

Parenteral Formulations of Small Molecules Therapeutics Marketed in the United States (1999) Part II

ROBERT G. STRICKLEY

Axys Pharmaceuticals, Inc., South San Francisco, California

[Editor's Note: This review article on Injectable Products is being published in three parts. The introduction and summary appeared in the November/December 1999 issue. The final Part will appear in the March/April 2000 issue of the *Journal*.]

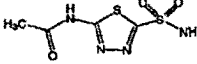
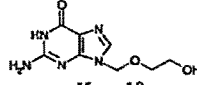
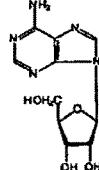
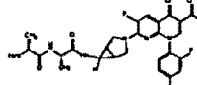
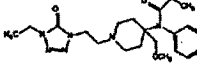
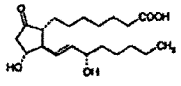
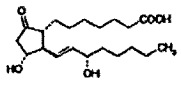
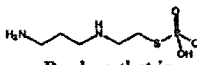
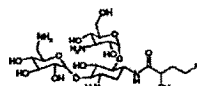
Injectable Products

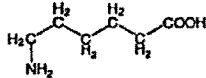
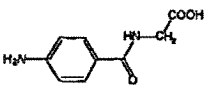
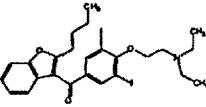
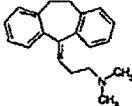
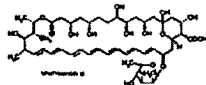
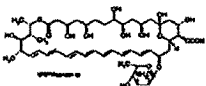
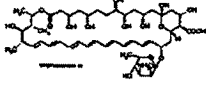
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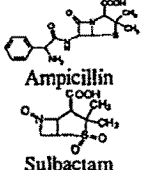
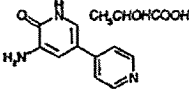
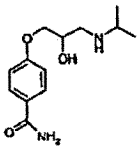
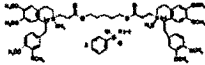
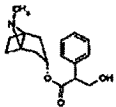
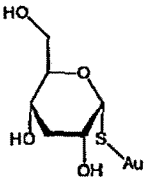
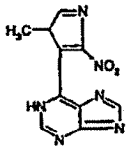
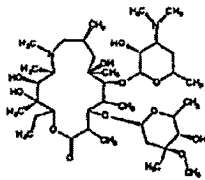
1. Physician's Desk Reference, 53rd ed., Medical Economics Company, Inc., Montvale, NJ, 1999.

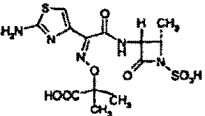
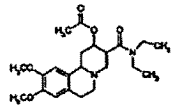
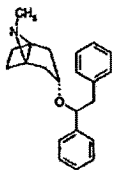
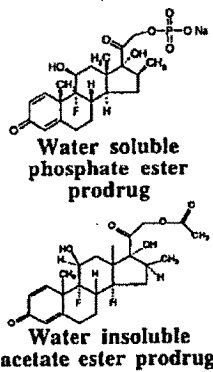
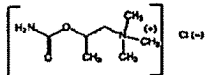
Correspondence address: 180 Kimball Way, South San Francisco, CA 94080

2. Lawrence A. Trissel, Handbook on Injectable Drugs, 10th ed., American Society of Health-System Pharmacists, Inc., Bethesda, MD, 1998.
3. Lynn D. Phillips and Merrily A. Kuhn, Manual of IV Medications, 2nd ed., Lippincott-Raven Publishers, Philadelphia, PA, 1999.
4. D. A. Hussar, "New drugs of 1998," *Journal of the American Pharmaceutical Association*, **39**, 151 (1999).
5. D. A. Hussar, "New drugs of 1997," *Journal of the American Pharmaceutical Association*, **38**, 155 (1998).
6. Food and Drug Administration internet website, <http://www.fda.gov/>, See human drugs, what's new, new and generics approvals.

