INSULIN (Systemic)

Introduction

This monograph includes information on the following:1) Buffered Insulin Human; 2) Extended Insulin Zinc a, b; 3) Extended Insulin Human Zinc; 4) Insulin; 5) Insulin Human; 6) Insulin Zinc; 7) Insulin Human Zinc; 8) Isophane Insulin; 9) Isophane Insulin Human; 10) Isophane Insulin Human and Insulin Human; 11) Prompt Insulin Zinc a, b.

INN:

Extended Insulin Zinc Suspension¾Insulin Zinc Suspension (Crystalline) 3

Insulin Zinc Suspension¾Compound Insulin Zinc Suspension 3

Prompt Insulin Zinc Suspension¾Insulin Zinc Suspension (Amorphous) 3

BAN:

Extended Insulin Zinc Suspension¾Insulin Zinc Suspension (Crystalline) 3

Prompt Insulin Zinc Suspension¾Insulin Zinc Suspension (Amorphous) 3

JAN:

Extended Insulin Zinc Suspension¾Crystalline Insulin Zinc Injection (Aqueous Suspension) 3

Insulin Human Injection¾Insulin Human (Biosynthesis) and Insulin Human (Synthesis) 3

Isophane Insulin Suspension¾Isophane Insulin Injection (Aqueous Suspension) 3

Insulin Zinc Suspension¾Insulin Zinc Injection (Aqueous Suspension) and Insulin Zinc Purified Porcine (Suspension) 3

Prompt Insulin Zinc Suspension¾Amorphous Insulin Zinc Injection (Aqueous Suspension) 3

VA CLASSIFICATION (Primary/Secondary)¾HS501/GA900; DX900

Commonly used brand name(s):Humulin 10/9010; Humulin 20/8010; Humulin 30/7010; Humulin 40/6010; Humulin 50/5010; Humulin 70/3010; Humulin 70/30 Pen10; Humulin L7; Humulin N9; Humulin N Pen9; Humulin R5; Humulin R, Regular U-500 (Concentrated)5; Humulin U3; Humulin-L7; Humulin-N9; Humulin-R5; Humulin-U3; Lente6; Lente Iletin6; Lente Iletin II6; NPH Iletin8; NPH Iletin II8; NPH Purified Insulin8; Novolin 70/3010; Novolin 70/30 PenFill10; Novolin 70/30 Prefilled10; Novolin L7; Novolin N9; Novolin N PenFill9; Novolin N Prefilled9; Novolin R5; Novolin R PenFill5; Novolin R Prefilled5; Novolin ge 10/90 Penfill10; Novolin ge 20/80 Penfill10; Novolin ge 30/7010; Novolin ge 30/70 Penfill10; Novolin ge 40/60 Penfill10; Novolin ge 50/50 Penfill10; Novolin ge Lente7; Novolin ge NPH9; Novolin ge NPH Penfill9; Novolin ge Toronto5; Novolin ge Toronto Penfill5;

Novolin ge Ultralente3; Regular (Concentrated) Iletin II, U-5004; Regular Iletin II4; Regular Insulin4; Velosulin BR1; Velosulin Human1.

Other commonly used names are:
Lente insulin Insulin Zinc.

NPH insulin Isophane Insulin.

Regular insulin Insulin.

Semilente insulin Prompt Insulin Zinc.

Ultralente insulin Extended Insulin Zinc.

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

a Not commercially available in the U.S.

b Not commercially available in Canada.

Category

Antidiabetic agent; diagnostic aid (pituitary growth hormone reserve).

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Diabetes, type 1¾Insulin is indicated in the treatment of type 1 diabetes (previously called Type I, ketosis-prone, brittle, or juvenile-onset diabetes), which occurs in individuals who produce little or no endogenous insulin. One of two regimens (conventional or intensive therapy) is commonly used to treat this condition. The intensive regimen provides more rigid control of blood glucose than the conventional regimen does, but requires more frequent monitoring and more frequent dosage adjustment, and, unless insulin is administered via an insulin pump, a larger number of injections. 48, 49, 54

Diabetes, type 2¾Insulin is indicated in the treatment of certain patients with type 2 diabetes (previously known as Type II, adult-onset, maturity-onset, ketosis-resistant, or stable diabetes), which occurs in individuals who produce or secrete insufficient quantities of endogenous insulin or who have developed resistance to endogenous insulin. Insulin therapy in type 2 diabetes is reserved for patients whose disease is not controlled by other measures, such as diet, exercise, or oral antidiabetic agents, or for patients who cannot tolerate oral antidiabetic agents. 48, 50, 54

Diabetes mellitus, gestational (GDM) 48, 49, 215

Diabetes mellitus, malnutrition-related 49 or

Diabetes mellitus, other, associated with certain conditions or syndromes, 48, 49 such as: Pancreatic disease (congenital absence of the pancreatic islets, transient diabetes of the newborn, functional immaturity of insulin secretion in the neonate, or cystic fibrosis); endocrine disease (endocrine overactivity due to Cushing's syndrome, hyperthyroidism, pheochromocytoma, somatostatinoma, or aldosteronoma; or endocrine underactivity due to hypoparathyroidism-hypocalcemia, type I isolated growth hormone deficiency, or multitropic pituitary deficiency); or genetic syndromes, including inborn errors of metabolism (glycogen-storage disease type I or insulin-resistant syndromes, such as muscular dystrophies, late onset proximal myopathy, and Huntington's chorea)¾Insulin is indicated for the treatment of GDM and for the treatment of diabetes mellitus associated with certain conditions and syndromes uncontrolled by other treatment measures (diet, exercise, and oral antidiabetic agents). Insulin requirements eventually increase during pregnancy for all patients with diabetes. Need for additional exogenous insulin usually stops postpartum for GDM patients due to hormonal and metabolic changes; however, in some patients, GDM progresses to type 1 or type 2 diabetes within 5 to 10 years. 215 Insulin also is used to treat diabetes induced by hormones, medications, or chemicals. Insulin has been added to total parenteral nutrition or glucose solutions in order to facilitate glucose utilization in patients with poor glucose tolerance. 40, 49, 55, 56, 57, 76

Insulin also is used to treat acute complications associated with diabetes, such as ketoacidosis, significant acidosis, ketosis, hyperglycemic hyperosmolar nonketotic coma, or diabetic coma. 54 Also, temporary insulin dosing for patients with diabetes who do not usually require insulin or an increased insulin dose for patients with type 1 diabetes or patients with type 2 diabetes who require insulin may be warranted when these patients are subjected to physical stress (e.g., pregnancy, fever, severe infection, severe burns, major surgery, or other severe trauma). 48, 50, 54

Combination use of insulin and oral antidiabetic agents in patients with type 1 diabetes is controversial because many studies have indicated that oral antidiabetic agents are not effective in the treatment of these patients. 58, 59 Some patients with type 2 diabetes who are resistant to sulfonylureas alone may benefit from the combination of low-dose insulin and oral sulfonylurea agents for diabetes; however, resultant weight gain and effects of hyperinsulinemia should be considered. In addition, the combination of metformin and sulfonylurea agents has been used successfully before discontinuation of oral agents and initiation of insulin therapy. 113

Concentrated insulin (500 USP Insulin Units per mL) is used only to treat insulin-resistant patients needing a high dose (over 200 USP units) of insulin. 27

[Growth hormone deficiency (diagnosis)] *¾Regular insulin administered intravenously is used to assess the capacity of the pituitary gland to release growth hormone. Reliable results may require that more than one test be performed, using either regular insulin or arginine. This test also may be used to obtain information regarding release of corticotropin from the pituitary. A physician experienced in the use of the insulin tolerance test should be present because of the risk of hypoglycemia. 2, 187, 192, 193

* Not included in Canadian product labeling.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Source¾Bovine: Obtained from the pancreas of oxen; differs from human insulin by two amino acids at positions 8 and 10 on the A-chain and from porcine insulin by one amino acid at position 30 on the B-chain. 53, 88

Human: Derived by enzymatic modification of the one different amino acid (threonine for alanine) in porcine insulin (semi-synthetic) or derived by microbial synthesis (recombinant DNA process involving genetically engineered Escherichia coli or baker's yeast); identical to naturally occurring human insulin; contains 21 amino acids in the A-chain and 30 amino acids in the B-chain. 53, 88

Porcine: Obtained from pork pancreas; differs from human insulin by one amino acid at position 30 on the B-chain. 53, 88

Molecular weight¾Insulin (beef): 5733.61 3

Insulin (pork): 5777.66 3

Insulin Human (semisynthetic, biosynthetic): 5807.69 3

Mechanism of action/Effect:

Insulin is a polypeptide hormone that controls the storage and metabolism of carbohydrates, proteins, and fats. This activity occurs primarily in the liver, in muscle, and in adipose tissues after binding of the insulin molecules to receptor sites on cellular plasma membranes. Although the mechanisms of insulin's molecular actions in the cellular area are still being explored, it is known that cell membrane transport characteristics, cellular growth, enzyme activation and inhibition, and alterations in protein and fat metabolism are all influenced by insulin. 50, 91 More specifically, insulin promotes uptake of carbohydrates, proteins, and fats in most tissues. Also, insulin influences carbohydrate, protein, and fat metabolism by stimulating protein and free fatty acid synthesis, and by inhibiting release of free fatty acid from adipose cells. 50, 54 Insulin increases active glucose transport through muscle and adipose cellular membranes, and promotes conversion of intracellular glucose and free fatty acid to the appropriate storage forms (glycogen and triglyceride, respectively). Although the liver does not require active glucose transport, insulin increases hepatic glucose conversion to glycogen and suppresses hepatic glucose output. Even though the actions of exogenous insulin are identical to those of endogenous insulin, the ability to negatively affect hepatic glucose output differs because a smaller quantity of exogenous insulin reaches the portal vein. 91

