

DRUG FACTS AND COMPARISONS.

2015

Facts & Comparisons®

DRUG FACTS

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2015

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Drug Facts and Comparisons,[®] 2015 Edition

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Foreword

Facts & Comparisons™, a part of Clinical Drug Information, LLC, has served the drug information needs of pharmacists and other health care professionals since its inception in 1946 by providing timely unbiased, comparative information on prescription and non-prescription medications. *Drug Facts and Comparisons*® (DFC), our flagship product, is the primary source of drug information and the reference of choice for our many loyal subscribers because of its uncompromising editorial quality, reliability, and ease of use. DFC has remained unique among other drug information resources because of its organization by therapeutic use, providing single drug monographs as well as in-depth comparisons of closely related agents. Over the years, DFC has changed in size and scope, but the concept has never changed. That is why health care professionals continue to look to Facts & Comparisons™ to keep them abreast of important information in their practice.

Customers who prefer the currency, speed, and efficiency of electronic products can access DFC through *Facts & Comparisons*® eAnswers, our electronic library of reference information, which is available on-line or CD ROM. In addition to DFC, other content sets available on *Facts and Comparisons*® eAnswers include *Drug Interaction Facts*, *A to Z Drug Facts*, *Briggs' Drugs in Pregnancy and Lactation*, *Med Facts* (patient drug information handouts), *Review of Natural Products*, and *Drug Identifier*. Recently, *Facts and Comparisons*® eAnswers has added more detailed product tables for certain drugs, which is based on Medi-Span data, and has also added comparative efficacy information to some monographs regarding certain disease states. Information about *Facts & Comparisons*® eAnswers can be accessed through www.factsandcomparisons.com. Facts & Comparisons™ also offers drug information for handheld personal data assistants, available for downloading at www.factsandcomparisons.com.

Drug Facts and Comparisons™ monographs are also integrated into Medi-Span's Drug Information Bridge, a pre-programmed application programming interface (API) that includes Medi-Span's drug files and clinical databases. The integration of the DFC referential content with Medi-Span's premier databases provides superior point-of-care solutions for our professional customers.

Facts & Comparisons™ takes our mission of providing drug information to health care professionals very seriously, which is why we continue to invest in technology, improve our current publications, and stay in contact with our customers to make sure we maintain the high standards we set many years ago when Erwin Kastrup, RPh, first developed this concept. We have many people to thank for helping us achieve these goals, including our Editorial Advisory Panel, reviewers, contributors, and our excellent, dedicated employees, but more than anything we want to thank our loyal subscribers who have helped us develop and improve our drug information publications that are so widely used today.

We are dedicated to maintaining the traditions that are important to both Facts & Comparisons™ and our customers, but we are also dedicated to evolving our products to meet the changing technologies and the changing needs of health care professionals. These goals only can be accomplished by responding to the comments and suggestions from our subscribers, which we encourage and appreciate. As always, let us know how we can better serve you and your drug information needs.

Preface

As the premier publisher of drug information, Facts & Comparisons™ provides a broad range of print and electronic resources to fulfill the day-to-day needs of practicing health care professionals. *Drug Facts and Comparisons® (DFC)*, our flagship publication developed in 1946 by pharmacist Erwin K. Kastrop, was initially designed to provide objective information in a format that facilitated unbiased comparisons of drug products in a timely manner. After more than 60 years, the basic concepts remain the same. However, the content and presentation of material in *DFC* continues to evolve to reflect the changing needs of the health care environment.

The annual bound edition is one of several formats in which *DFC* is available. The original loose-leaf version is kept up to date through monthly print updates. An electronic version, updated continuously, is available as part of *Facts & Comparisons® eAnswers* and can be accessed via www.factsandcomparisons.com.

Facts & Comparisons® eAnswers also provides full monographs with complete prescribing information for nearly every single agent drug product, while the print versions continue to present abbreviated drug monographs in instances where a class monograph exists.

The new 68th edition of *DFC* incorporates 35 new drugs: Ado-trastuzumab emtansine (*Kadcyla* by Genentech), afatinib dimaleate (*Gilotrif* by Boeringer Ingelheim), botulism antitoxin heptavalent (equine) (by Cangene), cabozantinib malate (*Cometriq* by Exelixis), canagliflozin (*Invokana* by Janssen), coagulation factor XIII A-Subunit, recombinant (*Tretten* by Novo Nordisk), conjugated estrogens/bazedoxifene (*Duavee* by Pfizer), dabrafenib mesylate (*Tafinlar* by GlaxoSmithKline), dapagliflozin propanediol (*Farxiga* by Bristol-Myers Squibb), dimethyl fumarate (*Tecfidera* by Biogen Idec), dolutegravir sodium (*Tivicay* by GlaxoSmithKline), eslicarbazepine acetate (*Aptiom* by Sunovion), ferric carboxymaltose (*Injectafer* by American Regent), fluticasone furoate/vilanterol trifenate (*Breo Ellipta* by GlaxoSmithKline), glycerol phenylbutyrate (*Ravicti* by Hyperion Therapeutics), ibrutinib (*Imbruvica* by Pharmacyclics), levomilnacipran (*Fetzima* by Forest), lorcaserin hydrochloride (*Belviq* by Eisai), luliconazole (*Luzu* by Medicis), macitentan (*Opsumit* by Actelion), metreleptin (*Myalept* by Bristol-Myers Squibb), obinutuzumab (*Gazyva* by Genentech), pomalidomide (*Pomalyst* by Celgene Corporation), ponatinib hydrochloride (*Iclusig* by ARIAD Pharmaceuticals), prothrombin complex concentrate (human) (*Kcentra* by CSL Behring), radium Ra 223 dichloride (*Xofigo* by Bayer), riociguat (*Adempas* by Bayer Healthcare), simeprevir sodium (*Olysio* by Janssen Therapeutics), sofosbuvir (*Sovaldi* by Gilead Sciences), sucroferric oxyhydroxide (*Velphoro* by Fresenius), trametinib dimethyl sulfoxide (*Mekinist* by GlaxoSmithKline), umeclidinium/vilanterol (*Anoro Ellipta* by GlaxoSmithKline), unoprostone isopropyl (*Rescula* by Sucampo), varicella-zoster immune globulin (human) (*Varizig* by Cangene), vortioxetine (*Brintellix* by Takeda).

As this edition goes to press, we continue to update our database daily for use in future editions and formats of *DFC*. We also continue to expand our extensive library of drug information resources to remain the full service drug information provider that our customers have come to expect. However, this can only be accomplished with feedback from the loyal health care professionals who use our information on a daily basis. Comments, criticisms, and suggestions are always welcome and encouraged. Please call or visit us at www.factsandcomparisons.com.

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DIETARY REFERENCE INTAKES OF VITAMINS AND MINERALS

In 1941, the Food and Nutrition Board (FNB) of the Institute of Medicine, National Academy of Sciences, published the first edition of the Recommended Dietary Allowances (RDAs) to be used to evaluate the nutritional intakes of large populations. The primary purpose for the RDAs was to prevent diseases caused by nutritional deficiencies. Over the years, these guidelines were periodically updated and revised based on cumulative scientific evidence, and the tenth edition was published in 1989. In response to the growth of scientific knowledge regarding the roles of nutrients in human health, the FNB in partnership with Health Canada revised the RDAs and developed the Dietary Reference Intakes (DRIs).

The DRIs were published as a series of 8 reports from 1997 to 2005 and include the following nutrient reference values: Estimated Average Requirement (EAR), RDAs, Adequate Intake (AI), and Tolerable Upper Intake Level (UL). EAR refers to the intake value of a nutrient that is estimated to meet the

nutritional needs by a specified indicator of adequacy in 50% of an age- and gender-specific group. RDAs are based on EARs and are estimated to meet the needs of most individuals (97% to 98%). AIs are used when an RDA cannot be determined. UL is the maximum amount of daily nutrient intake (from food, water, and supplements) that is likely to pose no risk of adverse reactions.

In the following DRI tables, the RDAs are in bold type and the AIs are in ordinary type followed by an asterisk (*). These values may be used as goals for individual intake. For healthy breast-fed infants, the AI represents mean intake. For all other life-stage groups, the AI is believed to cover the needs of all individuals, but a lack of data or uncertainty in the data prevent specifying with confidence the percentage of individuals covered by this intake.

DRIs: Recommended Intakes for Individuals (Vitamins)

Life-stage group	Vitamin A (mcg/d) ^a	Vitamin C (mg/d)	Vitamin D (mcg/d) ^{b,c}	Vitamin E (mcg/d) ^a	Vitamin K (mcg/d)	Thiamine (mg/d)	Riboflavin (mg/d)	Niacin (mg/d) ^a	Vitamin B ₆ (mg/d)	Folate (mcg/d) ^d	Vitamin B ₁₂ (mcg/d)	Pantothenic acid (mg/d)	Biotin (mcg/d)	Choline (mg/d) ^e
Infants														
0 to 6 mo	400*	40*	10*	4*	2*	0.2*	0.3*	2*	0.1*	65*	0.4*	1.7*	5*	125*
7 to 12 mo	500*	50*	10*	5*	2.5*	0.3*	0.4*	4*	0.3*	80*	0.5*	1.8*	6*	150*
Children														
1 to 3 y	300	15	15*	6	30*	0.5	0.5	6	0.5	150	0.9	2*	8*	200*
4 to 8 y	400	25	15*	7	55*	0.6	0.6	8	0.6	200	1.2	3*	12*	250*
Men														
9 to 13 y	600	45	15*	11	60*	0.9	0.9	12	1	300	1.8	4*	20*	375*
14 to 18 y	900	75	15*	15	75*	1.2	1.3	16	1.3	400	2.4	5*	25*	550*
19 to 30 y	900	90	15*	15	120*	1.2	1.3	16	1.3	400	2.4	5*	30*	550*
31 to 50 y	900	90	15*	15	120*	1.2	1.3	16	1.3	400	2.4	5*	30*	550*
51 to 70 y	900	90	15*	15	120*	1.2	1.3	16	1.7	400	2.4 ^f	5*	30*	550*
70 y	900	90	20*	15	120*	1.2	1.3	16	1.7	400	2.4 ^h	5*	30*	550*
Women														
9 to 13 y	600	45	15*	11	60*	0.9	0.9	12	1	300	1.8	4*	20*	375*
14 to 18 y	700	65	15*	15	75*	1.1	1.1	14	1.2	400 ^g	2.4	5*	25*	400*
19 to 30 y	700	75	15*	15	90*	1.1	1.1	14	1.3	400 ^g	2.4	5*	30*	425*
31 to 50 y	700	75	15*	15	90*	1.1	1.1	14	1.3	400 ^g	2.4	5*	30*	425*
51 to 70 y	700	75	15*	15	90*	1.1	1.1	14	1.5	400	2.4 ^h	5*	30*	425*
70 y	700	75	20*	15	90*	1.1	1.1	14	1.5	400	2.4 ^h	5*	30*	425*
Pregnancy														
14 to 18 y	750	80	15*	15	75*	1.4	1.4	18	1.9	600 ⁱ	2.6	6*	30*	450*
19 to 30 y	770	85	15*	15	90*	1.4	1.4	18	1.9	600 ⁱ	2.6	6*	30*	450*
31 to 50 y	770	85	15*	15	90*	1.4	1.4	18	1.9	600 ⁱ	2.6	6*	30*	450*
Lactation														
14 to 18 y	1,200	115	15*	19	75*	1.4	1.6	17	2	500	2.8	7*	35*	550*
19 to 30 y	1,300	120	15*	19	90*	1.4	1.6	17	2	500	2.8	7*	35*	550*
31 to 50 y	1,300	120	15*	19	90*	1.4	1.6	17	2	500	2.8	7*	35*	550*

NOTE: AIs are in ordinary type followed by an asterisk (*), and RDAs are in bold type.