Drug Name/ Marketed Name	Structure	Formulation	Preadministration preparation	Route of Administration	Company and Indication
Acetazol- amide sodium/ Diamox	 pKa = 7.2	Solution 500 mg pH 9.2	Constitute with 5 mL WFI to ≤ 100 mg/mL.	IV bolus/ IV infusion; IM but may be painful due to alkaline pH	Lederle, Antiglaucoma; diuretic in treatment of mountain sickness
Acyclovir sodium/ Zovirax	 pKa ~ 10	Lyophilized powder 500 - 1000 mg pH 10.5 - 11.6	Reconstitute with WFI to 50 mg/mL; Dilute with dextrose 5% or saline to < 7 mg/mL.	IV infusion over 1 hour	Glaxo Wellcome, Antiviral
Adenosine/ Adenocard IV (bolus), Adenoscan (IV infusion)		Solution 3 mg/mL, Sodium chloride 9 mg/mL, pH 4.5-7.5	None	IV bolus/ IV infusion at 0.14 mg/kg/min for 6 minutes	Fujisawa, Conversion to sinus rhythm of PSVT (bolus). Adjunct for thallium-201 myocardial perfusion scintigraphy (infusion)
Alatrofloxacin mesylate/ Trovan	 Amide prodrug for trovafloxacin	Solution 5 mg/mL pH 3.4-4.3	Dilute with dextrose 5% to 1-2 mg/mL. (potentially incompatible with saline and lactated Ringer's)	IV infusion over 60 minutes	Pfizer, Antibiotic
Alfentanil HCl/ Alfenta		Solution 0.5 mg/mL, Sodium chloride (isotonic) pH 4-6	None for bolus. For IV infusion dilute with saline, dextrose 5%, or lactated Ringer's to 0.025- 0.080 mg/mL.	IV bolus/ IV infusion at 0.5-3.0 ug/kg/min	Taylor, Analgesic
Alprostadil (prostaglan- dinE1/ Caverject		Lyophilized powder 6-46 ug Lactose 172 mg, Sodium citrate 47 mg, Benzyl alcohol 8.4 mg	Reconstitute with 1.2 mL water preserved with benzyl alcohol 0.95% w/v. (~ 0.5-1.1 ug is lost due to adsorption to the vial and syringe.)	Intra- cavernosal	Pharmacia & Upjohn, Erectile dysfunction
Alprostadil alfadex (prosta- glandinE1/ Edex	 complexed with α- cyclodextrin	Lyophilized powder 6-50 ug complexed with 200- 1610 ug of α-cyclodextrin Lactose 56 mg pH 4-8	Reconstitute with 1.2 mL saline.	Intra- cavernosal	Schwarz Pharma, Erectile dysfunction
Amifostine/ Ethiol	 Prodrug that is dephosphorylated by alkaline phosphatase to active free thiol	Lyophilized powder 500 mg	Reconstitute with saline to 50 mg/mL (stable at room temperature for 5 hours). May be further diluted with saline to 5 mg/mL.	IV infusion over 15-30 minutes	Alza, Antineoplastic adjuvant [cytoprotective and radioprotective (reduces toxic effect of cisplatin)]
Amikacin sulfate		Solution 250 mg/mL, Sodium metabisulfite 0.66% Sodium citrate 2.8 % pH 3.5 - 5.5	For IV infusion dilute with saline or dextrose 5% to 2.5-5 mg/mL.	IM/ IV Infusion over 30 - 60 minutes	Elkins-Sinn, Antibiotic