Antidiabetic agent¾

Administered insulin substitutes for the lack of endogenous insulin secretion and partially corrects the disordered metabolism and inappropriate hyperglycemia of diabetes mellitus, which are caused by either an absolute deficiency or a reduction in the biologic effectiveness of insulin, or possibly both. Maintenance of good blood glucose control by insulin, which is facilitated by increasing glucose uptake and use, may slow the progression of the serious long-term complications of diabetes. 48, 50, 54

Diagnostic aid, pituitary growth hormone reserve¾

Regular insulin administered intravenously stimulates growth hormone secretion by producing hypoglycemia, which is used to evaluate pituitary growth hormone reserve. 187, 192, 193

Other actions/effects:

Insulin increases the intracellular shift of potassium and magnesium and decreases renal excretion of sodium. Insulin decreases the synthesis of high density lipoprotein (HDL) cholesterol and increases the synthesis of very low density lipoprotein (VLDL) cholesterol in the liver. Insulin increases lipoprotein uptake and utilization in the lactating mammary gland. Also, insulin stimulates activity of and tissue response to the sympathetic nervous system. The growth-promoting action of insulin may contribute to an increase in peripheral vascular resistance through vascular hypertrophy. 50, 85, 86

USP Insulin Type	Onset of action b (hrs)	Time to peak b (hrs)	Duration of action
Intravenous Insulin injection U-100 (regular insulin) pork, purified pork, biosynthetic human, semisynthetic human	1/6-1/2	1/4-1/2	1/2-1
Subcutaneous Insulin injection U-100 (regular insulin) pork, purified pork, biosynthetic human, semisynthetic human	1/2-1	2-4	5-7
Insulin injection U-500 (regular insulin) purified pork, biosynthetic human			24 c
Isophane insulin suspension U-100 (NPH insulin) mixed a, pork, purified pork, biosynthetic human	3-4	6-12	18-28
Isophane insulin suspension (70%) and insulin injection (30%) U-100 biosynthetic human	1/2	4-8	24
Insulin zinc suspension U-100 (lente insulin) mixed a, pork, purified pork, biosynthetic human	1-3	8-12	18-28

Extended insulin zinc suspension U-100 (ultralente) biosynthetic human	4-6	18-24	36
Prompt insulin zinc suspension U-100 (semilente)	1-3	2-8	12-16

a Mixed = Mixture of beef and pork insulins.

b Mean values; individual responses vary widely.

c U-500 strength is absorbed slowly, resulting in a long duration of action. 198, 199

Absorption:

The rate of subcutaneous and intramuscular insulin absorption is highly variable (up to 50% interindividual and intraindividual variability) and is dependent on many factors including insulin formulation, injection site, injection technique, and route of injection. The addition of protamine or zinc to insulin produces a crystallized insulin in suspension that has a longer absorption phase (and a longer duration of action) than dissolved insulin does and is dependent on enzymatic degradation of the suspension at the injection site for absorption. 28, 50, 88, 89 Absorption of regular insulin, when mixed with equal or greater quantities of zinc insulin, may be slowed if the mixture is not injected immediately after preparation. Mixing regular insulin with isophane insulin does not alter the rate of absorption of either. 87, 90 Studies have shown that the absorption rate of human insulins is no different from, or only slightly higher than, the rate for animal insulins. 90 The speed of injection and temperature of insulin do not alter absorption; however, capillary surface area and exercise do affect the intramuscular blood flow and can alter absorption. Exercising the limb into which the insulin was injected within 30 to 40 minutes postinjection may increase insulin absorption (delay of exercise may be warranted). 87, 88, 170, 171 Although longer-acting insulins have less pronounced variability in absorption among injection sites, the absorption rate for 12 USP Units of regular insulin given subcutaneously declined per region as follows: abdominal (87 minutes), deltoid (141 minutes), gluteal (155 minutes), and femoral (164 minutes). 87 Finally, insulin absorption is faster with intramuscular injection than with subcutaneous injection, and is slower with very high insulin concentrations or high dose volumes. 87, 88

A subcutaneous depot of insulin forms slowly at the injection site when a continuous subcutaneous infusion insulin pump is used, resulting in less variation in insulin availability and a smaller depot than occurs with use of subcutaneous injections. When injection sites are rotated, continued absorption from the first depot usually prevents plasma concentrations from decreasing to subtherapeutic values while another depot is forming. 190

Distribution:

Distributed into most cells. 90

Biotransformation:

Insulin¾Hepatic and renal. 50, 91

Isophane or zinc insulins¾Split into protamine or zinc and insulin by subcutaneous enzymes prior to absorption. 50, 171

Half-life:

Insulin¾5 to 6 minutes; can be longer in some patients with diabetes. 91 Insulin antibodies, if present, bind to circulating plasma insulin and prolong its biologic half-life. 50, 171

Elimination:

Renal, 30 to 80%; unchanged insulin is reabsorbed. 50, 91

Precautions to Consider

Cross-sensitivity and/or related problems

Patients intolerant of beef or pork insulins may use the alternative single-source insulin under the direction of their physician. Intolerance of beef insulin is more common than intolerance of pork insulin. Intolerance is often reduced by the use of purified pork insulin, biosynthetic human insulin, or semisynthetic human insulin. 50

Patients hypersensitive to protamine sulfate also may be hypersensitive to protamine-containing insulins. Patients who have become sensitized to protamine through administration of a protamine-containing insulin are at risk for severe anaphylactoid reactions if protamine sulfate is subsequently administered for reversal of heparin effect. 63, 64

Pregnancy/Reproduction

Pregnancy¾Insulin does not cross the placenta. However, maternal glucose and maternal insulin antibodies do cross the placenta and can cause fetal hyperinsulinemia and related problems, such as large-for-gestational-age infants and macrosomnia, possibly resulting in a need for early induced or cesarean delivery. 66, 69, 70, 72, 73, 75 Furthermore, high blood glucose concentrations occurring during early pregnancy (5 to 8 weeks gestation) have been associated with a higher incidence of major congenital abnormalities and, later in pregnancy, increased perinatal morbidity and mortality. 66, 67, 215

Women with diabetes must be educated about the necessity of maintaining strict metabolic control before conception and throughout pregnancy, especially during early pregnancy, to significantly decrease the risk of maternal mortality, congenital anomalies, and perinatal morbidity and mortality. 66, 67, 68, 69, 75, 215 A study reported that initial glycosylated hemoglobin (hemoglobin A 1c, a measurement of blood glucose control for the preceding 3 months) concentrations of 10% or more, 8 to 9.9%, and below 8% produced infant malformation rates of 35%, 12.9%, and 4.8%, respectively; the malformation rate in infants born to mothers who do not have diabetes is approximately 2%. 73, 75 Use of insulin rather than oral antidiabetic agents for the treatment of type 2 diabetes and

gestational diabetes mellitus (GDM) permits maintenance of blood glucose at concentrations as close to normal as possible. 215 Insulin requirements in pregnant patients with diabetes often are decreased during the first trimester. Requirements usually are increased in the last two trimesters of pregnancy in response to the anti-insulin hormone activity associated with increased concentrations of human placental estrogen, progesterone, chorionic gonadotropin, and prolactin; peripheral insulin resistance due to increasing levels of fatty acids and triglycerides; and increased degradation of insulin by the placenta. 28, 76, 215

Postpartum¾Insulin requirements drop quickly after childbirth, and GDM patients usually no longer need insulin. Inadequately controlled maternal blood glucose late in pregnancy may cause increased insulin production in the fetus, resulting in neonatal hypoglycemia. Treatment may be necessary until euglycemic control is established by the neonate. 76, 215

Breast-feeding

Insulin is not distributed into breast milk. Problems in humans have not been documented. The insulin requirement in lactating women is reduced because of hormonal changes; in patients with type 1 diabetes, insulin requirements during lactation may be up to 27% lower than the patient's pre-pregnancy requirements. Daily monitoring for several months is important until insulin needs stabilize or until insulin is no longer needed. 85, 86

Pediatrics

Insulin therapy in pediatric patients is similar to that in other age groups. However, strict intensive insulin therapy is not generally used for this age group because noncompliance may be a problem and because this regimen may be less beneficial before puberty while risks of hypoglycemia may be higher due to greater insulin sensitivity. 50, 211

Adolescents

Insulin therapy in adolescents is similar to that in other age groups. Appropriate use of intensive insulin therapy may be beneficial when used cautiously. Patients with diabetes have a transient increase in insulin requirement (by approximately 20 to 50%) at puberty during the growth spurt only. 78, 79, 80, 81, 82, 83 Adolescent females usually require more insulin than do adolescent males because of increased insulin resistance; this is thought to be due, in part, to an increased secretion of growth hormone, but not to an increased secretion of sex hormones. Increased growth hormone secretion also may require alteration of the timing of insulin doses to overcome the prominent dawn phenomenon of hyperglycemia in adolescents of both sexes who have diabetes. 78, 79, 80, 81, 82, 83, 211

Geriatrics

Insulin therapy in older patients is similar to that in other age groups. However, strict intensive insulin therapy is not generally used. Also, dehydration, which may mask early symptoms of hypoglycemia and permit development of more severe symptoms; vision problems, which may lead to inaccurate dosage measurement and/or glucose monitoring; shakiness, which may interfere with measurement and self-administration of a dose; and lack of compliance with prescribed diet commonly occur in the elderly and may interfere with control of diabetes. Instructions may be

needed to help the patient monitor urine or blood glucose if visual problems are present or early symptoms of hypoglycemia are missing or delayed, a particular problem in this age group. Special devices are available to help administer the insulin dose when help with visual clarity or steadiness is needed. 84, 213

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

If the need exists to administer any medications that may affect metabolic or glycemic control of diabetes mellitus, blood glucose concentrations should be monitored by the patient or health care professional. This is particularly important when any medication is added to or removed from an established drug regimen. Subsequent adjustments in diet or insulin dosage or both may be necessary; these adjustments may differ depending on the severity of the diabetes mellitus and other factors. 94