^a As retinol activity equivalents (RAEs). 1 RAE = retinol 1 mcg, β -carotene 12 mcg, α -carotene 24 mcg, or β -cryptoxanthin 24 mcg. The RAE for dietary provitamin A carotenoids is 2-fold greater than retinol equivalents (RE), whereas the RAE for preformed vitamin A is the same as RE.

^b As cholecalciferol. Cholecalciferol 1 mcg = vitamin D 40 units.

^c Values based on the absence of adequate exposure to sunlight.

^d As α -tocopherol. α -Tocopherol includes RRR- α -tocopherol, the only form of α -tocopherol that occurs naturally in foods and the 2R-stereoisomeric forms of α -tocopherol (RRR-, RSR-, RRS-, and RSS- α -tocopherol) that occur in fortified foods and supplements. It does not include the 2S-stereoisomeric forms of α -tocopherol (SSR-, SSR-, and SSS- α -tocopherol), also found in fortified foods and supplements.

^e Includes nicotinic acid amide, nicotinic acid (pyridine-3-carboxylic acid), and derivatives that exhibit the biological activity of nicotinamide. As niacin equivalents (NE). Niacin 1 mg = tryptophan 60 mg; 0 to 6 months = preformed niacin (not NE).

^f As dietary folate equivalents (DFE). One DFE = food folate 1 mcg = folic acid 0.5 mcg from fortified food or as a supplement consumed with food = 0.5 mcg of a supplement taken on an empty stomach.

^g Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all stages of the life-cycle, and it may be that the choline requirement can be met by endogenous synthesis at some of these stages.

^h Because 10% to 30% of older people may malabsorb food-bound B₁₂, it is advisable for individuals older than 50 years of age to meet their RDA mainly by consuming foods fortified with B₁₂ or a supplement containing B₁₂.

ⁱ In view of evidence linking folate intake with neural tube defects in the fetus, it is recommended that all women capable of becoming pregnant consume 400 mcg from supplements or fortified foods in addition to intake of food folate from a varied diet.

It is assumed that women will continue consuming 400 mcg from supplements or fortified food until their pregnancy is confirmed and they enter prenatal care, which ordinarily occurs after the end of the preconceptional period—the critical time for formation of the neural tube.

DIETARY REFERENCE INTAKES OF VITAMINS AND MINERALS

Life-stage group	DRIs: Recommended Intakes for Individuals (Elements)														
	Calcium (mg/d)	Chromium (mcg/d)	Copper (mcg/d)	Fluoride (mg/d)	Iodine (mcg/d)	Iron (mg/d) ^a	Magnesium (mg/d)	Manganese (mg/d)	Molybdenum (mcg/d)	Phosphorus (mg/d)	Selenium (mcg/d)	Zinc (mg/d) ^b	Potassium (g/d)	Sodium (g/d)	Chloride (g/d)
Infants															
0 to 6 mo	200*	0.2*	200*	0.01*	110*	0.27*	30*	0.003*	2*	100*	15*	2*	0.4*	0.12*	0.18*
7 to 12 mo	260*	5.5*	220*	0.5*	130*	11	75*	0.6*	3*	275*	20*	3	0.7*	0.37*	0.57*
Children															
1 to 3 y	700*	11*	340	0.7*	90	7	80	1.2*	17	460	20	3	3*	1*	1.5*
4 to 8 y	1,000*	15*	440	1*	90	10	130	1.5*	22	500	30	5	3.8*	1.2*	1.9*
Men															
9 to 13 y	1,300*	25*	700	2*	120	8	240	1.9*	34	1,250	40	8	4.5*	1.5*	2.3*
14 to 18 y	1,300*	35*	890	3*	150	11	410	2.2*	43	1,250	55	11	4.7*	1.5*	2.3*
19 to 30 y	1,000*	35*	900	4*	150	8	400	2.3*	45	700	55	11	4.7*	1.5*	2.3*
31 to 50 y	1,000*	35*	900	4*	150	8	420	2.3*	45	700	55	11	4.7*	1.5*	2.3*
51 to 70 y	1,000*	30*	900	4*	150	8	420	2.3*	45	700	55	11	4.7*	1.3*	2*
70 y	1,200*	30*	900	4*	150	8	420	2.3*	45	700	55	11	4.7*	1.2*	1.8*
Women															
9 to 13 y	1,300*	21*	700	2*	120	8	240	1.6*	34	1,250	40	8	4.5*	1.5*	2.3*
14 to 18 y	1,300*	24*	890	3*	150	15	360	1.6*	43	1,250	55	9	4.7*	1.5*	2.3*
19 to 30 y	1,000*	25*	900	3*	150	18	310	1.8*	45	700	55	8	4.7*	1.5*	2.3*
31 to 50 y	1,000*	25*	900	3*	150	18	320	1.8*	45	700	55	8	4.7*	1.5*	2.3*
51 to 70 y	1,200*	20*	900	3*	150	8	320	1.8*	45	700	55	8	4.7*	1.3*	2*
70 y	1,200*	20*	900	3*	150	8	320	1.8*	45	700	55	8	4.7*	1.2*	1.8*
Pregnancy															
14 to 18 y	1,300*	29*	1,000	3*	220	27	400	2*	50	1,250	60	12	4.7*	1.5*	2.3*
19 to 30 y	1,000*	30*	1,000	3*	220	27	350	2*	50	700	60	11	4.7*	1.5*	2.3*
31 to 50 y	1,000*	30*	1,000	3*	220	27	360	2*	50	700	60	11	4.7*	1.5*	2.3*
Lactation															
14 to 18 y	1,300*	44*	1,300	3*	290	10	360	2.6*	50	1,250	70	13	5.1*	1.5*	2.3*
19 to 30 y	1,000*	45*	1,300	3*	290	9	310	2.6*	50	700	70	12	5.1*	1.5*	2.3*
31 to 50 y	1,000*	45*	1,300	3*	290	9	320	2.6*	50	700	70	12	5.1*	1.5*	2.3*

NOTE: AIs are in ordinary type followed by an asterisk (*) and RDAs are in bold type.

^aNon-heme iron absorption is lower for those consuming vegetarian diets than for those eating nonvegetarian diets. Therefore, it has been suggested that the iron requirement for individuals consuming a vegetarian diet is approximately 2-fold greater than for individuals consuming a nonvegetarian diet.

^bZinc absorption is lower for those consuming vegetarian diets than for those eating nonvegetarian diets. Therefore, it has been suggested that the zinc requirement for individuals consuming a vegetarian diet is approximately 2-fold greater than for individuals consuming a nonvegetarian diet.

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INTRAVENOUS NUTRITIONAL THERAPY

Protein Substrates

CRYSTALLINE AMINO ACIDS

	Amino acid concentration	Amino acids (essential) (mg/100 mL)										Amino acids (nonessential) mg/100 mL										Electrolytes (mEq/L)					Supplied in (mL) ^b		Labeled indications		
		Isoleucine	Leucine	Lysine	Methionine	Phenylalanine	Threonine	Tryptophan	Valine	Alanine	Arginine	Histidine ^a	Proline	Serine	Taurine	Tyrosine	Glycine	Aspartic acid	Cysteine	Sodium	Potassium	Chloride	Acetate	Phosphate (mM/L)							
Aminosyn 3.5% (Hospital)	3.5%	0.55	252	329	252	140	154	182	56	280	448	343	105	300	147	31	448						51		322	1,000	Yes	No	Yes		
Aminosyn II 3.5% (Hospital)	3.5%	0.54	231	350	368	60	104	140	70	175	348	356	105	253	186	95	175	258	245		16.3		25.2		308	1,000	Yes	No	Yes		
Aminosyn 5% (Abbott)	5%	0.79	360	470	360	200	220	260	80	400	640	490	150	430	210	44	640						86		462	500 ^c	1,000 ^c	Yes	Yes	Yes	
Aminosyn II 5% (Abbott)	5%	0.77	330	500	525	86	149	200	100	250	497	509	150	361	265	135	250	369	350		19.3		35.9		438	500	Yes	Yes	Yes		
TrophAmine 6% (B. Braun)	6%	0.93	490	840	490	200	290	250	120	470	320	730	290	410	230	15	140	220	300	190	< 14	5.5		54.4		525	500 ^d	Yes	Yes	No	
Aminosyn 7% (Hospital)	7%	1.1	510	660	510	280	310	370	120	560	900	680	210	610	300	44	900						105		655	500 ^e	Yes	Yes	Yes		
Aminosyn-PF 7% (Hospital)	7%	1.07	534	831	475	125	300	360	125	452	490	861	220	570	347	50	44	270	576	370			32.5		561	500 ^e	Yes	Yes	No		
Aminosyn II 7% (Hospital)	7%	1.07	462	700	735	120	209	280	140	350	695	713	210	505	371	189	350	517	490		25		50		589	500 ^e	Yes	Yes	Yes		
Aminosyn 8.5% (Hospital)	8.5%	1.34	620	810	624	340	380	460	150	680	1,100	850	260	750	370	44	1,100								802	500 ^f	Yes	Yes	Yes		
Aminosyn II 8.5% (Hospital)	8.5%	1.3	561	850	883	146	253	340	170	425	844	865	255	614	450	230	425	627	595		32		61		706	500 ^f	Yes	Yes	Yes		
FreAmine III 8.5% (B. Braun)	8.5%	1.3	590	770	620	450	480	340	130	560	600	810	240	950	500		1,190				< 14	10		72	10	810	500 ^f	Yes	Yes	Yes	
TrophAmine 10% (B. Braun)	10%	1.55	820	1,400	820	340	480	420	200	780	540	1,200	480	680	380	25	240	360	500	320	< 16		< 3	97		875	500 ^d	Yes	Yes	No	
Aminosyn 10% (Hospital)	10%	1.57	720	940	720	400	440	520	160	800	1,280	980	300	880	420	44	1,280							147		932	500 ^f	Yes	Yes	Yes	
Aminosyn-PF 10% (Hospital)	10%	1.52	780	1,200	677	180	427	512	180	673	698	1,227	312	812	495	70	385	820	527				46		788	1,000 ^f	Yes	Yes	No		
Aminosyn II 10% (Hospital)	10%	1.53	660	1,000	1,050	172	298	400	200	500	993	1,018	300	722	530	270	500	738	700		38		72		1,040	500 ^f	Yes	Yes	Yes		
Travasol 10% (Baxter)	10%	1.65	600	730	580	400	560	420	180	580	2,070	1,150	480	680	500	40	1,030						40	88		998	500	1,000	Yes	Yes	Yes
FreAmine III 10% (B. Braun)	10%	1.53	690	910	730	530	560	400	150	660	710	950	280	1,120	590		1,400				< 16	10		~ 89	10	950	500 ^f	Yes	Yes	Yes	
Aminosyn II 15% (Hospital)	15%	2.3	990	1,500	1,575	258	447	600	300	750	1,490	1,527	450	1,083	795	405	750	1,107	1,050		62.7		107.6		1,300	2,000	Yes	Yes	No		
Clinisol 15% (Baxter)	15%	2.37	749	1,040	1,180	749	1,040	749	250	960	2,170	1,470	894	894	592	39	1,040	749	434				127		1,357	5,000 ^f	Yes	Yes	No		
Premasol 6% (Baxter)	6%	0.93	490	840	490	200	290	250	120	470	320	730	290	410	230	15	140	220	300	190	< 14		< 3	57		520	500	Yes	Yes	No	
Premasol 10% (Baxter)	10%	1.55	820	1,400	820	340	480	420	200	780	540	1,200	480	680	380	25	240	360	500	320	< 16		< 3	94		865	500	1,000	Yes	Yes	No