Drug Name/ Marketed Name	Structure	Formulation	Preadministration preparation	Route of Administration	Company and Indication
Aminocaproic acid/ Amicar		Solution 250 mg/mL, Benzyl alcohol 0.9% pH 6.8	Dilute with saline or dextrose 5% to ~ 15- 20 mg/mL.	IV infusion at 4 grams/hour	Immunex, Enhancing hemostasis when fibrinolysis contributes to bleeding
Amino- hippurate sodium "PAH"		Solution 200 mg/mL	None	IV infusion at 6-10 mg/kg and 10-24 mg/min	Merck, Measures effective renal plasma flow
Amiodarone HCL/ Cordarone		Solution 50 mg/mL, TWEEN 80 at 10%, Benzyl alcohol 2% pH 4.1	Dilute with dextrose 5% to < 2 mg/mL.	IV infusion at 5-15 mg/min dextrose	Wyeth-Ayerst , Antiarrhythmic, Antianginal
Amitriptyline HCl/ Elavil		Solution 10 mg/mL, Dextrose 44 mg/mL, Methylparaben 1.5 mg/mL, Propylparaben 0.2 mg/mL pH 4-6	None	IM	Zeneca, Antidepressant
Amphoter- icin B/ Abelcet	 complexed 1:1 (drug-to- lipid molar ratio) with [L- α-dimyristoylphosphati- dylcholine (DMPC) and L- α-dimyristoylphosphati- dylglycerol (DMPG) in a 7:3 mole ratio]	Liposome opaque suspension 5 mg/mL DMPC 3.4 mg/mL, DMPG 1.5 mg/mL, Sodium chloride 9 mg/mL pH = 5-7	Dilute with dextrose 5% to 1-2 mg/mL.	IV infusion at 2.5 mg/kg/hr	The Liposome Company, Antifungal
Amphoter- icin B cholesteryl sulfate/ Amphotec	 complexed 1:1 molar with cholesteryl sulfate	Lyophilized powder 50 - 100 mg After reconstitution with WFI to a 5 mg/mL colloidal liposomal dispersion, Sodium cholesteryl sulfate 2.6 mg/mL, EDTA 0.037 mg/mL, Lactose 95 mg/mL, TRIS 0.56 mg/mL	Reconstitute with WFI to 5 mg/mL. Dilute with dextrose 5% to 0.16 - 0.83 mg/mL.	IV infusion at 3-4 mg/kg/hr	Sequus (Purchased by Alza), Antifungal
Amphoter- icin B/ Ambisome		Lyophilized powder 50 mg After reconstitution with WFI to a 4 mg/mL translucent liposomal suspension, Hydrogenated soy phosphatidylcholine 18 mg/mL, Distearoylphosphatidylglycerol 7 mg/mL, Cholesterol 4 mg/mL, Alpha tocopherol 0.05 mg/mL, Sucrose 75 mg/mL, Disodium succinate 2 mg/mL pH 5.0-6.0	Reconstitute with WFI to 4 mg/mL. Dilute with dextrose 5% to 1-2 mg/mL.	IV infusion at 3-5 mg/kg/hr	Fugisawa (developed by NeXstar, now Gilead), Antifungal