>> Alcohol

(consumption of moderate or large amounts of alcohol enhances insulin's hypoglycemic effect, increasing the risk of prolonged, severe hypoglycemia, especially under fasting conditions or when liver glycogen stores are low; small amounts of alcohol consumed with meals do not usually present problems 50, 95, 96, 97, 98, 99, 100)

Anabolic steroids, especially stanozolol, oxandrolone, and methandrostenolone or

Androgens

(increased tissue sensitivity to insulin and increased tissue resistance to glucagon may occur, resulting in hypoglycemia, especially when insulin resistance is present; a decrease in insulin dose may be required 50, 101, 102)

Antidiabetic agents, sulfonylurea or

Carbonic anhydrase inhibitors, especially acetazolamide

(these medications chronically stimulate the pancreatic beta cell to release insulin and increase receptor and tissue sensitivity to insulin; although concurrent use of these medications with insulin may increase the hypoglycemic response, the effect may be unpredictable 50, 91, 93, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114)

(sulfonylurea antidiabetic agents have been used concurrently with insulin in treating a select group of patients with type 2 diabetes whose condition is not well-controlled with either agent alone; however, the long-term benefit of this use has not been established; many studies have shown there

is generally no additional benefit from using sulfonylurea antidiabetic agents for the treatment of patients with type 1 diabetes [50, 91, 93, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114]

Anti-inflammatory drugs, nonsteroidal (NSAIDs) or

Salicylates, large doses

(these medications inhibit synthesis of prostaglandin E [which inhibits endogenous insulin secretion], thereby increasing basal insulin secretion, the response to a glucose load, and the hypoglycemic effect of concurrently administered insulin; dosage adjustment of the NSAID or salicylate and/or insulin may be necessary, especially during and following chronic concurrent use [50, 91, 114, 115, 116, 117])

>> Beta-adrenergic blocking agents, including ophthalmics, if significant systemic absorption occurs

(beta-adrenergic blocking agents may inhibit insulin secretion, modify carbohydrate metabolism, and increase peripheral insulin resistance, leading to hyperglycemia; however, they also may cause hypoglycemia and block the normal catecholamine-mediated response to hypoglycemia [glycogenolysis and mobilization of glucose], thereby prolonging the time it takes to achieve euglycemia and increasing the risk of a severe hypoglycemic reaction. Selective beta 1-adrenergic blocking agents [such as acebutolol, atenolol, betaxolol, bisoprolol, and metoprolol] exhibit the above actions to a lesser extent; however, any of these agents can blunt some of the symptoms of developing hypoglycemia, such as increased heart rate or blood pressure [increased sweating may not be altered], 113 making detection of this complication more difficult [50, 91, 119, 120, 121, 122, 123, 124, 125, 126, 127])

Chloroquine or

Quinidine or

Quinine

(concurrent use with insulin may increase the risk of hypoglycemia and increased blood insulin concentrations because of decreased insulin degradation [50, 93, 129, 130, 131, 132])

>> Corticosteroids

(these agents antagonize insulin's effects by stimulating release of catecholamines, causing hyperglycemia; corticosteroid-induced diabetes can occur in up to 14% of the patients taking systemic corticosteroids for several weeks or with prolonged use of topical corticosteroids, but this condition rarely produces acidosis or ketonuria even with high glucose concentrations; reversal of effects may take several weeks or months; changes in insulin dose may be necessary for patients with diabetes during and following concurrent use [50, 91, 133, 134, 135])

Diuretics, loop or

Diuretics, thiazide

(concurrent use with insulin may increase the risk of hyperglycemia because the potassium-depleting effect of these diuretics may inhibit insulin secretion and decrease tissue sensitivity to insulin 50, 139, 140, 141, 142)

Guanethidine or

Monoamine oxidase (MAO) inhibitors, including furazolidone, procarbazine, and selegiline

(epinephrine release by these agents may cause hyperglycemia; however, chronic use results in hypoglycemia; the mechanism of the latter is unknown but may include stored catecholamine depletion and interference with the compensatory adrenergic response to a fall in blood glucose; a change in dose of insulin before, during, and after treatment with these agents may be necessary 143, 144, 145, 146, 147, 148, 149, 150)

Hyperglycemia-causing agents, such as:

Calcium channel blocking agents

Clonidine

Danazol

Dextrothyroxine

Diazoxide, parenteral

Epinephrine

Estrogen

Estrogen-progestin-containing oral contraceptives

Glucagon

Growth hormone

Heparin

Histamine H 2-receptor antagonists

Marijuana

Morphine

Nicotine

Phenytoin

Sulfinpyrazone

Thyroid hormones 28, 50, 91, 179, 181

(these medications may change metabolic control of glucose concentrations and, unless the changes can be controlled with diet, may necessitate an increase in the amount or a change in the timing of the insulin dose 50, 91)

Hypoglycemia-causing agents, such as:

Angiotensin-converting enzyme inhibitors

Bromocriptine

Clofibrate

Ketoconazole

Lithium

Mebendazole

Pyridoxine

Sulfonamides

Theophylline 28, 50, 91

(these medications may change metabolic control of glucose concentrations and, unless the changes can be controlled with diet, may necessitate a decrease in the amount or a change in the timing of the insulin dose 50, 91)

Octreotide

(octreotide can cause changes in the counterregulatory hormones secretion [insulin, glucagon, and growth hormone] and slow gastric emptying and gastrointestinal contractility, resulting in delayed meal absorption and mild transient hypoglycemia or hyperglycemia in individuals with or without diabetes; in patients with diabetes, insulin therapy may need to be reduced following the initiation of octreotide and monitored for adjustments during and after octreotide treatment 21, 22, 200, 201)

>> Pentamidine

(pentamidine has a toxic effect on pancreatic beta cells, resulting in a biphasic effect on glucose concentration, i.e., initial insulin release and hypoglycemia followed by hypoinsulinemia and hyperglycemia with continued use of pentamidine; initially, insulin dose should be reduced, then the dose should be increased with continued use of pentamidine 50, 91, 153)

Tetracycline

(a delayed onset of increased tissue sensitivity to insulin may occur in patients with diabetes; this reaction has not occurred in individuals with normal glucose tolerance 153, 154, 155, 156)

Tobacco, smoking 151, 152

(may antagonize insulin effects by stimulating release of catecholamines, causing hyperglycemia; also, smoking reduces subcutaneous insulin absorption; dosage reduction of insulin may be necessary when an insulin-dependent patient suddenly stops smoking 50, 91, 136, 137, 151, 152)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).

Risk-benefit should be considered when the following medical problems exist

Note: The following medical problems may necessitate a change in insulin therapy and are not intended as contraindications.

Allergy or local skin sensitivity to insulins

>> Diarrhea or

>> Gastroparesis or

>> Intestinal obstruction or

>> Vomiting or

>> Other conditions causing delayed food absorption or malabsorption 50

(vomiting or delayed stomach emptying may require a change in timing of the insulin dose to realign peak action to peak blood glucose concentrations)

Hepatic disease 50

(insulin requirements are complex, and an increase or decrease of dosage may be needed partly because of modifications in hepatic metabolism of insulin and alterations in hepatic and plasma glucose concentrations)

>> Hyperglycemia-causing conditions, 50 such as:

Female hormonal changes or

Fever, high or

Hyperadrenalism, not optimally controlled or

Infection, severe or

Psychological stress

(these conditions may increase blood glucose, increase or change the insulin requirement, and necessitate more frequent blood glucose monitoring)

(insulin requirements may be increased near or during a menstrual cycle and may return to normal after menstruation; also, a change to intravenous insulin administration may be needed during labor when close glucose control is needed 50)

Hyperthyroidism, not optimally controlled

(hyperthyroidism increases both the activity and the clearance of insulin, making glycemic control difficult until the patient is euthyroid 50, 91)

>> Hypoglycemia-causing conditions, such as:

Adrenal insufficiency, not optimally controlled or

Pituitary insufficiency, not optimally controlled

(these conditions, by reducing blood glucose concentrations, may decrease the insulin requirement and necessitate more frequent blood glucose monitoring)

(also, untreated or not optimally controlled adrenal or pituitary insufficiency may increase tissue sensitivity to insulin and reduce the patient's insulin requirement 50, 91)

Renal disease 50

(insulin requirements are complex, and an increase or decrease of dosage may be needed due to modifications in renal clearance of insulin)

Surgery or

Trauma

(hypoglycemia or hyperglycemia may occur, depending on the surgery or trauma; a change to intravenous insulin administration may be needed when close glucose control is necessary 50)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):

>> Blood glucose determinations

(the concentration of blood or plasma glucose reflects the current degree of metabolic control and should be routinely monitored by the patient at home and by the physician [every 3 months and more often when the patient is not stabilized] to confirm that blood glucose concentration is maintained within agreed upon targets by the selected diet and dosing regimen; this is particularly important during dosage adjustments. Self-monitoring of blood glucose by the patient may require testing at multiple times during the day for intensive insulin therapy or once to several times a week for conventional insulin therapy 50, 91, 202)

(caution in interpreting blood glucose concentrations is needed because normal whole blood glucose values are approximately 15% lower than plasma glucose values. Normal fasting whole blood glucose for adults of all ages is 65 to 95 mg/dL [3.6 to 5.3 mmol/L]. Normal fasting serum glucose is 70 to 105 mg/dL [3.9 to 5.8 mmol/L] for adults younger than 60 years of age and 80 to 115 mg/dL [4.4 to 6.4 mmol/L] for adults 60 years of age or older. For children, normal fasting serum glucose is less than 130 mg/dL [7.2 mmol/L] and fasting whole blood glucose is less than 115 mg/dL [5.6 mmol/L]. 50, 91, 183, 184, 185 For pregnant women with diabetes, normal fasting serum glucose is less than 105 mg/dL [5.8 mmol/L] and fasting whole blood glucose is less than 120 mg/dL [6.7 mmol/L]. 61, 69, 71, 215 Goals of intensive insulin therapy are to maintain fasting blood glucose between 60 and 120 mg/dL [3.3 and 6.7 mmol/L] and postprandial blood glucose at less than 180 mg/dL [10 mmol/L], while goals of conventional insulin therapy are based on the absence of symptoms of hyperglycemia and hypoglycemia 164)