^a Histidine is considered an essential amino acid in infants and in renal failure.
^b Values are for 50 mL solution.
^c Contains calcium.
^d Contains sodium.
^e Contains potassium.
^f Contains aluminum.

^a Metabolites to be considered an essential amino acid in infants and in renal failure.
^b Product contains 10% amino acid solution.
^c Sodium free.
^d With < 50 mg sodium metabolite per 100 mL.
^e With < 50 mg sodium metabolite per 100 mL.
^f TPN - total parenteral nutrition.

Protein Substrates

CRYSTALLINE AMINO ACIDS — INJECTION

For complete and comparative prescribing information, refer to the Amino Acid Injection (General Formulation) class monograph. For additional information, refer to the Dietary Reference Intakes of Vitamins and Minerals table.

Indications

► **Nutritional supplementation:** For nutritional support of patients requiring TPN via either central or peripheral infusion routes. Parenteral nutrition with amino acids is indicated to prevent nitrogen loss or treat negative nitrogen balance in patients in whom the alimentary tract by the oral, gastrostomy, or jejunostomy route cannot or should not be used or adequate protein intake is not feasible by these routes; GI absorption of protein is impaired; or protein requirements are substantially increased as with extensive burns.

The following products are approved only for use in children: Premasol 6% and 10%, TrophAmine 6% and 10%, and Aminosyn-PF 7% and 10%.

► **Protein sparing (Aminosyn, Aminosyn II, FreAmine III, Travasol):** Dilute amino acid solutions for peripheral administration may be used in patients who exemplify no clinically significant protein malnutrition. The purpose of the solution is to replace protein losses that occur in relation to an intercurrent phenomenon that is known or suspected to be productive of a protein loss condition for short or moderate period of time. In well-nourished, mildly catabolic patients, such as routine postsurgical patients who require only short-term parenteral nutrition, protein sparing can be achieved by peripheral infusion of amino acid solutions with or without dextrose.

Administration and Dosage

► **General dosing considerations:** The total daily dose of the solution depends on the daily protein requirements and on the patient's metabolic and clinical response. The determination of nitrogen balance and accurate daily body weights, corrected for fluid balance, are probably the best means of assessing individual protein requirements.

The primary aim is to provide sufficient water to compensate for insensible, urinary, and other (nasogastric suction, fistula drainage, diarrhea) fluid losses. Total fluid requirements, as well as electrolyte and acid-base needs, should be estimated and appropriately administered.

For an amino acid solution of specified total concentration, the volume required to meet amino acid requirements per 24 hours can be calculated. After making an estimate of the total daily fluid (water) requirement, the balance of fluid needed beyond the volume of amino acid solution required can be provided either as a noncarbohydrate or a carbohydrate-containing electrolyte solution. Intravenous (IV) lipid emulsion may be substituted for part of the carbohydrate-containing solution.

Each gram of dextrose provides approximately 3.4 kcal. Each gram of fat provides 9 kcal.

Adults:**Nutritional supplementation —****Aminosyn and Aminosyn II:**

• **Usual dosage** — TPN may be started with dextrose 10% added to the calculated daily requirement of amino acids (1.5 g/kg for a metabolically stable patient). Dextrose content is gradually increased over the next few days to the estimated daily caloric need as the patient adapts to the increasing amounts of dextrose.

The average depleted major surgical patient with complications requires between 2,500 and 4,000 kcal and between 12 and 24 g of nitrogen per day. An adult patient in an acceptable weight range with restricted activity who is not hypermetabolic, requires approximately 30 kcal/kg of body weight per day. Average daily adult fluid requirements are between 2,500 and 3,000 mL and may be much higher with losses from fistula drainage or severe burns. Typically, a hospitalized patient may lose 12 to 18 g of nitrogen a day and, in severe trauma, the daily loss may be 20 to 25 g or more.

• **Peripheral venous infusion** — 1 to 1.5 g/kg/day of total amino acids will reduce protein catabolism. Infusion or ingestion of carbohydrate or lipid will not reduce the nitrogen-sparing effect of IV amino acid infusions at this dose.

If desired, only one-half of an estimated daily amino acid requirement of 1.5 g/kg can be given on the first day. Amino acids together with dextrose in concentrations of 5% to 10% infused into a peripheral vein can be continued while oral nutrition is impaired. However, if a patient is unable to take oral nourishment for a prolonged period of time, institution of TPN with exogenous calories should be considered.

Clinisol: The dosage on the first day should be approximately half the anticipated optimal dosage and should be increased gradually to minimize glycosuria; similarly, withdrawal should be accomplished gradually to avoid rebound hypoglycemia.

• **Central venous infusion** — In unstressed adults with no unusual nitrogen losses, a minimum dosage of 0.1 g of nitrogen (4.2 mL of Clinisol) plus 4.4 g (15 calories) of dextrose/fat emulsion per kilogram of body weight per day is required to achieve nitrogen balance and weight stability. For patients stressed by surgery, trauma, or sepsis, and those with unusual nitrogen losses, the dosage required for maintenance may be as high as 0.3 to 0.4 g/kg/day of nitrogen (13 to 17 mL of Clinisol), with proportionate increases in nonprotein calories. Periodic assessment of nitrogen balance of the individual patient is the best indicator of proper dosage. Use of an infusion pump is advisable to maintain a steady infusion rate during central venous infusion.

• **Peripheral venous infusion** — May be administered by peripheral vein. Dilute 250 mL of Clinisol 15% in 750 mL of dextrose 10% to reduce the osmolality to 718 mOsm/L.

FreAmine III:

• **Usual dosage** — Daily amino acid doses of approximately 1 to 1.5 g/kg of body weight for adults with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance in such patients, although higher doses may be required in severely catabolic states. Such higher doses must be accompanied by frequent laboratory evaluation. Fat emulsion may be supplied to help meet energy requirements.

• **Protein sparing** — For protein sparing in well-nourished patients not receiving significant additional calories, amino acid dosages of 1 to 1.7 g/kg/day significantly reduce nitrogen losses and spare body protein. If rises in serum urea nitrogen (BUN) exceed 20 mg in 48 hours, amino acid infusion should be discontinued or rate of administration reduced.

• **Central venous nutrition** — Calorie-to-nitrogen ratios of at least 100 to 150 nonprotein calories per gram of nitrogen have been recommended to achieve positive nitrogen balance in severely catabolic patients.

• **Peripheral parenteral nutrition** — For moderately catabolic, depleted patients requiring parenteral nutrition in whom the central venous route is not indicated, FreAmine III can be mixed with dextrose 5% solutions and administered by peripheral vein.

Travasol:

• **Usual dosage** — Daily amino acid doses of approximately 1 to 1.5 g/kg of body weight for adults with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance. For the initial treatment of trauma or protein calorie malnutrition, higher doses of protein with corresponding quantities of carbohydrate will be necessary to promote adequate patient response to therapy. The severity of the illness being treated is the primary consideration in determining proper dose level. Such higher doses must be accompanied by more frequent laboratory evaluation.

• **Protein sparing** — For protein sparing in well-nourished patients not receiving significant additional calories, amino acid dosages of 1 to 1.7 g/kg/day reduce nitrogen losses and spare body protein. If daily percent increases in BUN in the range of 10 to 15 mg for more than 3 days should occur, protein-sparing therapy should be discontinued and a regimen with full nonprotein calorie substrates should be adopted.

• **Central vein administration** — In addition to meeting nitrogen needs, the administration rate is governed, especially during the first few days of therapy, by the patient's tolerance to dextrose. Daily intake of amino acids and dextrose should be increased gradually to the maximum required dose as indicated by frequent determinations of urine and blood sugar levels.

► **Children:** Pediatric requirements for parenteral nutrition are constrained by the greater relative fluid requirements of the infant and greater caloric requirements per kilogram.

Amino acids are probably best administered in a 2.5% concentration.

Premature infants with respiratory distress syndrome suspected of having a patent ductus arteriosus should be given fluids more cautiously.

Nutritional supplementation —

Aminosyn and Aminosyn II: For most children receiving IV nutrition, 2.5 g/kg/day of amino acids with dextrose alone or with IV lipid calories of 100 to 130 kcal/kg/day is recommended. In cases of malnutrition or stress, these requirements may be increased. It is acceptable in children to start with a nutritional solution of half strength at a rate of approximately 60 to 70 mL/kg/day. Within 24 to 48 hours, the volume and concentration of the solution can be increased until the full strength pediatric solution (amino acids and dextrose) is given at a rate of 125 to 150 mL/kg/day.

A basic solution for pediatric use should contain 25 g of amino acids and 200 to 250 g of glucose per 1,000 mL, administered from bottles containing 250 or 500 mL. Such a solution given at the rate of 145 mL/kg/day provides 130 kcal/kg/day.

Aminosyn-PF: For infants up to 10 kg, the dosage is up to 2.5 g/kg/day of amino acid. For infants and children larger than 10 kg, the dosage is a total of up to 25 g/day of amino acids for the first 10 kg of body weight plus 1 to 1.25 g of amino acid for each kg of body weight over 10 kg. Initial amino acid dosage levels of 1 g/kg/day may be increased gradually in increments of 0.5 g/kg/day to approximate desired intake levels.