Drug Name/ Marketed Name	Structure	Formulation	Preadministration preparation	Route of Administration	Company and Indication
Ampicillin and Sulbactam sodium/ Unasyn	 Ampicillin Sulbactam	Powder 1-2 grams (ampicillin), 0.5-1.0 grams (sulbactam) pH = 8-10	Reconstitute with WFI to 250 mg/mL ampicillin and 125 mg/mL sulbactam. For IV dilute with saline or dextrose 5% to 3-45 mg/mL.	IM/ IV infusion over 10-30 minutes	Pfizer, Antibacterial (ampicillin)
Amrinone lactate/ Inocor (not in 1999 PDR)		Solution 5 mg/mL, Sodium metabisulfite 0.25 mg/mL, pH = 3-4	None or dilute with saline or half-saline to 1-3 mg/mL.	Slow IV bolus over 2-3 minutes IV infusion at 5-10 ug/kg/min	Sanofi Winthrop, Inotropic and vasodilator (short term management of CHF)
Atenolo/ Tenormin		Solution 0.5 mg/mL, Sodium chloride (to isotonic), Citric acid to pH = 5.5 - 6.2	None, or dilution with saline or dextrose 5%.	IV infusion at 1 mg/min	Zeneca, Antihypertensive and treatment of acute myocardial infarction
Atracurium besylate/ Tracrium		Solution 10 mg/mL w/wo Benzyl alcohol 0.9% pH = 3.2-3.6 (benzene sulfonic acid)	None for IV bolus For IV infusion dilute with saline or dextrose 5% to 0.2- 0.5 mg/mL.	IV bolus/ IV infusion at 5-13 ug/kg/min	Glaxo Wellcome, General anesthesia (Skeletal muscle relaxant)
Atrophine sulfate		Solution 0.1-1.0 mg/mL, Sodium chloride 9 mg/mL, w/wo Benzyl alcohol 1.5% pH 3-6	None	SC/ IM/ IV bolus	Elkins-Sinn, Astra, and Baxter, Anticholinergic, Antispasmodic
Aurothio- glucose/ Solganal		Suspension 50 mg/mL in sesame oil Aluminum monostearate 2%, Propylparaben 0.1%	None	IM (oil) Prolonged release due to slow absorption	Schering Corp., Antirheumatic
Azathioprine sodium/ Imuran		Lyophilized power 100 mg pH = 9.8-11	Reconstitute with 10 mL WFI. For IV infusion dilute with saline or dextrose 5%.	IV bolus/ IV Infusion	Glaxo Wellcome, Immuno- suppressive anti- metabolite; management of severe rheumatoid arthritis
Azithromy- cin/ Zithromax		Lyophilized powder, 500 mg, Citric acid 414 mg	Reconstitute with 5 mL WFI, and dilute to 1-2 mg/mL with saline, dextrose 5%, or lactated Ringer's.	IV infusion of 500 mg at 1 mg/mL over 3 hours, or 2 mg/mL over 1 hour	Pfizer, Antibiotic

Drug Name/ Marketed Name	Structure	Formulation	Preadministration preparation	Route of Administration	Company and Indication
Aztreonam/ Azactam		1) Lyophilized powder 0.5-2 g, L-arginine 780mg/gram aztreonam pH = 4.5-7.5 2) Frozen Solution 20-40 mg/mL Lactose 14-34 mg/mL, Arginine 16-32 mg/mL pH 4.5-7.5	For IM reconstitute with at least 3 mL WFI or saline to ~ 100-500 mg/mL. For IV bolus reconstitute with WFI to 50-200 mg/mL. For IV infusion reconstitute with 3 mL WFI, then dilute with saline, dextrose 5%, lactated Ringer's to ≤ 20 mg/mL.	IM/ IV bolus/ IV Infusion/	BMS, Antibiotic
Benzquin- amide (Not in 1999 PDR)		Powder 50 mg pH = 3-4	Reconstitute with WFI to 25 mg/mL.	IM/ IV infusion	Pfizer, Prevent nausea with surgery anesthesia
Benztropine mesylate/ Cogentin		Solution 1 mg/mL, Sodium chloride 9 mg/mL pH = 5-8	None	IM/ (IV bolus is alright, but has no advantage over IM)	Merck, Anticholinergic used in psychotic patients with acute dystonic reactions, and in Parkinson's disease
Betametha- sone Phosphate sodium and Betametha- sone Acetate/ Celestone soluspan	 Water soluble phosphate ester prodrug Water insoluble acetate ester prodrug	Suspension Betamethasone sodium phosphate 3 mg/mL, Betamethasone acetate 3 mg/mL, Sodium phosphate dibasic 7.1 mg/mL, Sodium phosphate monobasic 3.4 mg/mL, EDTA 0.1 mg/mL, Benzalkonium chloride 0.2 mg/mL, pH 6.8-7.2	None	IM	Schering, Anti- inflammatory and for allergies
Bethanechol chloride/ Urecholine		Solution 5.1 mg/mL, pH neutral	None	SC	Merck, Cholinergic

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