(capillary blood glucose measurement provides important information when done properly, but caution is warranted because of potential errors in technique and readings; it has been suggested that the values be relied upon only if the reported glucose concentration for patients in whom diabetes is stable is between 75 mg/dL and 325 mg/dL [4.12 mmol/L and 17.88 mmol/L, respectively] 50, 157)

Body weight determinations

(significant increase in body weight may require increase in insulin dosage 50, 91)

Glucose, urine 50, 91 or

Ketones, urine

(if blood glucose concentrations exceed 200 mg/dL [11.1 mmol/L], it may be necessary to monitor urine for the presence of glucose and ketones; normalization of glucose in the urine generally lags quantitatively behind serum glucose concentrations; test methods are generally capable of detecting serum glucose concentrations greater than 180 mg/dL [10 mmol/L])

Glycosylated hemoglobin (hemoglobin A 1c) determinations

(hemoglobin A 1c values [normal whole blood hemoglobin A 1c is 4 to 6% of total hemoglobin; specific values are laboratory-dependent] reflect the metabolic control over the preceding 3 months, but assessment of this parameter does not eliminate the need for daily blood glucose monitoring. Hemoglobin A 1c is falsely elevated in patients whose diabetes is unstable when the intermediate precursor is elevated [e.g., in alcoholism] and falsely lowered in conditions of shortened red blood cell life-span [e.g., in anemia and acute or chronic blood loss] or in patients with hemoglobinopathies [e.g., sickle cell disease] 50, 91, 185, 202)

pH measurements, serum or

Potassium concentrations, serum

(determinations may be important if the patient is hypoglycemic and ketoacidotic 50)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Those indicating need for medical attention

Incidence more frequent

Hypoglycemia¾mild, including nocturnal hypoglycemia (anxiety; behavior change similar to drunkenness; blurred vision; cold sweats; confusion; cool, pale skin; difficulty in concentrating; drowsiness; excessive hunger; fast heartbeat; headache; nausea; nervousness; nightmares; restless sleep; shakiness; slurred speech; unusual tiredness or weakness) 50, 91; hypoglycemia¾severe (coma; seizures) 50; weight gain 164

Note: The occurrence of a recent episode of hypoglycemia may result in less severe symptoms appearing during a second episode. In children and the elderly, symptoms of hypoglycemia are variable and harder to identify. Furthermore, nocturnal hypoglycemia may be asymptomatic in 33% or more of affected patients. 50, 159, 160 Also, rebound hyperglycemia may appear from 1/2 to 24 hours after moderate to severe hypoglycemia (Somogyi phenomenon). 91, 204, 212

Hypoglycemic episodes, including severe hypoglycemic coma, occur three times more frequently with intensive insulin therapy than with conventional therapy. 164

Weight gain of 120% above ideal weight (mean of 4.6 kg after 5 years of treatment) is experienced by 12.7 patients per 100 patient-years during intensive insulin therapy and by 9.3 patients per 100 patient-years during conventional insulin therapy. 164

Incidence rare

Edema (swelling of face, fingers, feet, or ankles) 50, 91; lipoatrophy at injection site (depression of the skin at the injection site) 50, 91; lipohypertrophy at injection site (thickening of the skin at the injection site) 50, 91

Note: Edema due to sodium retention caused by insulin is reversible over several days to a week after euglycemic recovery from severe hyperglycemia or ketoacidosis. 91

The risk of lipoatrophy may be reduced by injecting insulin into the periphery of the atrophic site in order to restore subcutaneous adipose tissue. 91 The risk of lipohypertrophy may be decreased by rotating injection sites. 91

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Insulin (Systemic) .

In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):

Before using this medication

>> Conditions affecting use, especially:

Allergy or local skin sensitivity to insulins

Pregnancy¾Importance of controlling and monitoring blood glucose to meet changing needs for insulin during and after pregnancy and to prevent maternal and fetal problems, including fetal macrosomnia, congenital anomalies, and hyperglycemia; alerting physician to plans before becoming pregnant when possible

Breast-feeding¾Insulin is not distributed into breast milk; however, the maternal requirement for insulin is less during breast-feeding because of hormonal changes; checking blood glucose every day for several months to help determine variable insulin dosing needs

Use in children¾Use in children is similar to use in other age groups. However, prepubertal children have increased risk of hypoglycemia because they have greater sensitivity to insulin than do pubertal children

Use in adolescents¾Use in adolescents is similar to use in other age groups. However, insulin needs increase by 20 to 50% at puberty and decrease afterwards; girls may need higher insulin doses than boys

Use in the elderly¾Dehydration may mask early symptoms of hypoglycemia and permit development of more severe symptoms.Vision problems and shakiness may make accurate dosing and glucose monitoring difficult; special training and equipment are available to help overcome these problems

Other medications, especially alcohol, beta-adrenergic blocking agents, corticosteroids, or pentamidine

Other medical problems, especially adrenal insufficiency, pituitary insufficiency, or other conditions causing hypoglycemia; diarrhea, gastroparesis, intestinal obstruction, vomiting, or other conditions

causing delayed food absorption or malabsorption; female hormonal changes, high fever, hyperadrenalism, psychological distress, severe infection, or other conditions causing hyperglycemia

Proper use of this medication

>> Understanding what is meant by source of insulin (beef and pork, pork, mixed insulins, and human) and only buying insulin derived from the source and of the type and strength that are prescribed; otherwise, consulting physician

>> Selecting syringe of proper units of measure for insulin capacity; syringe should be made to measure insulin in units to facilitate accurate dose measurement; a 3/10 cc syringe measures up to 30 USP Units, a 1/2 cc syringe measures up to 50 USP Units, and a 1 cc syringe measures up to 100 USP Units

Carefully selecting and rotating injection sites, following physician's recommendations 204, 205, 207

>> Proper preparation of medication

>> Measuring one type of insulin per dose

>> Measuring and mixing two types of insulin per dose

>> Proper administration technique

>> Using various injection devices

Carefully reading patient instruction sheet contained in insulin or device package

Understanding how to use insulin in insulin devices such as automatic injectors, continuous subcutaneous insulin infusion pumps, disposable and nondisposable syringes, insulin pen devices, and insulin spray injectors

Disposing of syringes by separating needle from syringe, capping or clipping needle, and disposing in puncture-resistant container

>> Compliance with therapy, including not taking more or less medication than directed

>> Importance of adherence to recommended regimens for diet, exercise, blood sugar testing, changes in dose, and sick-day management

>> Proper dosing

>> Proper storage

Precautions while using this medication

>> Regular visits to physician to check progress, especially during the first few weeks of treatment

>> Carefully following special instructions of health care team

Discussing use of alcohol

Discussing plans to stop chronic smoking of tobacco

Not taking other medications unless discussed with physician

Getting counseling for family members to help them assist the patient with diabetes; also, special counseling for pregnancy planning and contraception

Discussing travel arrangements, including transporting insulin and carrying medical history and extra supplies of insulin and syringes

>> Preparing for and knowing what to do in case of an emergency by carrying medical history and current medication list; wearing medical identification; and keeping extra needed medical supplies, quick acting sugar, and nonexpired glucagon kit nearby

>> Recognizing symptoms of hypoglycemia: Anxiety; behavior change similar to drunkenness; blurred vision; cold sweats; confusion; cool, pale skin; difficulty in concentrating; drowsiness; excessive hunger; fast heartbeat; headache; nausea; nervousness; nightmares; restless sleep; shakiness; slurred speech; and unusual tiredness or weakness

>> Recognizing what brings on symptoms of hypoglycemia, such as delaying or missing a meal or snack, exercising more than usual, drinking significant amounts of alcohol, taking certain medications, using too much insulin, or sickness, including vomiting or diarrhea

>> Knowing what to do if symptoms of hypoglycemia occur, such as eating glucose tablets or gel, corn syrup, honey, or sugar cubes; or drinking fruit juice, nondiet soft drink, or sugar dissolved in water; also, eating small snack, such as cheese and crackers, milk, or half sandwich when scheduled meal is longer than 1 hour away; not eating foods high in fat, such as chocolate because fat slows gastric emptying; or using glucagon injection if the patient becomes unconscious

>> Recognizing symptoms of hyperglycemia and ketoacidosis: Blurred vision; drowsiness; dry mouth; flushed, dry skin; fruit-like breath odor; increased urination (frequency and volume); ketones in urine; loss of appetite; stomachache, nausea, or vomiting; tiredness; troubled breathing (rapid and deep); unconsciousness; and unusual thirst

>> Recognizing what brings on symptoms of hyperglycemia, such as diarrhea, fever, or infection; not taking enough or skipping a dose of insulin; exercising less than usual; or overeating or not following meal plan

>> Knowing what to do if symptoms of hyperglycemia occur, such as checking blood glucose and increasing the insulin dose (short term for supplementary or anticipatory doses) according to the individualized dosing schedule developed; contacting physician for more permanent dose changes; changing only one type of insulin dose (usually the first dose); anticipating how one change in an insulin dose affects other doses of the day; delaying a meal if blood glucose concentration exceeds

200 mg/dL (11.1 mmol/L); checking with physician when blood glucose concentration is above 240 mg/dL (13.3 mmol/L); not exercising when blood glucose concentration is above 240 mg/dL (13.3 mmol/L); or being hospitalized if ketoacidosis or coma occurs