Aminosyn-PF should be diluted with dextrose prior to use. Nonprotein calories should constitute approximately 100 to 130 kcal/kg/day. Part of the nonprotein caloric requirement may be provided as lipid emulsion administered concurrently to provide up to 60% of daily calories at a dose not to exceed 4 g/kg/day of fat. Fluid intake for the infant receiving central venous TPN should be approximately 125 mL/kg/day (range, 100 to 175 mL/kg/day), depending on the clinical condition of the patient.

Clinisol, Travasol: Two to 3 g/kg of body weight for infants with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance.

FreAmine III: Two to 3 g/kg of body weight for infants with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance. Higher doses must be accompanied by frequent laboratory evaluation.

Infants (up to 10 kg) receiving TPN generally receive 2 to 3 g of protein, 120 to 150 calories, and 120 to 150 mL of fluid per kilogram of body weight per day. This can be provided in a solution containing approximately 2.125% of FreAmine III (diluted from FreAmine III 8.5% or 10%) and dextrose 20%. Less hypertonic mixtures may be administered by peripheral vein. Because physiological changes occur rapidly in small infants, the daily dose of nutrients should initially be increased slowly with frequent monitoring of pertinent clinical and metabolic parameters. Children weighing more than 10 kg require fewer calories and slightly less protein; generally 50 to 80 calories and 2 g/kg/day of protein is sufficient.

Premasol, TrophAmine: For infants up to 10 kg, the dosage is 2 to 2.5 g/kg/day of amino acids. For infants and young children larger than 10 kg, the total dosage of amino acids should include the 20 to 25 g/day for the first 10 kg of body weight, plus 1 to 1.25 g/day for each kg of body weight over 10 kg.

CRYSTALLINE AMINO ACIDS — INJECTION

A fluid dosage of 125 mL/kg/day is appropriate for most infants receiving TPN. Although nitrogen requirements may be higher in severely hypercatabolic or depleted patients, provision of additional nitrogen may not be possible because of fluid intake limits, nitrogen, or glucose intolerance.

►Elderly: In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. Amino acid injections are known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function.

►Concomitant therapy:

Dextrose/Insulin — In many patients, provision of adequate calories in the form of hypertonic dextrose may require the administration of exogenous insulin to prevent hyperglycemia and glycosuria. To prevent rebound hypoglycemia, a solution containing dextrose 5% should be administered when hypertonic dextrose infusions are abruptly discontinued.

Lipid emulsion — Fat emulsion coadministration should be considered when prolonged parenteral nutrition is required in order to prevent essential fatty acid deficiency (EFAD). Serum lipids should be monitored for evidence of EFAD in patients maintained on fat-free TPN.

IV fat emulsions provide approximately 1.1 kcal/mL (10%) or 2 kcal/mL (20%) and may be administered along with amino acid-dextrose solutions by means of a short Y-connector near the infusion site to supplement caloric intake. Fat, however, should not be the sole caloric intake because studies have indicated that glucose is more nitrogen sparing in the stressed patient.

Electrolytes — Crystalline amino acid solutions without electrolytes are intended for patients requiring individualized electrolyte therapy. The electrolyte content of amino acid solutions with electrolyte therapy must be considered when calculating daily electrolyte intake. Serum electrolytes should be monitored as indicated. Sodium, chloride, potassium, phosphate, calcium, and magnesium are major electrolytes that should be added to amino acid as required. For adults, approximately 60 to 180 mEq of potassium, 10 to 30 mEq of magnesium, and 20 to 80 mEq of phosphate per day appear necessary to achieve optimum metabolic response. In addition, sufficient quantities of the major extracellular electrolytes (sodium, calcium, and chloride) must be given.

In patients with hyperchloremic or other metabolic acidosis, sodium and potassium may be added as the acetate or lactate salts to provide bicarbonate alternatives.

Trace minerals/vitamins — Vitamins, including folic acid and vitamin K, are required additives. The trace element supplements should be given when long-term parenteral nutrition is undertaken.

Vitamin B₁₂, vitamin K, and folic acid are given intramuscularly (IM) or added to the solution as desired.

Iron is added to the solution or given IM in depot form as indicated. Iron supplementation is more critical in children.

Trace metal additives, including zinc, copper, manganese, and chromium, should also be provided, especially when long-term parenteral therapy is anticipated.

Cysteine — Cysteine is considered to be an essential amino acid in infants and young children. An admixture of cysteine hydrochloride to the TPN solution is therefore recommended. Based on clinical studies, the recommended dosage is 1 mmol of cysteine hydrochloride monohydrate per kilogram of body weight per day. An alternative recommendation is to give 500 mg of cysteine per 12.5 g of Aminosyn-PF.

►Preparation for administration: Color variation from pale yellow to yellow is normal and does not alter efficacy.

Do not use flexible container in series connections.

Solutions should be used promptly after mixing. Storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours.

►Administration: Administration time for a single bottle and set should never exceed 24 hours.

Central venous administration — Hypertonic mixtures of amino acids and dextrose may be safely administered by continuous infusion through a central venous catheter with the tip located in the vena cava. For adults, the 7%, 8.5%, or 10% solution may be used in equal volume with dextrose 50% to provide an admixture containing amino acids 3.5%, 4.25%, or 5% and dextrose 25%.

For adults, the rate of IV infusion of Aminosyn initially should be 2 mL/min and may be increased gradually. After dilution of FreAmine, the admixture is typically administered over an 8-hour period. For children, the initial infusion rate should be slow and gradually increased to 60 to 125 mL/kg/day. If administration should fall behind schedule, no attempt to "catch up" to planned intake should be made. In addition to meeting protein needs, the rate of administration is governed by the patient's glucose tolerance estimated by glucose levels in blood and urine.

Peripheral parenteral administration —

Children: Solutions administered by peripheral vein should not exceed twice the normal serum osmolality (718 mOsm/L).

Aminosyn: Aminosyn 3.5%, together with dextrose in concentrations of 5% to 10%, is suitable for administration by peripheral vein. This solution is not intended for central vein infusion because it does not contain adequate amounts of amino acids or electrolytes for administration with high concentrations of dextrose. Aminosyn 7%, 8.5%, or 10% may be diluted with sterile

water for injection or dextrose 5% to 10% injection to achieve a final amino acid concentration of 3.5%, 4.25%, or 5% for peripheral administration.

Aminosyn-PF: For patients in whom the central venous route is not indicated and who can consume adequate calories enterally, Aminosyn-PF may be administered by peripheral vein with parenteral nonprotein calories. A concentration of dextrose in the final admixture is 5% to 10%, and simultaneous administration of lipid emulsion is recommended both as a caloric source and to attenuate the potentially irritating effects of the hypertonic admixture.

Clinisol: In patients for whom central vein catheterization is not advisable, admixtures with Clinisol can be administered by peripheral vein. Dilution of 250 mL of Clinisol in 750 mL of dextrose 10% will reduce the osmolality to a level (718 mOsm/L) that is more favorable to the maintenance of the integrity of the walls of the veins.

FreAmine III: For moderately catabolic, depleted patients in whom the central venous route is not indicated, FreAmine III 8.5% or 10% can be mixed with dextrose 5% solutions and administered by peripheral vein.

Premasol, TrophAmine: For patients in whom the central venous route is not indicated and who can consume adequate calories enterally, Premasol and TrophAmine may be administered by peripheral vein with or without parenteral carbohydrate calories. Such infusates can be prepared by diluting with sterile water for injection or dextrose 5% to 10% injection to provide isotonic or slightly hypertonic solutions for peripheral infusion. It is essential that peripheral infusion be accompanied by adequate caloric intake.

►Admixture compatibility: Calcium and phosphate additives are potentially incompatible when added to the TPN admixture. However, if one additive is added to the amino acid bottle, and the other to the dextrose or concentrated dextrose, and if the contents of both bottles are swirled before they are combined, the likelihood of physical incompatibility is reduced. Calcium and phosphate may also be added to alternative infusate bottles to avoid precipitation.

Premasol and TrophAmine may be admixed with solutions that contain phosphate or that have been supplemented with phosphate. The presence of calcium and magnesium ions in an additive solution should be considered when phosphate is also present, in order to avoid precipitation.

►Storage/Stability: Store at 20° to 25°C (68° to 77°F). Protect from freezing. Avoid exposure to light.

Admixtures must be stored under refrigeration and used within 24 hours of admixing.

Clinisol, Travasol, Premasol — Store at 25°C (77°F). Brief exposure up to 40°C (104°F) does not adversely affect the product. Avoid excessive heat. Protect from freezing. Protect from light. Do not remove contents from overpouch until ready to use. Do not use if overpouch has been previously opened or damaged.

Actions

►Pharmacology: Crystalline amino acids solution promotes protein synthesis and wound healing and reduces the rate of endogenous protein catabolism. Amino acids, when given by central venous infusion in combination with concentrated dextrose, electrolytes, vitamins, trace metals, and ancillary fat supplements, constitutes TPN. When administered peripherally, the amino acid solution enhances the conservation of body protein.

FreAmine III — Phosphate, a component of FreAmine III, is a major intracellular anion that participates in providing energy for metabolism of substrates and contributes to significant metabolic and enzymatic reactions in all organs and tissues. It exerts a modifying influence on calcium levels, buffering effect on acid-base equilibrium, and has a primary role in the excretion of hydrogen ions.

Aminosyn PF, Premasol, TrophAmine — Aminosyn PF, Premasol, and TrophAmine contain a mixture of essential and nonessential amino acids, as well as taurine and a soluble form of tyrosine. The amino acid composition has been specifically formulated to provide a well-tolerated nitrogen source for nutritional support and therapy for infants and young children. When administered in conjunction with cysteine, amino acid solution results in plasma amino acid concentrations approximating a profile consistent with that of a breast-fed infant.

The rationale for these amino acid solutions is based on the observation of inadequate levels of essential amino acids in the plasma of infants receiving TPN using conventional amino acid solutions. These formulas were developed through the application of specific pharmacokinetic multiple regression analysis relating amino acid intake to the resulting plasma amino acid concentrations.

Clinical studies in infants and young children who required TPN therapy showed that infusion of amino acid 6% and 10% with a cysteine admixture resulted in plasma amino acid concentrations approximating those of normal breast- or formula-fed infants. In addition, weight gains, nitrogen balance, and serum protein concentrations were consistent with an improved nutritional status.

When infused with hypertonic dextrose as a caloric source, supplemented with cysteine, electrolytes, vitamins, and minerals, amino acid solution provides TPN for infants and young children, with the exception of essential fatty acids.

