (Roche)SolutionIB, IF9.2NaOHLasix FluorouraciFluorouracil (Roche) Fluorouracil (Roche)SolutionIB, IF8-11NaOHLasix FurosemideSolutionIB, IF, IF9.2NaOHLasix FluorouraciFluorouracil (Roche) FluorouraciSolutionIB, IF, IF, IF, IF, IF, IF, IF, IF, IF, I	92	HCI/NaOH	Acetazolamide Na	Diamox (Lederle)	Powder	IM IB IF.
8.6-9 Aminophylline Aminophylline Aminophylline (Abbott, Elkins-Sinn, American Regent) Solution IB, IF 9.6-10.4 Amobarbital Na Amyial Na (Lilly) Powder IM, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IB, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IM, IF, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Amooth Betamethasone Na Celestone Phosphate Solution IB, IM 8.5 Na2HPO4, NaOH Betamethasone Na Celestone Phosphate Solution IB, IF 9.2-10 NaOH Chlorothiazide Na Sodium Diuril (Merck) Powder IB, IF 9.16.5 Diethylstilbestrol Stilphostrol (Miles) Solution IB 9.2 NaOH Fluorouracil Fluorouracil (Roche) <t< td=""><td>10.5-11.6</td><td>4.4.004, 4.104.074 A</td><td>Acyclovir Na</td><td>Zovirax (Burroughs Wellcome)</td><td>Powder</td><td>ÎF îF</td></t<>	10.5-11.6	4.4.004, 4.104.074 A	Acyclovir Na	Zovirax (Burroughs Wellcome)	Powder	ÎF îF
9.6-10.4 Amobarbital Na Amytal Na (Lily) Powder IM, IF 9.6 NaOH Azathioprine Na Imuran (Burroughs Powder IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Powder IM, IB, IF 8-10 Ampicillin Na Celestone Phosphate Solution IB, IM 9.2-10 NaOH Betamethasone Na Celestone Phosphate Solution IB, IF 9.2-10 NaOH Diazoxide Hyperstat (Schering) Solution IB 9.10.5 Diethylstilbestrol Stilphostrol (Miles) Solution IF 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB, IF 8-11 NaOH Folic acid Folivite (Lederle) Solution IB, IF 8-9.3 NaOH Lasix Furosemide Solution	8.6-9		Aminophylline	Aminophylline (Abbott, Elkins-Sinn, American Regent)	Solution	IB, IF
9.6 NaOH Azathoprine Na Imuran (Burtoughs Wellcome) Powder IB, IF 8-10 Ampicillin Na Polycillin-N (Apothecon) Totacillin-N (Beecham) Omnipen-N (Wyeth) Powder IM, IB, IF 8.5 Na ₂ HPO ₄ , NaOH Betamethasone Na PO ₄ Celestone Phosphate Solution IB, IM 9.2–10 NaOH Chlorothiazide Na Diazoxide Sodium Diuril (Merck) Powder IB, IF 11.6 NaOH Diazoxide Hyperstat (Schering) Solution IB 9-10.5 Diethylstilbestrol Stilphostrol (Miles) Solution IB, IF 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB, IF 8-11 NaOH Folic acid Folivite (Lederle) Solution IB, IF 8-9.3 NaOH Lasix Furosemide Solution IB, IF 11 Ganciclovir Na Cytovene (Syntex) Powder IF, IB, IF 8.1 Leucovorin Ca Wellcovorin (Immunex, Burroughs Wellcome) Powder IB, IB, IF 9.5–10.5 Na carbonate Methobevital Na Brevital Na (Lilib) Powder IB,	9.6-10.4	NT: 2NTY	Amobarbital Na	Amytal Na (Lilly)	Powder	IM, IF