Side/adverse effects

Signs of potential side effects, especially mild hypoglycemia, including nocturnal hypoglycemia; severe hypoglycemia; weight gain; edema; lipoatrophy or lipohypertrophy at injection site

General Dosing Information

In the U.S., the potency of insulin is expressed in terms of USP Insulin Units or USP Insulin Human Units. Bovine or porcine insulin contains not less than 26 USP Insulin Units per mg of insulin on the dried basis. Human insulin contains not less than 27.5 USP Insulin Human Units per mg of insulin on the dried basis. 53, 91 International Units cannot be compared directly to USP Units because the reference standards and the methodologies for manufacturing are different. 91

It is generally not recommended that patients whose diabetes is well-controlled with animal insulins automatically be switched to human insulins. Human insulins may not offer any significant advantage over the highly purified pork insulins, with the exception of reduced antibody concentrations, which may be a consideration for some patients, especially children, young adults, patients who are pregnant or considering pregnancy, patients with allergies, or patients using insulin intermittantly. 50, 176, 208 Patients should be informed of the possible need for dosage adjustment during the first 1 to 2 weeks following a change in the source (bovine and porcine, porcine, or human) of their insulin products and advised not to make such a change without first consulting their physicians. 47, 87, 88, 89, 90, 176

Transferring patients from oral hypoglycemic agents to insulin can be immediate, although blood glucose concentrations should be evaluated for several days following the change and the prolonged effects of chlorpropamide should be considered when determining the insulin dose. 50

The vial of insulin must not be shaken hard before being used. Frothing or bubble formation can cause an incorrect dose. Contents are mixed well by rolling the bottle slowly between the palms of the hands or by gently tipping the bottle over a few times. Insulin should not be used if it looks lumpy or grainy, or sticks to the bottle. Also, regular insulin should not be used if it becomes viscous or cloudy; only clear, colorless solutions should be used. 23, 26, 41

Dilution of insulin preparations generally should be avoided. However, some pediatric doses may be too small to measure accurately. If needed, diluting from U-100 to U-10 has been suggested to aid in accurate dosing for very small doses in pediatric patients. 205 Such dilutions are stable for 2 months when stored at 4 °C (39 °F) or until the date of expiration of the insulin, whichever occurs first. Occasionally insulin must be diluted to avoid crystallization in the catheters when it is administered as a low-dose infusion via an insulin pump. In these rare cases, dilution should be performed aseptically in a laminar flow hood using diluents and mixing vials provided or recommended by the manufacturer. The differences in strength, dosage volume, and expiration date should be clearly labeled by the pharmacist and emphasized to the patient. If insulin needs to be diluted during an emergency and the diluents are not readily available, 0.9% sodium chloride injection without preservative may be used for dilution of small insulin doses. However, these solutions are not stable

and should be used promptly. Stinging or burning at the site of injection also may occur due to the lower pH of these solutions. 50, 77, 188

Different types of insulin are sometimes mixed in the syringe in proportions ordered by the physician in order to achieve a more accurate matching of insulin availability to the patient's requirements in a single dose. If insulins are to be mixed, several factors should be considered:

· Each patient should always follow the same sequence of mixing the separate insulin preparations. As a general rule, regular insulin should be drawn first to avoid contamination and clouding of the vial of regular insulin by the other insulin. A mixture of regular insulin and another insulin will have a longer duration of action than does regular insulin alone. 50, 208

· Insulin zinc, prompt insulin zinc, and extended insulin zinc may be mixed in any proportion without loss of the characteristics of the individual insulins. Such mixtures are stable for up to 18 months. 50, 206, 208

· Unbuffered regular insulin and isophane insulin may be mixed in any proportion in a syringe and stored upright if possible. The prefilled syringe can be used immediately, stored at room temperature and used within 14 days, or stored in a refrigerator for use within 3 weeks. Mixtures containing buffered regular insulin should be used immediately. 208

· Mixing unbuffered regular insulin and insulin zinc insulins (lente, semilente, and ultralente) is not recommended because the excess zinc in the insulin zinc insulin can form an extra zinc insulin complex with the regular insulin. This can lengthen the insulin's duration of action and give unpredictable clinical results. However, if these insulins are combined, it is recommended that the mixture be used immediately. 208

· Phosphate buffered regular insulin or isophane insulins should not be mixed with insulin zinc insulins. Zinc phosphate may precipitate from the mixture, which can shorten the expected duration of action and provide unpredictable clinical results. 208

· Phosphate buffered regular insulin should not be mixed with any other insulin when used in an external insulin infusion pump because of the potential problem of precipitation. 194

After receiving insulin at first diagnosis of type 1 diabetes, 20 to 30% of patients appear to normalize for a few weeks or months (called the honeymoon phase). Some clinicians continue insulin treatment in small doses of 0.2 to 0.5 USP Units per kg of body weight during this time. 50

Conventional and intensive insulin therapies are individualized insulin regimens that provide different levels of blood glucose control. Conventional therapy consists of one or two insulin injections a day and daily self-monitoring of urine or blood glucose, but not daily adjustments of insulin dose. Intensive insulin therapy provides tighter blood glucose control via administration of three or more injections a day or by use of an insulin pump. Also, adjustments of insulin dose according to the results of self-monitoring of blood glucose determinations are performed at least four times a day and before anticipated dietary intake and exercise. Close glucose control has been proven to delay the onset and slow the progression of diabetic retinopathy, nephropathy, and neuropathy. 164, 165, 166, 167, 209, 210, 214 The dosage and the timing of administration of insulin can vary greatly and must therefore be determined for each individual patient by the attending physician. Matching the patient's specific insulin needs over a 24-hour period through the

use of short-acting and longer-acting preparations may decrease long-term complications of diabetes mellitus. 209, 210, 211, 212, 213, 214

If a pattern of metabolic noncontrol ensues (blood glucose concentrations changing for 3 days), the total daily insulin dose usually is adjusted by changing only one type of insulin and only one segment of the daily dose; the first preprandial dose is the one most commonly changed because it more prominently affects the other doses of the day. 50, 209, 212

Insulin requirements may change with diet or physical activity. Algorithms can be developed to aid a patient with supplemental or anticipatory insulin dosing needs based on the patient's sensitivity to insulin. Supplemental doses of regular insulin can be used to correct excessive preprandial blood glucose concentrations after the basic dose of insulin is established. Anticipatory insulin doses are based on anticipated dietary or physical activity changes. Because of the increased risk of secondary hyperglycemia due to exercise, patients should be cautioned against exercising if the blood glucose concentration exceeds 240 mg/dL (13.3 mmol/L) or when a condition exists that causes low glucagon stores. 50, 209

Additional low doses of regular insulin (1 to 2 USP Units for each 30 to 40 mg/dL [1.7 to 2.2 mmol/L] incremental rise above the target blood glucose concentration) every 3 to 4 hours may be needed on sick days. Patients should be warned to inform the physician if the concentration remains above 240 mg/dL (13.3 mmol/L) after three supplementary insulin doses or if symptoms of ketoacidosis develop. 50

The patient should always use only one brand or type of syringe and should consult the physician before changing brands or syringe types. Among different brands or syringe types, the unmeasured volume between the needle point and the bottom calibration on the syringe barrel (called dead space) may differ enough to cause improper dosage. 45, 47, 209, 213

The use of a disposable syringe and needle to administer more than one injection is controversial. Although USP medical advisory panels do not recommend this practice, it must be recognized that some patients reuse disposable syringes and needles because of economic constraints. Where this is occurring, it must be emphasized that the syringe and needle be used only for one particular patient, the needle should be wiped with alcohol, and the needle's cap replaced after each use. Also, the syringe and needle should be reused only for a limited number of injections. Disposable syringes and needles should not be reused on a continuing basis. 110, 172, 173, 174, 208

For intravenous infusion

Regular insulin (Insulin Injection USP and Insulin Human Injection USP) in the 100-USP-Unit concentration is the only insulin type suitable for intravenous administration.

Insulin can be adsorbed to the surfaces of glass and plastic intravenous infusion containers (including polyvinyl chloride [PVC], ethylene vinyl acetate, and polyethylene). Adsorption is unpredictable and the clinical significance is uncertain. Recommendations for minimizing adsorption include adding 0.35% serum albumin human or approximately 5 mL of the patient's blood or using a syringe pump with a short cannula. For admixtures of insulin greater than 100 USP Units per 500 mL of intravenous solution, decant 50 mL of intravenous solution containing insulin through the administration apparatus and store for 30 minutes before using for optimal results. 205, 206 Afterwards, insulin

dosage should be adjusted to meet the patient's targeted blood glucose concentration. Regular insulin is compatible with dextrose injection, 0.9% sodium chloride injection, and combinations of these. 206

For continuous subcutaneous insulin infusion pump

Generally, buffered regular insulin is used in insulin pumps, although unbuffered regular insulin has been used. Phosphate buffered regular insulin is less likely to crystallize and block insulin pump catheters and is preferred over unbuffered regular insulin. 194 Following insulin pump manufacturers' recommendations and suggested maintenance procedures is important to ensure optimal performance and to avoid problems, such as insulin adhesion or clogging. 23, 26, 41, 42, 47 Consult individual manufacturer's package inserts. 23, 26, 41, 42, 47

When initiating a continuous subcutaneous insulin infusion with an insulin pump, a priming dose may be needed. Without an initial priming dose, the depot forms at a very slow rate. Pumps with a short pulse-rate interval have little superiority over pumps with a longer interval in relation to the depot formation. An additional priming dose is not necessary when the infusion site is changed. Absorption of insulin from the depot at the first site continues after discontinuation of the infusion, preventing insulin concentrations from decreasing to subtherapeutic values while another depot is forming at the new site. 50, 88