It is thought that the acetate from lysine acetate, under the conditions of parenteral nutrition, does not impact net acid-base balance when renal and respiratory functions are normal. Clinical evidence seems to support this thinking; however, confirmatory experimental evidence is not available.

The human newborn conjugates bile with taurine, which becomes the primary method of biliary excretion. Taurine deficiency, because of its effect on

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CRYSTALLINE AMINO ACIDS — INJECTION

bile salt conjugation and, therefore, on bile salt flow, may be of major importance in the genesis of cholestasis. Taurine has also been shown to play a role in CNS development.

Contraindications

Anuria, hepatic coma, hypersensitivity to one or more amino acids present in the solution.

► **Aminosyn, Aminosyn II:** Metabolic disorders involving impaired nitrogen utilization.

► **Clinisol, Travasol:** Severe liver disease, metabolic disorders involving impaired nitrogen utilization (*Clinisol* only).

► **Aminosyn PF, Premasol, TrophAmine, FreAmine III 10%:** In patients with inborn errors of amino acid metabolism (including those involving branched chain amino acid metabolism, such as maple syrup urine disease and isovaleric acidemia).

► **FreAmine III 8.5%:** In patients with hepatic encephalopathy or inborn errors of amino acid metabolism.

Warnings/Precautions

► **Administration:** Initiation and termination of infusions of TPN fluids must be gradual to permit adjustment of endogenous insulin release.

Peripheral administration — Peripheral administration of amino acid solutions requires appropriate dilution and provision of adequate calories. Take care to ensure proper placement of the needle within the lumen of the vein. Frequently inspect the venipuncture site for signs of infiltration. If venous thrombosis or phlebitis occurs, discontinue infusion or change infusion site and initiate appropriate treatment. In children, the final solution should not exceed twice normal serum osmolality (718 mOsmol/L).

Central venous administration — Administer strongly hypertonic nutrient solutions via an IV catheter placed in a central vein, preferably the superior vena cava. Regard the placement of a central venous catheter as a surgical procedure. One should be fully acquainted with various techniques of catheter insertion, as well as recognition and treatment of complications. For details of technique and placement sites, consult the medical literature. X-ray is the best means of verifying catheter placement. Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formation of arteriovenous fistula, phlebitis, thrombosis, cardiac arrhythmia, and air and catheter emboli. Other complications known to occur from the placement of central venous catheters include sepsis and vein irritation because of hypertonicity of the infused solution. The risk of sepsis is present during IV therapy, especially when using central venous catheters for prolonged periods. It is imperative that the preparation of admixtures and the placement and care of the catheters be accomplished under controlled aseptic conditions.

► **Serum urea nitrogen changes:** IV infusion of amino acids may induce a rise in BUN, especially in patients with impaired hepatic or renal function. Perform appropriate laboratory tests periodically and discontinue infusion if BUN levels exceed normal postprandial limits and continue to rise. A modest rise in BUN normally occurs as a result of increased protein intake.

► **Hyperammonemia:** Hyperammonemia is of special significance in infants, because its occurrence in the syndrome caused by genetic metabolic defects is sometimes associated, although not necessarily in a causal relationship, with mental retardation. This reaction appears to be dose related and is more likely to develop during prolonged therapy. This reaction appears to be related to a deficiency of the urea cycle amino acids of genetic or product origin. Therefore, it is essential that blood ammonia levels be measured frequently in infants. The mechanisms of this reaction are not clearly defined, but may involve genetic defects and immature or subclinically impaired liver function.

Instances of asymptomatic hyperammonemia have been reported in patients without overt liver dysfunction. The mechanisms of this reaction are not clearly defined, but may involve genetic defects and immature or subclinically impaired liver function.

Give conservative doses of amino acids dictated by the nutritional status of the patient. If symptoms of hyperammonemia develop, reduce amino acid dosage levels and titrate against serum ammonia levels.

► **Fluid and/or solute overload:** Administration of IV solutions can cause fluid and/or solute overload, resulting in dilution of serum electrolyte concentrations, overhydration, congested states, or pulmonary edema. The risk of dilutional states is inversely proportional to the electrolyte concentrations of the solutions. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of the solutions.

► **Aluminum toxicity:** Some products contain aluminum, which may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with CNS and bone toxicity. Tissue loading may occur at even lower rates of administration.

► **Cardiovascular considerations:** Avoid circulatory overload, particularly in patients with cardiac insufficiency.

In patients with myocardial infarction, infusion of amino acids should always be accompanied by dextrose because in anoxia, free fatty acids cannot be utilized by the myocardium, and energy must be produced anaerobically from glycogen or glucose.

► **Diabetes:** Take special care when giving dextrose to a diabetic or prediabetic patient. To prevent severe hyperglycemia in such patients, insulin may be required. Concomitant administration with highly concentrated dextrose solutions may result in hyperglycemia, glycosuria, and hyperosmolar syndrome. Routinely monitor blood and urine glucose in patients receiving this therapy.

► **Exogenous calories:** For long-term total nutrition, or if a patient has inadequate fat stores, it is essential to provide adequate exogenous dextrose calories concurrently with the amino acids. Administration of amino acids without carbohydrates may result in the accumulation of ketone bodies in the blood. Correction of this ketonemia may be achieved by the administration of carbohydrate. Concentrated dextrose solutions are an effective source of such calories. Administer such strongly hypertonic nutrient solutions through an indwelling IV catheter with the tip located in the superior vena cava.

In order for parenterally administered amino acids to be retained by the body and utilized for protein synthesis, adequate calories must be coadministered.

► **Electrolyte supplementation:** Extraordinary electrolyte losses, such as may occur during protracted nasogastric suction, vomiting, diarrhea, or GI fistula drainage may necessitate additional electrolyte supplementation.

Aminosyn PF, TrophAmine, and Premasol contain no added phosphorus. **FreAmine III** contains phosphorus 10 mmol/L. Patients, especially those with hypophosphatemia, may require the addition of phosphate. To prevent hypocalcemia, calcium supplementation should always accompany phosphate administration. To ensure adequate intake, monitor serum levels frequently.

► **Metabolic acidosis:** Metabolic acidosis can be prevented or readily controlled by adding a portion of the cations in the electrolyte mixture as acetate salts and, in the case of hyperchloremic acidosis, by keeping the total chloride content of the infusate to a minimum. **FreAmine III, Premasol, and TrophAmine** contain less than 3 mEq/L of chloride.

The metabolizable acetate anion and amino acid profile in **Travasol** were designed to minimize or prevent occurrences of hyperchloremic metabolic acidosis and hyperammonemia. However, be aware of appropriate countermeasures if they become necessary.

► **Essential fatty acid deficiency:** EFAD is becoming increasingly recognized in patients receiving long-term (more than 5 days) TPN. The use of fat emulsion to provide 4% to 10% of total caloric intake as linoleic acid may prevent EFAD.

During parenteral nutrition with concentrated dextrose and amino acid solutions, EFAD syndrome may develop but may not be clinically apparent. Early demonstration of this condition can only be accomplished by analysis of plasma lipids.

► **Protein-sparing therapy:** During protein-sparing therapy in the absence of supporting carbohydrate metabolism, an accumulation of ketone bodies in the blood often occurs. Correction of ketonemia usually can be accomplished by administering some carbohydrates.

Protein-sparing therapy is useful for periods of up to 10 to 12 days. Place patients requiring nutritional support thereafter on oral or parenteral regimens that employ adequate nonprotein calorie components.

► **Sepsis:** The constant risk of sepsis is present during administration of TPN. Because contaminated solutions and infusion catheters are potential sources of infection, it is imperative that the preparation of the solution and the placement and care of catheters be accomplished under strict aseptic conditions. If fever develops, change the solution, its delivery system, and the site of the indwelling catheter.

Ideally, prepare solutions in the hospital pharmacy in a laminar flow hood using careful aseptic technique to avoid inadvertent touch contamination during mixing of solutions and subsequent admixtures.

Consult the medical literature for a discussion of the management of sepsis during central venous nutrition. In brief, typical management includes replacing the solution being administered with a fresh container and set, and the remaining contents are cultured for bacterial or fungal contamination. If sepsis persists and another source of infection is not identified, the catheter is removed, the proximal tip cultured, and a new catheter reinserted when the fever has subsided. Nonspecific, prophylactic antibiotic treatment is not recommended. Clinical experience indicates that the catheter is likely to be the prime source of infection as opposed to aseptically prepared and properly stored solutions.

► **Metabolic complications:** The following metabolic complications have been reported with TPN administration: metabolic acidosis and alkalosis, hypophosphatemia, hypocalcemia, osteoporosis, glycosuria, hyperglycemia, hyperosmolar nonketotic states and dehydration, rebound hypoglycemia, osmotic diuresis and dehydration, elevated liver enzymes, hypo- and hypervitaminosis, electrolyte imbalances, and hyperammonemia in children. Frequent evaluations are necessary especially during the first few days of therapy to prevent or minimize these complications.

Administration of glucose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, coma, and death.

► **Sulfite sensitivity:** Some products contain a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown.

Protein Substrates

CRYSTALLINE AMINO ACIDS WITH ELECTROLYTES

	ProcalAmine (B. Braun Medical)	FreAmine III 3% w/Electrolytes (B. Braun Medical)	Aminosyn 3.5% M ^a (Hospira)	Aminosyn 7% w/Electrolytes (Hospira)	Aminosyn 8.5% w/Electrolytes (Hospira)	Aminosyn II 8.5% w/Electrolytes (Hospira)
Threonine	120	120	182	370	460	340
Tryptophan	46	46	56	120	150	170
Valine	200	200	280	560	680	425
Amino acids (nonessential) (mg/100 mL)						
Alanine	210	210	448	900	1,100	844
Arginine	290	290	343	690	850	865
Histidine	85	85	105	210	260	255
Proline	340	340	300	610	750	614
Serine	180	180	147	300	370	450
Tyrosine			31	44	44	230
Glycine	420	420	448	900	1100	425
Glutamic acid						627
Aspartic acid						595
Cysteine	< 20	< 20				
Electrolytes (mEq/L)						
Sodium chloride			234 ^c	28 ^c	28 ^c	
Potassium acetate			128 ^d			
Phosphoric acid			40 ^e			
Magnesium acetate, anhydrous			21 ^f			
Magnesium chloride, hexahydrate				102 ^g	102 ^g	
Sodium phosphate, dibasic				425 ^h	425 ^h	
Potassium chloride				487 ⁱ	487 ⁱ	
Sodium	35	35	40	65	65	80
Potassium	24.5	24.5	13	65	65	66
Magnesium	5	5	3	10	10	10
Chloride	41	41	40	96 ^j	96 ^j	86
Acetate	47 ^k	44 ^l	65 ^m	124 ⁿ	142 ⁿ	61
Phosphate (mM/L)	3.5 ^c	3.5	3.5	30 ^o	30 ^o	30
Osmolality (mOsm/L)	735	405	421	883	1,040	999
Nonprotein calories (g per 100 mL) (glycerin)	3			500	500	500
Supplied in (mL) ^p	1,000	1,000	1,000	500	1,000	500
pH			5.2 (4.5 to 6) ^q	5.2 (4.5 to 6) ^r	5.2 (4.5 to 6) ^r	
Labeled indications						
Peripheral parenteral nutrition	Yes	Yes	Yes	Yes	Yes	Yes
Central TPN ^s	No	No	No	Yes	Yes	Yes
Protein sparing	Yes	Yes	Yes	Yes	Yes	Yes

^a Contains maintenance electrolytes.