8-10 Ampletinin Na Polyettini-N (Apothecon) Powder IM, IB, IF Totacillin-N (Beecham) Omnipen-N (Wyeth) 8.5 Na ₂ HPO ₄ , NaOH Betamethasone Na Celestone Phosphate Solution IB, IM 9.2-10 NaOH Chlorothiazide Na Sodium Diuril (Merck) Powder IB, IF 11.6 NaOH Diazoxide Hyperstat (Schering) Solution IB 9-10.5 Diethylstilbestrol Stilphostrol (Miles) Solution IB 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB, IF 8-11 NaOH Folic acid Folvite (Lederle) Solution IB 8-9.3 NaOH Lasix Furosemide Solution IM, IB, IF 11 Ganciclovir Na Cytovene (Syntex) Powder IF 8.1 Leucovorin Ca Wellcovorin (Immunex, Powder IM, IB, IF 9.5–10.5 Na carbonate Methobevital Na Brevital Na (Lilly) Powder IB	9.0	NaOH	Azaimoprine Na	Wellcome)	Powder	IB, IF
8.5 Na ₂ HPO ₄ , NaOH Betamethasone Na PO ₄ Celestone Phosphate Solution IB, IM 9.2-10 NaOH Chlorothiazide Na Sodium Diuril (Merck) Powder IB, IF 11.6 NaOH Diazoxide Hyperstat (Schering) Solution IB 9-10.5 Diethylstilbestrol Stilphostrol (Miles) Solution IF 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB, IF 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB, IF 8-11 NaOH Folic acid Folvite (Lederle) Solution IB 8-9.3 NaOH Lasix Furosemide Solution IM, IB, IF 11 Ganciclovir Na Cytovene (Syntex) Powder IF 8.1 Leucovorin Ca Wellcovorin (Immunex, Powder Powder IM, IB, IF 9.5-10.5 Na carbonate Methobevital Na Brevital Na (Lilby) Powder IB	0-10		Ampichan Na	Totacillin-N (Apointecon) Omnipen-N (Wyeth)	rowaer	1м, 1В, 1г
9.2-10 NaOH Chlorothiazide Na Sodium Diuril (Merck) Powder IB, IF 11.6 NaOH Diazoxide Hyperstat (Schering) Solution IB 9-10.5 Diethylstilbestrol Stilphostrol (Miles) Solution IF 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB, IF 8-11 NaOH Folic acid Folvite (Lederle) Solution IB 8-9.3 NaOH Lasix Furosemide Solution IB 11 Ganciclovir Na Cytovene (Syntex) Powder IF 8.1 Leucovorin Ca Wellcovorin (Immunex, Powder IM, IB, IF 9.5-10.5 Na carbonate Methobevital Na Brevital Na (Lilby) Powder IB	8.5	Na ₂ HPO ₄ , NaOH	Betamethasone Na PO₄	Celestone Phosphate (Schering)	Solution	IB, IM
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9-10.5 Diethylstilbestrol Diphosphate Stilphostrol (Miles) Solution IF 9.2 NaOH Fluorouracil Fluorouracil (Roche) Solution IB, IF 8-11 NaOH Folic acid Folvite (Lederle) Solution IB 8-9.3 NaOH Lasix Furosemide Solution IM, IB, IF 11 Ganciclovir Na Cytovene (Syntex) Powder IF 8.1 Leucovorin Ca Wellcovorin (Immunex, Burroughs Wellcome) Powder IM, IB, IF 9.5-10.5 Na carbonate Methobevital Na Brevital Na (Lille) Powder IB	11.6	NaOH	Diazoxide	Hyperstat (Schering)	Solution	IB
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95-105 Na carbonate Methohevital Na Brevital Na (Lilly) Powder IB IF	8.1		Leucovorin Ca	Wellcovorin (Immunex,	Powder	IM, IB, IF
THE AVAILABLE AVAI	9,5-10.5	Na carbonate	Methohexital Na	Brevital Na (Lilly)	Powder	IB. IF

IM = intramuscular, IF = intravenous infusion, IB = intravenous direct injection.

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