For treatment of adverse effects and/or overdose

Recommended treatment may include:
· For mild to moderate hypoglycemia:
¾Treating with immediate ingestion of a source of sugar, such as glucose gel, glucose tablets, fruit juice, corn syrup, nondiet soft drink, honey, sugar cubes, or table sugar dissolved in water. A frequently used source of sugar is a glassful of orange juice containing 2 or 3 teaspoonfuls of table sugar.
¾Documenting blood glucose and rechecking in 15 minutes.
¾Counseling patient to seek medical assistance promptly. 191

¾For severe hypoglycemia or acute overdose, including coma:
¾Need for patient to obtain emergency medical assistance immediately.
¾Immediately treating with 50 mL of 50% dextrose injection given intravenously to stabilize the patient. Then administering a continuous infusion of 5 to 10% dextrose injection to maintain slight hyperglycemia (approximately 100 mg/dL blood glucose concentration) for up to 12 days. An adult who does not have diabetes usually exhibits a higher maximal hypoglycemic effect from insulin than does an adult who has diabetes. It is important to note that oral glucose cannot be relied upon to maintain euglycemia because 60% of an oral glucose dose is stored as hepatic glycogen with only 15% left for brain utilization and 15% for insulin-dependent tissues. 189

¾Glucagon, 1 to 2 mg administered intramuscularly, is useful for fast onset of action to mobilize hepatic glucose stores but may be ineffective or variable in its effect if glycogen stores are depleted. 23, 189

¾Monitoring vital signs, arterial blood gases, blood glucose, and serum electrolytes (especially calcium, potassium, and sodium) as required. Initially, blood glucose concentrations should be

monitored as frequently as every 1 to 3 hours. Blood urea nitrogen and serum creatinine concentrations also should be obtained. 50, 189

¾Cerebral edema¾Managed with mannitol and dexamethasone. 189

¾Hypokalemia¾Managed with potassium supplements. 189

Other supportive measures also should be employed as needed.

BUFFERED INSULIN HUMAN

Parenteral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

BUFFERED INSULIN HUMAN INJECTION

Usual adult and adolescent dose

Type 1 diabetes¾Initial¾

Subcutaneous or continuous subcutaneous insulin infusion, a total insulin dose, using one or more types of insulin, is 0.5 to 1.2 USP Insulin Human Units per kg of body weight a day in divided doses, taking body fat, blood glucose, and insulin sensitivity into consideration. A few patients will require less than 0.5 USP Insulin Human Unit per kg of body weight a day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose.

When using a continuous subcutaneous insulin infusion pump, the basal insulin dose (usually forty to sixty percent of the total insulin daily dose) is divided into a dose that can be continuously infused subcutaneously over twenty-four hours. Also, a premeal injection (also, forty to sixty percent of total insulin dose) can be delivered preprogrammed or manually by the patient through the insulin pump. 221

When using subcutaneous injections, regular human insulin is usually injected in low doses, i.e., less than 10 USP Insulin Human Units a dose.

Both subcutaneous injections and premeal injections of regular human insulin using a continuous subcutaneous insulin infusion pump generally are given fifteen to thirty minutes before one or more meals and/or a bedtime snack. 50, 209, 210, 219, 221

Maintenance¾

Subcutaneous or continuous subcutaneous insulin infusion, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial¾

Subcutaneous, a total insulin dose, using one or more types of insulin, may vary from 5 to 10 USP Insulin Human Units per day to 0.7 to 2.5 USP Insulin Human Units per kg of body weight a day in divided doses, taking body fat, blood glucose, and insulin sensitivity into consideration. Dose

titration to a targeted blood glucose goal is achieved over several days with changes of no more than 2 to 6 USP Insulin Human Units a day in the existing total daily insulin dose; again, with consideration of body weight. Very insulin-resistant patients using large doses, 200 USP Insulin Human Units or greater, may need to use a concentrated regular insulin (U-500) instead. Regular human insulin is usually given in low doses, i.e., often less than 10 USP Insulin Human Units a dose, fifteen or thirty minutes before one or more meals and/or a bedtime snack. 50, 209, 215, 218

Maintenance¾
Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: For treatment of diabetic ketoacidosis, an optional loading dose of 0.15 USP Insulin Human Unit per kg of body weight is given intravenously, followed by 0.1 USP Insulin Human Unit per kg of body weight per hour by continuous infusion. 218 The rate of insulin infusion should be decreased when the plasma glucose concentration reaches 300 mg per dL. Infusion of 5% dextrose injection should be started separately from the insulin infusion when plasma glucose concentration reaches 250 mg per dL. Thirty minutes before discontinuing the insulin infusion, an appropriate dose of insulin should be injected subcutaneously; intermediate-acting insulin has been recommended. 50, 218 Alternatively, a loading dose of 0.5 USP Insulin Human Unit per kg of body weight is injected intramuscularly, followed by 0.1 USP Insulin Human Unit per kg of body weight injected intramuscularly every hour until the blood glucose concentration reaches 300 mg per dL. Then to maintain blood glucose concentration at 250 mg per dL, 0.1 USP Insulin Human Unit per kg of body weight is injected intramuscularly every two hours as needed. With either type of insulin administration, capillary blood glucose should be monitored at least hourly and the insulin dose adjusted accordingly. 204, 216, 218

Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50, 91, 138

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

[Growth hormone deficiency, diagnosis of] *¾Intravenous, 0.05 to 0.15 USP Insulin Human Unit per kg of body weight as a single rapid injection. 192, 193

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50, 218

Strength(s) usually available

U.S.¾100 USP Insulin Human Units per mL (OTC)[Velosulin BR (semisynthetic) (phosphate buffered) 194]

Canada¾100 USP Insulin Human Units per mL[Velosulin Human (semisynthetic) (phosphate buffered) 34]

Note: Velosulin Human is available only through the Special Access Program in Ottawa. 34

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from freezing.

Stability:

Do not use if cloudy, discolored, or unusually viscous. 194

Auxiliary labeling:

· Refrigerate.
· Do not freeze.

Note: Patients should be advised not to mix phosphate buffered insulin with zinc-containing insulins. 9, 47, 50

Also, patients should be advised not to mix phosphate buffered insulin with any other insulin when using a continuous subcutaneous external insulin pump. 194

Buffered insulin human is the preferred regular insulin for use in continuous subcutaneous infusion insulin pumps, but also may be injected subcutaneously or intramuscularly with an insulin syringe, or used intravenously. 194 When this insulin is used in a continuous subcutaneous infusion insulin pump, the catheter tubing and the insulin in the reservoir must be changed every 48 hours or the manufacturer's recommendations followed for specific external insulin pumps. 194

EXTENDED INSULIN ZINC

Parenteral Dosage Forms

EXTENDED INSULIN ZINC SUSPENSION (ULTRALENTE INSULIN) USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Unit per kg of body weight sometimes as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Units per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Extended insulin zinc is given once or twice a day thirty to sixty minutes before a meal and/or a bedtime snack. 50, 190, 209, 215, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Units per day to 0.7 to 2.5 USP Insulin Units per kg of body weight per day, taking body fat, blood glucose, and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Units a day; again, body weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Units or greater, may need to use a concentrated regular insulin (U-500) instead. Extended insulin zinc is given once or twice a day thirty or sixty minutes before a meal and/or a bedtime snack. 50, 190, 209, 210, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50

Strength(s) usually available

U.S.¾Not commercially available.

Canada¾Not commercially available. 161

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from freezing. 11, 33, 41

Stability:

Do not use if precipitate has become clumped or granular in appearance. 11, 33, 41

Auxiliary labeling:

· Shake gently. 11, 33, 41

· Refrigerate. 11, 33, 41

· Do not freeze. 11, 33, 41

Note: Extended insulin zinc suspension is sometimes mixed with other insulin types as directed by the physician. 11, 33, 41

EXTENDED INSULIN HUMAN ZINC

Parenteral Dosage Forms

EXTENDED INSULIN HUMAN ZINC SUSPENSION USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Human Unit per kg of body weight as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Human Units per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Human Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Extended

insulin human zinc is given once or twice a day thirty to sixty minutes before a meal and/or a bedtime snack. 50, 190, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Human Units per day to 0.7 to 2.5 USP Human Insulin Units per kg of body weight per day, taking body fat, blood glucose, and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Human Units a day; again, body weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Human Units or greater, may need to use a concentrated regular insulin (U-500) instead. Extended insulin human zinc is given once or twice a day thirty to sixty minutes before a meal and/or a bedtime snack. 50, 138, 218, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50, 91, 138, 218

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 217, 218

Strength(s) usually available

U.S.¾100 USP Insulin Human Units per mL (OTC)[Humulin U (biosynthetic)] 20

Canada¾100 USP Insulin Human Units per mL (OTC)[Humulin-U (biosynthetic) 6, 7, 28] [Novolin ge Ultralente (biosynthetic) 10, 33]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from freezing. 6, 7, 10, 28, 33, 52

Stability:

Do not use if precipitate has become clumped or granular in appearance. 6, 7, 10, 28, 33

Auxiliary labeling:

· Shake gently. 6, 7, 10, 28, 33, 52

· Refrigerate. 6, 7, 10, 28, 33, 52

· Do not freeze. 6, 7, 10, 28, 33, 52

INSULIN

Parenteral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

INSULIN INJECTION (REGULAR INSULIN, CRYSTALLINE ZINC INSULIN) USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial¾
Subcutaneous or continuous subcutaneous insulin infusion, a total insulin dose, using one or more types of insulin, is 0.5 to 1.2 USP Insulin Units per kg of body weight a day in divided doses, taking body fat, blood glucose, and insulin sensitivity into consideration. A few patients will require less than 0.5 USP Insulin Unit per kg of body weight a day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose.
When using a continuous subcutaneous insulin infusion pump, the basal insulin dose (usually forty to sixty percent of the total insulin daily dose) is divided into a dose that can be continuously infused subcutaneously over twenty-four hours. Also, a premeal injection (also, forty to sixty percent of total insulin dose) can be delivered preprogrammed or manually by the patient through the insulin pump. 221

When using subcutaneous injections, regular insulin usually is injected in low doses, i.e., often less than 10 USP Insulin Units a dose.