^b Amount cited is for lysine alone and does not include the acetate salt.

^c Sodium chloride (NaCl) is a white, crystalline powder freely soluble in water.

^d Potassium acetate (CH₃COOK) consists of colorless crystals or white crystalline powder and is very soluble in water.

^e Phosphoric acid (H₃PO₄) is a colorless, syrupy liquid miscible with water.

^f Magnesium acetate (Mg(CH₃COO)₂·4H₂O).

^g Magnesium chloride (MgCl₂·6H₂O), deliquescent crystals and very soluble in water.

^h Sodium phosphate (Na₂HPO₄) is white granules and very soluble in water.

ⁱ Potassium chloride (KCl) is a white, granular powder and is freely soluble in water.

^j Includes chloride from hydrochloride added for processing and pH adjustment.

^k Acetate is provided as inorganic acetate salts (23 mEq/L), acetic acid (9 mEq/L), and lysine acetate (15 mEq/L). It is thought that acetate from lysine acetate and acetic acid, under the conditions of parenteral nutrition, does not impact net acid/base balance when renal and respiratory functions are normal. Clinical experience seems to support this thinking, although confirmatory experimental evidence is not available.

^l Acetate provided as inorganic acetate salts (20 mEq/L), acetic acid (9 mEq/L), and lysine acetate (15 mEq/L).

^m Includes acetate from acetic acid used in processing and the acetate salts of potassium, magnesium, and lysine.

ⁿ Includes acetate from acetic acid used in processing and from lysine acetate.

^o 1 mM of phosphorus = 31 mg.

^p Product contains aluminum.

^q Contains acetic acid for pH adjustment.

^r Contains hydrochloric acid and acetic acid for pH adjustment.

^s TPN = total parenteral nutrition.

CRYSTALLINE AMINO ACIDS WITH ELECTROLYTES — INJECTION

For complete and comparative prescribing information, refer to the Amino Acid Injection (General Formulation) class monograph. For additional information, refer to the Dietary Reference Intakes of Vitamins and Minerals table.

Indications

➤ **Aminosyn:** Infused with dextrose by peripheral vein infusion, indicated as a source of nitrogen in the nutritional support of patients with adequate stores of body fat in whom, for short periods of time, oral nutrition cannot be tolerated, is undesirable, or inadequate.

Aminosyn can be administered peripherally with dilute (5% to 10%) dextrose solution and intravenous (IV) fat emulsion as a source of nutritional support. This form of nutritional support can help to preserve protein and reduce catabolism in stress conditions in which oral intake is inadequate.

When administered with concentrated dextrose solution with or without fat emulsions, Aminosyn is also indicated for central vein infusion to prevent or reverse negative nitrogen balance in patients for whom the alimentary tract by the oral, gastrostomy, or jejunostomy route cannot or should not be used; GI absorption of protein is impaired; metabolic requirements for protein are substantially increased, as with extensive burns; and morbidity and mortality may be reduced by replacing amino acids lost from tissue breakdown, thereby preserving tissue reserves, as in acute renal failure.

➤ **FreAmine III:** For peripheral administration to well-nourished, mildly catabolic adults who require only short-term parenteral nutrition. In medical or routine postsurgical patients in whom enteral nutrition is not desirable or cannot be tolerated, protein sparing can be achieved by the peripheral infusion of amino acid solutions with or without nonprotein calories.

Protein Substrates

CRYSTALLINE AMINO ACIDS WITH ELECTROLYTES — INJECTION

metals, and ancillary fat supplements, constitutes TPN. *Aminosyn* can also be administered by peripheral vein with dextrose and maintenance electrolytes. IV fat emulsion may be substituted for part of the carbohydrate calories during either TPN or peripheral vein administration of *Aminosyn*.

FreAmine III — *FreAmine III* with electrolytes provides a physiological ratio of biologically utilizable essential and nonessential amino acids and a balanced pattern of maintenance electrolytes designed to meet adult requirements. The amino acids provide a substrate for protein synthesis as well as sparing body protein and muscle mass. Peripheral IV infusions of amino acids administered for short periods in selected patients promote protein anabolism and prevent protein breakdown to meet caloric requirements.

Sodium, the major cation of the extracellular fluid, functions primarily in the control of water distribution, fluid balance, and osmotic pressure of body fluids. Sodium is also associated with chloride and bicarbonate in the regulation of the acid-base equilibrium of body fluid. Potassium, the principal cation of intracellular fluid, participates in carbohydrate utilization and protein synthesis and is critical in the regulation of nerve conduction and muscle contraction, particularly in the heart.

Chloride, the major extracellular anion, closely follows the metabolism of sodium, and changes in the acid-base balance of the body are reflected by changes in the chloride concentration. Magnesium, a principal cation of soft tissue, is primarily involved in enzyme activity associated with the metabolism of carbohydrates and protein. Magnesium is also involved in neuromuscular irritability.

Phosphate is a major intracellular anion that participates in providing energy for metabolism of substrates and contributes to significant metabolic and enzymatic reactions in almost all organs and tissues. It exerts a modifying influence on calcium levels, a buffering effect on acid-base equilibrium, and has a primary role in the renal excretion of hydrogen ions.

Inorganic acetate salts serve as bicarbonate precursors. It is thought that the acetate from lysine acetate and acetic acid, under the condition of parenteral nutrition, does not impact net acid-base balance when renal and respiratory functions are normal. Clinical evidence seems to support this thinking; however, confirmatory experimental evidence is not available.

ProcalAmine — *ProcalAmine* provides a physiological ratio of biologically utilizable essential and nonessential amino acids, a nonprotein energy source, and a balanced pattern of maintenance electrolytes. The amino acids provide substrates for protein synthesis, as well as sparing body protein and muscle mass.

Glycerin (glycerol), a utilizable energy substrate, is also provided and serves to preserve body protein. Glycerol participates as an active energy substrate through its phosphorylation to a-glycerophosphate and subsequent conversion to dihydroxyacetone phosphate, 1 of the 2 key trioses in the metabolism of glucose for energy generation.

The metabolism of glycerol has been investigated in both animals and humans. The liver is chiefly responsible for the high potential of glycerol utilization for gluconeogenesis, accounting for at least three-fourths of the total capacity of the body to utilize glycerol. Further, the kidney accounts for up to one-fifth of this total capacity. Among other kinds of cells and tissues shown to utilize glycerol at various rates are the brain, intestine, muscle, leukocytes, lungs, and spermatozoa.

In a multicenter clinical study, mildly catabolic postsurgical patients receiving *ProcalAmine* showed a significant improvement in nitrogen balance compared with patients receiving isonitrogenous amino acids.

Contraindications

► **Aminosyn:** Hepatic coma, metabolic disorders involving impaired nitrogen utilization.

► **FreAmine III:** Anuria; hepatic coma or encephalopathy; inborn errors of amino acid metabolism; hypersensitivity to one or more amino acids present in the solution; when the administration of sodium, potassium, magnesium, chloride, or phosphate could be clinically detrimental (eg, hyperkalemia; heart block or myocardial damage; edema due to cardiovascular, renal, or hepatic failure; acid-base imbalance).

► **ProcalAmine:** Renal failure; severe liver disease or hepatic coma; metabolic disorders involving impaired nitrogen utilization; hypersensitivity to one or more amino acids present in the solution.

Warnings/Precautions

► **Administration:** During peripheral vein infusions of amino acids and electrolytes, take care to ensure proper placement of the needle or catheter.

Inspect the venipuncture site frequently for signs of infiltration or inflammation. If venous thrombosis or phlebitis occurs, discontinue infusions or change infusion site and initiate appropriate treatment.

Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formation of arteriovenous fistula, phlebitis, thrombosis, and air and catheter emboli.

Peripheral infusion therapy is intended to provide nutritional support for a limited period of time. If a patient requires an extended period of nutritional support, enteral or parenteral regimens should include nonprotein calories adequate for weight maintenance.

► **Serum urea nitrogen changes:** IV infusion of amino acids may cause a normal, modest rise in serum urea nitrogen (BUN) as a result of increased protein intake. The BUN may become elevated in patients with impaired renal or hepatic function. Periodically perform appropriate laboratory tests and, if the BUN levels exceed postprandial limits and continue to rise, discontinue the infusion. A modest rise in BUN normally occurs as a result of increased protein intake.

► **Hyperammonemia:** Give conservative doses of amino acids dictated by the nutritional status of the patient. If symptoms of hyperammonemia develop, discontinue amino acid administration and reevaluate the patient's clinical status.

Hyperammonemia is of special significance in infants, because it can result in mental retardation. Therefore, it is essential that blood ammonia levels be measured frequently in infants.

Instances of asymptomatic hyperammonemia have been reported in patients without overt liver dysfunction. The mechanisms of this reaction are not clearly defined, but may involve genetic defects and immature or subclinically impaired liver function.

► **Glycerol effects:** Undesirable adverse effects of glycerol reported in the literature include hemolysis, hemoglobinuria, and renal damage. None of these adverse effects was observed in clinical trials with *ProcalAmine*. The manifestation of these adverse effects is highly dependent on dose and route of administration, as well as on formulation. In general, high concentrations of glycerol (up to 40%) are not hemolytic, provided the solution is prepared with isotonic saline. Subcutaneous injection of low doses of glycerol alone (eg, 3% without other solutes) can cause hemolysis. Much higher doses, up to 20 times that of subcutaneous injection, are required to obtain similar effects IV. Subcutaneous injection of glycerol at low doses can produce hemoglobinuria. Therefore, perform frequent monitoring to ensure early detection of infiltrations.

► **Fluid and/or solute overload:** The IV administration of these solutions can cause fluid and/or solute overload, resulting in dilution of serum electrolyte concentrations, overhydration, congested states, or pulmonary edema. The risk of dilutional states is inversely proportional to the solute concentration of the solution infused. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the concentration of the solution.

► **Aluminum toxicity:** These products contain aluminum, which may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at more than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with CNS and bone toxicity. Tissue loading may occur at even lower rates of administration.

► **Cardiovascular considerations:** Take care to avoid circulatory overload, particularly in patients with cardiac insufficiency.

In patients with myocardial infarction, always accompany the infusion of amino acids by dextrose because in anoxia, free fatty acids cannot be utilized by the myocardium, and energy must be produced anaerobically from glycogen or glucose.