Both subcutaneous injections and premeal injections using a continuous subcutaneous insulin infusion pump of regular insulin generally are given fifteen to thirty minutes before one or more meals and/or a bedtime snack. 50, 209, 210, 219, 221

Maintenance¾

Subcutaneous or continuous subcutaneous insulin infusion, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial¾

Subcutaneous, a total insulin dose, using one or more types of insulin, may vary from 5 to 10 USP Insulin Units per day to 0.7 to 2.5 USP Insulin Units per kg of body weight a day in divided doses, taking body fat, blood glucose, and insulin sensitivity into consideration. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Units a day; again, with consideration of body weight. Very insulin-resistant patients using large doses, 200 USP Insulin Units or greater, may need to use a concentrated regular insulin (U-500) instead. Regular insulin usually is given in low doses, i.e., often less than 10 USP Insulin Units a dose, fifteen to thirty minutes before one or more meals and/or a bedtime snack. 50, 209, 210, 219

Maintenance¾

Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: For treatment of diabetic ketoacidosis, an optional loading dose of 0.15 USP Insulin Unit per kg of body weight is given intravenously, followed by 0.1 USP Insulin Unit per kg of body weight per hour by continuous infusion. 218 The rate of insulin infusion should be decreased when the plasma glucose concentration reaches 300 mg per dL. Infusion of 5% dextrose injection should be started separately from the insulin infusion when plasma glucose concentration reaches 250 mg per dL. Thirty minutes before discontinuing the insulin infusion, an appropriate dose of insulin should be injected subcutaneously; intermediate-acting insulin has been recommended. 50, 218 Alternatively, a loading dose of 0.5 USP Unit per kg of body weight is injected intramuscularly, followed by 0.1 USP Insulin Unit per kg of body weight injected intramuscularly every hour until the blood glucose concentration reaches 300 mg per dL. Then to maintain blood glucose concentration at 250 mg per dL, 0.1 USP Insulin Unit per kg of body weight is injected intramuscularly every two hours as needed. With either type of insulin administration, capillary blood glucose should be monitored at least hourly and the insulin dose adjusted accordingly. 204, 209, 216, 218

Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a

physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50, 138, 190

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

[Growth hormone deficiency, diagnosis of] *¾Intravenous, 0.05 to 0.15 USP Insulin Unit per kg of body weight as a single rapid injection. 192, 193

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50, 218

Strength(s) usually available

U.S.¾100 USP Insulin Units per mL (OTC)[Regular Iletin II (purified pork) 26] [Regular Insulin (pork) 41] [Regular Insulin (purified pork) 32]

500 USP Insulin Units per mL (Rx)[Regular (Concentrated) Iletin II, U-500 (purified pork)] 27

Canada¾100 USP Insulin Units per mL (OTC)[Regular Iletin II (pork) 8]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from sunlight and from freezing. 52

Stability:

Do not use if cloudy, discolored, or unusually viscous.

Auxiliary labeling:

· Refrigerate. 52

· Do not freeze. 52

Note: The 500-Unit strength is available only with a prescription and is used only for the treatment of patients with insulin-resistant diabetes.

Insulin Injection USP is sometimes mixed with other insulin types as directed by physician.

Patients should be advised not to mix regular insulin with any other insulin when using a continuous subcutaneous external insulin pump. 194

Regular insulin can be used in continuous subcutaneous infusion insulin pumps, but also may be injected subcutaneously or intramuscularly with an insulin syringe, or used intravenously. Phosphate buffered insulin is preferred over non-phosphate buffered insulin in insulin pumps. 194 When this insulin is used in a continuous subcutaneous infusion insulin pump, the catheter tubing and the insulin in the reservoir must be changed every 48 hours or the manufacturer's recommendations followed for specific external insulin pumps. 194

INSULIN HUMAN

Parenteral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

INSULIN HUMAN INJECTION (REGULAR INSULIN HUMAN) USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial¾

Subcutaneous or continuous subcutaneous insulin infusion, a total insulin dose, using one or more types of insulin, is 0.5 to 1.2 USP Insulin Human Units per kg of body weight a day in divided doses, taking body fat, blood glucose, and insulin sensitivity into consideration. A few patients will require less than 0.5 USP Insulin Human Unit per kg of body weight a day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose.

When using a continuous subcutaneous insulin infusion pump, the basal insulin dose (usually forty to sixty percent of the total insulin daily dose) is divided into a dose that can be continuously infused subcutaneously over twenty-four hours. Also, a premeal injection (also, forty to sixty percent of total insulin dose) can be delivered preprogrammed or manually by the patient through the insulin pump. 221

When using subcutaneous injections, regular human insulin usually is injected in low doses, i.e., often less than 10 USP Insulin Human Units a dose.

Both subcutaneous injections and premeal injections of regular human insulin using a continuous subcutaneous insulin infusion pump generally are given fifteen to thirty minutes before one or more meals and/or a bedtime snack. 50, 209, 210, 218, 219, 221

Maintenance¾

Subcutaneous or continuous subcutaneous insulin infusion, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial¾

Subcutaneous, a total insulin dose, using one or more types of insulin, may vary from 5 to 10 USP Insulin Human Units per day to 0.7 to 2.5 USP Insulin Human Units per kg of body weight a day in divided doses, taking body fat, blood glucose, and insulin sensitivity into consideration. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the

existing total daily insulin dose of no more than 2 to 6 USP Insulin Human Units a day; again, with consideration of body weight. Very insulin-resistant patients using large doses, 200 USP Insulin Human Units or greater, may need to use a concentrated regular insulin (U-500) instead. Regular human insulin usually is given in low doses, i.e., often less than 10 USP Insulin Human Units a dose, fifteen to thirty minutes before one or more meals and/or a bedtime snack. 50, 190, 209, 210, 215, 219

Maintenance¾
Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 190, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: For treatment of diabetic ketoacidosis, an optional loading dose of 0.15 USP Insulin Human Unit per kg of body weight is given intravenously, followed by 0.1 USP Insulin Human Unit per kg of body weight per hour by continuous infusion. 50, 218 The rate of insulin infusion should be decreased when the plasma glucose concentration reaches 300 mg per dL. Infusion of 5% dextrose injection should be started separately from the insulin infusion when plasma glucose concentration reaches 250 mg per dL. Thirty minutes before discontinuing the insulin infusion, an appropriate dose of insulin should be injected subcutaneously; intermediate-acting insulin has been recommended. 50, 218 Alternatively, a loading dose of 0.5 USP Insulin Human Unit per kg of body weight is injected intramuscularly, followed by 0.1 USP Insulin Human Unit per kg of body weight injected intramuscularly every hour until the blood glucose concentration reaches 300 mg per dL. Then, to maintain blood glucose concentration at 250 mg per dL, 0.1 USP Insulin Human Unit per kg of body weight is injected intramuscularly every two hours as needed. With either type of insulin administration, capillary blood glucose should be monitored at least hourly and the insulin dose adjusted accordingly. 204, 216, 218

Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50, 91, 138, 190

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 217

[Growth hormone deficiency, diagnosis of] *¾Intravenous, 0.05 to 0.15 USP Insulin Human Unit per kg of body weight as a single rapid injection. 192, 193

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50, 211, 217, 218

Strength(s) usually available

U.S.¾100 USP Insulin Human Units per mL (OTC)[Humulin R (biosynthetic) 18, 19] [Novolin R (biosynthetic) 46] [Novolin R PenFill (biosynthetic) 46, 48] [Novolin R Prefilled (biosynthetic) (prefilled single use syringe contains 150 USP Units in 1.5 mL) 195]

500 USP Insulin Human Units per mL (Rx)[Humulin R, Regular U-500 (Concentrated) (biosynthetic) 29]

Canada¾100 USP Insulin Human Units per mL (OTC)[Humulin-R (biosynthetic) 6, 28] [Novolin ge Toronto (biosynthetic) 10] [Novolin ge Toronto Penfill (biosynthetic) 10]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from sunlight 52 and from freezing. 9, 18, 19, 28, 38, 46, 47, 48, 52

Stability:

Do not use if cloudy, discolored, or unusually viscous. 9, 18, 19, 38, 46, 47, 48

Auxiliary labeling:

· Refrigerate. 9, 18, 19, 28, 38, 46, 47, 48, 52

· Do not freeze. 9, 18, 19, 28, 38, 46, 47, 48, 52

Note: The 500-Unit strength is available only with a prescription and is used only for the treatment of patients with insulin-resistant diabetes.

Insulin Human Injection USP is sometimes mixed with other insulin types as directed by the physician.