► **Diabetes:** Take special care when administering glucose to provide calories in diabetic or prediabetic patients.

Frequently monitor blood sugar levels in diabetic patients.

► **Exogenous calories:** For long-term total nutrition or if a patient has inadequate fat stores, it is essential to provide adequate exogenous calories concurrently with amino acids. Concentrated dextrose solutions are an effective source of such calories. Administer such strongly hypertonic nutrient solutions through an indwelling IV catheter with the tip located in the superior vena cava.

► **Phlebitis:** The use of hypertonic solutions has been associated with an increased incidence of phlebitis. The incidence of phlebitis with *ProcalAmine* was marginally higher than that observed with a less hypertonic solution. Phlebitis can be minimized by using an in-line filter and/or by changing the site of infusion.

► **Protein-sparing therapy:** Protein-sparing therapy is intended for short-term use only. If a patient requires an extended period of nutritional support, ensure that oral or parenteral regimens include adequate nonprotein calorie components.

► **Sepsis:** The constant risk of sepsis is present during administration of TPN. It is imperative that the preparation of the solution and the placement and care of catheters be accomplished under strict aseptic conditions.

Ideally, prepare solutions in the hospital pharmacy under a laminar flow hood using careful aseptic technique to avoid inadvertent touch contamination.

► **Metabolic complications:** The following metabolic complications have been reported with TPN administration: metabolic acidosis and alkalosis, hypophosphatemia, hypocalcemia, osteoporosis, hyperglycemia, hyperosmolar nonketotic states and dehydration, glycosuria, rebound hypoglycemia, osmotic diuresis and dehydration, elevated liver enzymes, hypo- and hyper-vitaminosis, electrolyte imbalances, and hyperammonemia in children. Frequent evaluations are necessary, especially during the first few days of therapy to prevent or minimize these complications.

CRYSTALLINE AMINO ACIDS WITH ELECTROLYTES — INJECTION

Administration of glucose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, coma, and death.

Administration of amino acids without carbohydrates may result in the accumulation of ketone bodies in the blood. Correction of this ketonemia may be achieved by the administration of carbohydrate.

► **Sulfite sensitivity:** Some of these products contain a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

► **Renal function impairment:** Administration of amino acid solutions in the presence of impaired renal function may augment an increasing BUN, as does any protein dietary component.

In patients with diminished renal function, administration of solutions containing sodium or potassium ions may result in sodium or potassium retention.

► **Hepatic function impairment:** Administration of amino acid solutions to a patient with hepatic insufficiency may result in plasma amino acid imbalances, metabolic alkalosis, hyperammonemia, prerenal azotemia, stupor, and coma.

► **Special risk:** Use solutions containing sodium ions with great care, if at all, in patients with congestive heart failure, severe renal insufficiency, and clinical states in which sodium retention with edema exists.

Use solutions containing potassium ions with great care, if at all, in patients with hyperkalemia, severe renal failure, and in conditions in which potassium retention is present.

Use solutions containing acetate ions with care in patients with metabolic or respiratory alkalosis. Administer acetate with great care in those conditions for which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

Administer sodium-containing solutions with caution to patients receiving corticosteroids or corticotropin, or to other salt-retaining patients. Exercise care when administering solutions containing sodium or potassium to patients with renal or cardiovascular insufficiency, with or without congestive heart failure, particularly if they are postoperative or elderly.

Potassium therapy should be guided primarily by serial electrocardiograms, especially in patients receiving digitalis. Serum potassium levels are not necessarily indicative of tissue potassium levels. Use solutions containing potassium or magnesium with caution in the presence of cardiac disease, particularly in the presence of renal disease.

Use feeding regimens that include amino acids with caution in patients with a history of renal disease, pulmonary disease, or cardiac insufficiency to avoid excessive fluid accumulation.

► **Pregnancy:** Category C. Animal reproduction studies have not been conducted with amino acids with electrolytes. It is also not known whether amino acid with electrolytes causes fetal harm when administered to a pregnant woman or if it affects reproduction capacity. Give amino acid with electrolytes to a pregnant woman only if clearly needed.

► **Lactation:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when amino acid with electrolytes is administered to a breast-feeding woman.

► **Children:** The effect of infusion of amino acids without dextrose on carbohydrate metabolism of children is not known at this time.

Safety and effectiveness of amino acid injections in children have not been established by adequate and well-controlled studies. However, the use of amino acid injections in children as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance is well established in the medical literature.

Aminosyn may not be suitable for use in infants who require individualized electrolyte therapy.

► **Elderly:** In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, take care in dose selection; it may be useful to monitor renal function.

► **Monitoring:** The electrolyte pattern is designed for maintenance only during protein sparing therapy in adults. Clinical evaluation and periodic

laboratory determinations are necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance, whenever the condition of the patient warrants such evaluation. Significant deviations from normal concentrations may require administration of additional electrolytes.

Do not withdraw venous blood for blood chemistries through the peripheral infusion site, because interference with estimations of nitrogen-containing substances may occur. Include glucose, urea nitrogen, serum electrolytes, ammonia, cholesterol, acid-base balance, serum proteins, kidney and liver function tests, osmolality, and hemogram in blood studies. White blood cell count and blood cultures are to be determined if indicated. Determine urinary osmolality and glucose as necessary.

Frequently monitor blood sugar levels in diabetic patients.

Carefully monitor nitrogen intake in patients with impaired renal function.

Drug Interactions

Amino Acids With Electrolytes Drug Interactions		
Precipitant drug	Object drug*	Description
CNS depressants (ie, barbiturates, hypnotics, narcotics, systemic anesthetics)	Amino acids with electrolytes	↑ Adjust dose with caution in patients receiving magnesium-containing solutions because of additive central depressive effects.
Amino acids with electrolytes	CNS depressants (eg, barbiturates, hypnotics, narcotics, systemic anesthetics)	
Tetracycline	Amino acids with electrolytes	↓ Because of its antianabolic activity, tetracycline may reduce the potential anabolic effects of amino acids.

* ↑ = object drug increased; ↓ = object drug decreased.

Adverse Reactions

► **Local:** Local reactions of the infusion site, consisting of erythema, phlebitis, thrombosis, and a warm sensation, have been reported with peripheral amino acid infusions, especially if other substances, such as antibiotics, are also administered through the same site.

► **Miscellaneous:** Generalized flushing, fever, and nausea have been reported during peripheral administration of amino acids.

► FreAmine III:

Local — Reactions that may occur because of the solution or the technique of administration include extravasation, febrile response, hypervolemia, infection at the site of injection, and venous thrombosis or phlebitis extending from the site of injection.

Metabolic/Nutritional — Symptoms may result from an excess or deficit of one or more of the ions present in the solution; therefore, frequent monitoring of electrolyte levels is essential.

Hypnatremia may be associated with edema and exacerbation of congestive heart failure due to the retention of water, resulting in an expanded extracellular fluid volume.

Reactions reported with the use of potassium-containing solutions include abdominal pain, diarrhea, nausea, and vomiting. The signs and symptoms of potassium intoxication include areflexia, cardiac arrest, cardiac arrhythmias, electrocardiographic abnormalities, heart block, hypotension, mental confusion, muscular or respiratory paralysis, paresthesias of the extremities, and weakness. Potassium deficits result in disruption of neuromuscular function and intestinal dilatation and ileus.

If infused in large amounts, chloride ions may cause a loss of bicarbonate ions, resulting in an acidifying effect.

Abnormally high plasma levels of magnesium can result in circulatory collapse, depression of cardiac and CNS function, flushing, hypotension, and sweating. Respiratory depression is the most immediate threat to life. Magnesium deficits can result in hyperirritability, hypertension, psychotic behavior, and tachycardia.

Phosphorus deficiency may lead to acute hemolytic anemia and impaired tissue oxygenation. Relative to calcium, excessive phosphorus intake can precipitate hypocalcemia with cramps, muscular hyperexcitability, and tetany.

Protein Substrates

AMINO ACID FORMULATION IN HEPATIC FAILURE/HEPATIC ENCEPHALOPATHY — INJECTION

Administration of glucose at a rate exceeding the patient's utilization rate may lead to hyperglycemia, coma, and death.

► **Sulfite sensitivity:** HepatAmine contains a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

► **Renal function impairment:** Administration of amino acids in the presence of impaired renal function or GI bleeding may augment an already elevated serum urea nitrogen (BUN). Do not infuse patients with azotemia from any cause with amino acids without regard to total nitrogen intake.

► **Hepatic function impairment:** Infusion of amino acid may not affect the clinical course of patients with fulminant hepatitis who have a poor prognosis and who are generally unresponsive to treatment. It has been shown that the abnormal plasma amino acid pattern in fulminant hepatitis differs from that in chronic liver disease.

► **Pregnancy:** Category C. Animal reproduction studies have not been conducted with amino acids. It is also not known whether amino acid injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Give amino acid injection to a pregnant woman only if clearly needed.

Amino acid injection has not been adequately studied in pregnant women and children; therefore, its safe use in such patients has not been demonstrated.

► **Lactation:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when amino acid injection is administered to a breast-feeding woman.

► **Children:** Safety and effectiveness of amino acid injections in children have not been established by adequate and well-controlled studies. However, the use of amino acid injections in children as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance is well established in the medical literature.

► **Elderly:** In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the

greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Amino acid injection is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, take care in dose selection; it may be useful to monitor renal function.

► **Monitoring:** General clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance, electrolyte concentrations, and acid base balance during prolonged parenteral therapy or whenever the condition of the patient warrants such evaluation. Significant deviations from normal concentrations may require the use of additional electrolyte supplements.

Studies should include blood sugar, serum proteins, kidney and liver function tests, electrolytes, hemogram, carbon dioxide content, serum osmolality, blood cultures, and blood ammonia levels.

Drug Interactions

Name well documented.

Adverse Reactions

► **CNS:** Asterixis was reported to have worsened in one patient during infusion of amino acid injection.

► **Local:** Extravasation, infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection.

► **Metabolic/Nutritional:** Reactions reported in clinical studies as a result of infusion of the parenteral fluid were dilutional hyponatremia, edema, and water weight gain.

Hypervolemia may occur because of the solution or technique of administration.

Phosphorus deficiency may lead to acute hemolytic anemia and impaired tissue oxygenation. Relative to calcium, excessive phosphorus intake can produce hypocalcemia with cramps, muscular hyperexcitability, and tetany.

► **Miscellaneous:** Febrile response, increase in BUN.

CYSTEINE HYDROCHLORIDE

Rx	Cysteine Hydrochloride (Various, eg, Hospira)	Injection, solution, concentrate:	In 10 mL single-dose vials and 50 mL multidose vial.
Rx	L-Cysteine Hydrochloride (Various, eg, American Regent, Sandoz)	50 mg/mL	In 10 mL single-dose syringes.

CYSTEINE HYDROCHLORIDE — INJECTION**Indications**

► **Cysteine supplement:** For use only after dilution as an additive to a crystalline amino acid solution to meet the intravenous (IV) amino acid nutritional requirements of infants receiving total parenteral nutrition (TPN).

Administration and Dosage

► **General dosing considerations:** Use only after dilution in crystalline amino acid injection. (See Preparation for Administration.)

► **Adults:** Not intended for use in adults.

► **Children:**

Cysteine supplementation in patients receiving TPN — Individualize dosage according to the needs of the neonate. (See also Preparation for Administration.)

Off-label dosing —

Cysteine supplementation in patients receiving TPN: One reference suggests cysteine supplementation at a rate of approximately 30 to 40 mg/g of protein.

► **Preparation for administration:** Use only after dilution in crystalline amino acid injection. Each 500 mg (10 mL) of cysteine injection should be combined aseptically with 12.5 g of crystalline amino acid injection, such as that present in 250 mL of crystalline amino acid injection 5%. The admixture is then diluted with 250 mL of dextrose 50% or such lesser volume as indicated. Equal volumes of crystalline amino acid 5% injection and dextrose 50% produce a final solution that contains crystalline amino acid 2.5% injection in dextrose 25%, which is suitable for administration by central venous infusion.

Administration of the final admixture should begin within 1 hour of mixing. Otherwise, the admixture should be refrigerated immediately and used within 24 hours of the time of mixing.

When using dispensing (multiple dose) vials, use aseptic technique. Dispense entire contents in aliquots under a laminar flow hood within 4 hours after entry or discard remaining contents after first withdrawal. Prepare stoppers with a suitable antiseptic solution.

► **Administration:** Use of large peripheral veins, in-line filters, and slowing the rate of infusion may reduce the incidence of local venous irritation. Electrolyte additives should be spread throughout the day. Irritating additive medications may need to be injected at another venous site.

Strong hypertonic nutrient solutions should be administered through an indwelling IV catheter with the tip located in the superior vena cava.

► **Storage/Stability:** Store between 15° and 30°C (59° and 86°F). After dilution in crystalline amino acid injection, administer within 1 hour of mixing. Otherwise, the admixture should be refrigerated immediately and used within 24 hours of the time of mixing.

Actions

► **Pharmacology:** Cysteine is a sulfur-containing amino acid. Cysteine is synthesized from methionine via the transsulfuration pathway in adults, but newborn infants lack the enzyme cystathionase, which is necessary to affect this conversion. Therefore, cysteine is generally considered to be an essential amino acid in infants.

Contraindications

Hepatic coma; metabolic disorders involving impaired nitrogen utilization.

Warnings/Precautions

► **Hyperammonemia:** Hyperammonemia is of special significance in infants, as it can result in mental retardation. Therefore, it is essential that blood ammonia levels be measured frequently in infants.

Instances of asymptomatic hyperammonemia have been reported in patients without overt liver dysfunction. The mechanisms of this reaction are not clearly defined but may involve genetic defects and immature or subclinically impaired liver function.

► **Aluminum toxicity:** This product contains aluminum, which may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum of more than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with CNS toxicity. Tissue loading may occur at even lower rates of administration.

► **Exogenous calories:** For long-term total nutrition, or if a patient has inadequate fat stores, it is essential to provide adequate exogenous calories concurrently with the amino acids. Concentrated dextrose solutions are an effective source of such calories. Such strong hypertonic nutrient solutions should be administered through an indwelling IV catheter, with the tip located in the superior vena cava.

Protein Substrates

CYSTEINE HYDROCHLORIDE — INJECTION

► **Diabetes:** Special care must be taken when administering hypertonic glucose to provide calories in diabetic or prediabetic patients.

► **Renal function impairment:** This product contains aluminum, which may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired.

Peripheral IV infusion of amino acids may induce a rise in serum urea nitrogen (BUN), especially in patients with impaired renal function. Periodically perform appropriate laboratory tests and discontinue the infusion if BUN levels exceed normal postprandial limits and continue to rise. A modest rise in BUN normally occurs as a result of increased protein intake.

Administration of amino acid solutions in the presence of impaired renal function may augment an increasing BUN, as does any protein dietary component.

► **Hepatic function impairment:** Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, metabolic alkalosis, prerenal azotemia, hyperammonemia, stupor, and coma.

Peripheral IV infusion of amino acids may induce a rise in BUN, especially in patients with hepatic impairment.

► **Special risk:** Use IV feeding regimens that include amino acids with caution in patients with a history of renal disease, pulmonary disease, or with cardiac insufficiency, so as to avoid excessive fluid accumulation.

Solutions with sodium — Use solutions containing sodium ion with great care, if at all, in patients with congestive heart failure, severe renal insufficiency, and in clinical states in which there exists edema with sodium retention.

Solutions with potassium — Use solutions that contain potassium ion with great care, if at all, in patients with hyperkalemia, severe renal failure, and in conditions in which potassium retention is present.

Solutions with acetate — Use solutions containing acetate ion with great care in patients with metabolic or respiratory alkalosis. Administer acetate with great care in those conditions for which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

► **Pregnancy:** Safe use during pregnancy has not been established; therefore, infusion of amino acids should be undertaken during pregnancy only when this is deemed essential to the patient's welfare, as judged by the health care provider.

This medicine is not indicated for use in pregnant women.

► **Lactation:** This medication is not indicated for use in breast-feeding women.

► **Children:** The effect of infusion of amino acids without dextrose upon carbohydrate metabolism of children is not known at this time. Hyperammonemia is of special significance in infants, as it can result in mental retardation. Monitor blood ammonia levels frequently.

This product contains aluminum, which may be toxic. Premature neonates are particularly at risk because their kidneys are immature and they require large amounts of calcium and phosphate solutions, which contain aluminum.

► **Monitoring:** Frequent clinical evaluations and laboratory determinations are necessary for proper monitoring during administration. Blood studies should include glucose, urea nitrogen, serum electrolytes, ammonia, cholesterol, acid-base balance, serum proteins, kidney and liver function tests, osmolality, and hemogram. White blood cell count and blood cultures are to be determined if indicated. Frequently determine urinary osmolality and glucose.

Carefully monitor nitrogen intake in patients with impaired renal function.

Drug Interactions

► **Tetracycline:** Because of its antianabolic activity, coadministration of tetracycline may reduce the nitrogen-sparing effects of infused amino acids.

Adverse Reactions

► **Local:** Local reactions consisting of a warm sensation, erythema, phlebitis, and thrombosis at the infusion site have occurred with peripheral IV infusion of amino acids, particularly if other substances, such as antibiotics, are also administered through the same site. In such cases, promptly change the infusion site to another vein. Use of large peripheral veins, in-line filters, and slowing the rate of infusion may reduce the incidence of local venous irritation.

► **Systemic:** Generalized flushing, fever, and nausea have been reported during peripheral infusions of amino acid solutions.

Caloric Intake

DEXTROSE (d-GLUCOSE)

Rx	D-2.5-W (Various, eg, Abbott)	2.5%	In 1000 mL.
Rx	D-5-W (Various, eg, Abbott, IMS, McGaw)	5%	In 25, 50, 100, 150, 250, 500 and 1000 mL vials and 10 mL syringes, 25 mL fill in 150 mL, 50 mL fill in 250 mL and 100 mL fill in 250 mL vials.
Rx	D-10-W (Various, eg, Hospira, Solopak, Winthrop)	10%	In 3 mL amps, 250, 500 and 1000 mL vials, 17 mL fill in 20 mL, 500 mL fill in 1000 mL, and 1000 mL fill in 2000 mL vials.
Rx	D-20-W (Various, eg, Abbott)	20%	In 500 mL vials, 500 mL fill in 1000 mL and 1000 mL fill in 2000 mL.
Rx	D-25-W (Various, eg, Abbott, IMS)	25%	In 10 mL syringes.
Rx	D-30-W (Various, eg, Abbott, McGaw)	30%	In 500 and 1000 mL, 500 mL fill in 1000 mL and 1000 mL fill in 2000 mL.
Rx	D-40-W (Various, eg, Abbott, McGaw)	40%	In 500 and 1000 mL, 500 mL fill in 1000 mL and 1000 mL fill in 2000 mL.
Rx	D-50-W (Various, eg, Abbott, IMS, McGaw, Pasadena)	50%	In 500, 1000 and 2000 mL and 50 mL amps, vials and syringes and 500 mL fill in 1000 mL and 1000 mL fill in 2000 mL.
Rx	D-60-W (Various, eg, Abbott, McGaw)	60%	In 500 and 1000 mL, 500 mL fill in 1000 mL and 1000 mL fill in 2000 mL.
Rx	D-70-W (Various, eg, Abbott, McGaw)	70%	In 70, 1000 and 2000 mL, 500 mL fill in 1000 mL and 1000 mL fill in 2000 mL.

DEXTROSE — INJECTION**Indications**

► **2.5%, 5%, and 10% solutions:** Used for peripheral infusion to provide calories whenever fluid and caloric replacement are required.

► **25% (hypertonic) solutions:** Acute symptomatic episodes of hypoglycemia in the neonate or older infant to restore depressed blood glucose levels and control symptoms.

► **50% solution:** Used in the treatment of insulin hypoglycemia (hyperinsulinemia or insulin shock) to restore blood glucose levels.

► **10%, 20%, 30%, 40%, 50%, 60%, and 70% (hypertonic) solutions:** For infusion after admixture with amino acids or dilution with other compatible IV fluids to provide variable final dextrose concentrations for intravenous infusion in patients whose condition requires parenteral nutrition.

► **Off-label uses:** Hypertonic solutions of 25% to 50% have been used as a sclerosing agent for the treatment of varicose veins and to reduce cerebrospinal pressure and cerebral edema caused by delirium tremens or acute alcohol intoxication.

Administration and Dosage

► **General dosing considerations:** Dosage is dependent upon age, weight, clinical condition of the patient and laboratory determinations. Frequent laboratory determinations and clinical evaluation are essential to monitor changes in blood glucose and electrolyte concentrations, and fluid and electrolyte balance during prolonged parenteral therapy.

Fluid administration should be based on calculated maintenance or replacement fluid requirements for each patient.

Adults:

Fluid and caloric replacement (2.5%, 5%, and 10% solutions) — Individualize dosage.

Insulin-induced hypoglycemia (50% solution) — 10 to 25 g intravenously (IV). Repeated doses may be required in severe cases. Determine blood glucose before injecting dextrose. In emergencies, promptly administer without waiting for pretreatment test results.

Parenteral nutrition (10%, 20%, 30%, 40%, 50%, 60%, and 70% [hypertonic] solutions) — Concentrated dextrose in water is administered by slow IV infusion a) after admixture with amino acid solutions or b)