Patients should be advised not to mix insulin human with any other insulin when using a continuous subcutaneous infusion insulin pump. 194

Insulin human may be used in continuous subcutaneous infusion insulin pumps, but also may be injected subcutaneously or intramuscularly with an insulin syringe, or used intravenously. Phosphate buffered insulin is preferred over non-phosphate buffered insulin in insulin pumps. 194 When this insulin is used in a continuous subcutaneous infusion insulin pump, the catheter tubing and the insulin in the reservoir must be changed every 48 hours or the manufacturer's recommendations followed for specific external insulin pumps. 194

INSULIN ZINC

Parenteral Dosage Forms

INSULIN ZINC SUSPENSION (LENTE INSULIN) USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Unit per kg of body weight as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Units per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Insulin zinc is given thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 215, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Units per day to 0.7 to 2.5 USP Insulin Units per kg of body weight per day, taking body fat, blood glucose, and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Units a day; again, body weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Units or greater, may need to use a concentrated regular insulin (U-500) instead. Insulin zinc is given thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 210, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50

Strength(s) usually available

U.S.¾100 USP Insulin Units per mL (OTC)[Lente Iletin II (purified pork) 24] [Lente (purified pork) 39]

Canada¾100 USP Insulin Units per mL (OTC)[Lente Iletin (beef and pork) 8] [Lente Iletin II (pork) 8]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from freezing. 53

Stability:

Do not use if precipitate has become clumped or granular in appearance. 8, 21, 41

Auxiliary labeling:

· Shake gently. 8, 21, 41, 53

· Refrigerate. 8, 21, 41, 53

· Do not freeze. 8, 21, 41, 53

Note: Insulin zinc suspension is sometimes mixed with other insulin types as directed by the physician. 8, 21, 41

INSULIN HUMAN ZINC

Parenteral Dosage Forms

INSULIN HUMAN ZINC SUSPENSION USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Human Unit per kg of body weight as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Human Units

per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Human Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Insulin human zinc is given thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 215, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Human Units per day to 0.7 to 2.5 USP Insulin Human Units per kg of body weight per day, taking body fat, blood glucose, and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Human Units a day; again, body weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Human Units or greater, may need to use a concentrated regular insulin (U-500) instead. Insulin human zinc is given thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 210, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50

Strength(s) usually available

U.S.¾100 USP Insulin Human Units per mL (OTC)[Humulin L (biosynthetic) 15] [Novolin L (biosynthetic) 44]

Canada¾100 USP Insulin Human Units per mL (OTC)[Humulin-L (biosynthetic) 6, 7, 15] [Novolin ge Lente (biosynthetic) 10, 36]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from sunlight 52 and from freezing. 6, 7, 10, 15, 36, 52

Stability:

Do not use if precipitate has become clumped or granular in appearance. 6, 7, 10, 15, 36

Auxiliary labeling:

· Shake gently. 6, 7, 10, 15, 36, 52

· Refrigerate. 6, 7, 10, 15, 36, 52

· Do not freeze. 6, 7, 10, 15, 36, 52

ISOPHANE INSULIN

Parenteral Dosage Forms

ISOPHANE INSULIN SUSPENSION (NPH INSULIN) USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Unit per kg of body weight as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Units per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Isophane insulin is given thirty to sixty minutes before a meal and/or a bedtime snack. 50, 190, 209, 215, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Units per day to 0.7 to 2.5 USP Insulin Units per kg of body weight per day, taking body fat, blood glucose,

and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Units a day; again, body weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Units or greater, may need to use a concentrated regular insulin (U-500) instead. Isophane insulin is given thirty to sixty minutes before a meal and/or a bedtime snack. 50, 190, 209, 210, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50

Strength(s) usually available

U.S.¾100 USP Insulin Units per mL (OTC)[NPH Iletin II (purified pork) 25] [NPH Purified Insulin (purified pork) 42]

Canada¾100 USP Insulin Units per mL (OTC)[NPH Iletin (beef and pork) 8] [NPH Iletin II (pork) 8]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from freezing. 8, 22, 25, 53

Stability:

Do not use if precipitate has become clumped or granular in appearance or clings to sides of vial. 8, 22, 25

Auxiliary labeling:

· Shake gently. 8, 22, 25, 53

· Refrigerate. 8, 22, 25, 53

· Do not freeze. 8, 22, 25, 53

Note: Isophane insulin suspension is sometimes mixed with insulin injection as directed by the physician. 8, 22, 25

ISOPHANE INSULIN HUMAN

Parenteral Dosage Forms

ISOPHANE INSULIN HUMAN SUSPENSION USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Human Unit per kg of body weight as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Human Units per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Human Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Isophane insulin human is given thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 215, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Human Units per day to 0.7 to 2.5 USP Insulin Human Units per kg of body weight per day, taking body fat, blood glucose, and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Human Units a day; again, body weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Human Units or greater, may need to use a concentrated regular insulin (U-500) instead. Isophane insulin human is given thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 210, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50

Strength(s) usually available

U.S.¾100 USP Insulin Human Units per mL (OTC)[Humulin N (biosynthetic) 16, 17] [Humulin N Pen (biosynthetic) 30] [Novolin N (biosynthetic) 45] [Novolin N PenFill (biosynthetic) 45] [Novolin N Prefilled (biosynthetic) (prefilled single-use syringe contains 150 USP Insulin Human Units in 1.5 mL) 45, 196]

Canada¾100 USP Insulin Human Units per mL (OTC)[Humulin-N (biosynthetic) 6, 7, 28] [Novolin ge NPH (biosynthetic) 10, 37] [Novolin ge NPH Penfill (biosynthetic) 10, 37]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from sunlight 52 and from freezing. 6, 7, 10, 16, 17, 28, 37, 45, 52

Stability:

Do not use if precipitate has become clumped or granular in appearance or clings to sides of vial. 6, 7, 10, 16, 17, 28, 37, 45

Auxiliary labeling:

· Shake gently. 6, 7, 10, 16, 17, 28, 37, 45, 52

· Gently rotate prefilled syringe up and down before injection. 196

· Refrigerate. 6, 7, 10, 16, 17, 28, 37, 45, 52

· Do not freeze. 6, 7, 10, 16, 17, 28, 37, 45, 52

ISOPHANE INSULIN HUMAN AND INSULIN HUMAN

Parenteral Dosage Forms

ISOPHANE INSULIN HUMAN SUSPENSION AND INSULIN HUMAN INJECTION

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Human Unit per kg of body weight as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Human Units per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Human Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Isophane insulin human and insulin human is given fifteen to thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 215, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Human Units per day to 0.7 to 2.5 USP Insulin Human Units per kg of body weight per day, taking body fat, blood glucose, and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Human Units a day; again, body weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Human Units or greater, may need to use a concentrated regular insulin (U-500) instead. Isophane insulin human and insulin human is given fifteen to thirty minutes before a meal and/or a bedtime snack. 50, 190, 209, 210, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50

Strength(s) usually available

U.S.¾100 USP Insulin Human Units per mL (50% isophane insulin human suspension and 50% insulin human injection) (OTC)[Humulin 50/50 (biosynthetic) 12]

100 USP Insulin Human Units per mL (70% isophane insulin human suspension and 30% insulin human injection) (OTC)[Humulin 70/30 (biosynthetic) 13, 14] [Humulin 70/30 Pen (biosynthetic) 31] [Novolin 70/30 (biosynthetic) 43] [Novolin 70/30 PenFill (biosynthetic) 43] [Novolin 70/30 Prefilled (biosynthetic) (prefilled single-use syringe contains 150 USP Insulin Human Units in 1.5 mL) 197]

Canada¾100 USP Insulin Human Units per mL (10% insulin human injection and 90% isophane insulin human suspension) (OTC)[Humulin 10/90 (biosynthetic) 6, 7, 28] [Novolin ge 10/90 Penfill (biosynthetic) 10, 40]

100 USP Insulin Human Units per mL (20% insulin human injection and 80% isophane insulin human suspension) (OTC)[Humulin 20/80 (biosynthetic) 6, 7, 28] [Novolin ge 20/80 Penfill (biosynthetic) 10, 40]

100 USP Insulin Human Units per mL (30% insulin human injection and 70% isophane insulin human suspension) (OTC)[Humulin 30/70 (biosynthetic) 6, 7, 14, 28] [Novolin ge 30/70 (biosynthetic) 10, 35] [Novolin ge 30/70 Penfill (biosynthetic) 10, 40]

100 USP Insulin Human Units per mL (40% insulin human injection and 60% isophane insulin human suspension) (OTC)[Humulin 40/60 (biosynthetic) 6, 7, 28] [Novolin ge 40/60 Penfill (biosynthetic) 10, 40]

100 USP Insulin Human Units per mL (50% insulin human injection and 50% isophane insulin human suspension) (OTC)[Humulin 50/50 (biosynthetic) 6, 7, 28] [Novolin ge 50/50 Penfill (biosynthetic) 10, 40]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F), unless otherwise specified by manufacturer. Protect from freezing.

Stability:

Do not use if precipitate has become clumped or granular in appearance.

Auxiliary labeling:

· Shake gently.
· Gently rotate prefilled syringe up and down before injection. 197

· Refrigerate.
· Do not freeze.

PROMPT INSULIN ZINC

Parenteral Dosage Forms

PROMPT INSULIN ZINC SUSPENSION (SEMILENTE INSULIN) USP

Usual adult and adolescent dose

Type 1 diabetes¾Initial: Subcutaneous, a total insulin dose is 0.5 to 0.8 USP Insulin Unit per kg of body weight as a single dose, depending on insulin type, or 0.5 to 1.2 USP Insulin Units per kg of body weight per day in divided doses. Body fat, blood glucose, and insulin sensitivity also should be considered. This total daily dose of insulin may be provided by one or more types of insulin. A few patients will require less than 0.5 USP Insulin Unit per kg of body weight per day. Dose titration to a targeted blood glucose goal is achieved over several days; a change in total daily insulin dose does not usually exceed 10% of the existing total daily insulin dose. Prompt insulin zinc is given thirty to sixty minutes before a meal and/or a bedtime snack. 50, 190, 209, 215, 218

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 218

Type 2 diabetes¾Initial: Subcutaneous, a total insulin dose may vary from 5 to 10 USP Insulin Units per day to 0.7 to 2.5 USP Insulin Units per kg of body weight per day, taking body fat, blood glucose, and insulin sensitivity into consideration. This total daily dose of insulin may be provided by one or more types of insulin and, depending on insulin type, may be given as a single dose or as divided doses. Dose titration to a targeted blood glucose goal is achieved over several days with changes from the existing total daily insulin dose of no more than 2 to 6 USP Insulin Units a day; again, body

weight should be considered. Very insulin-resistant patients using large doses, 200 USP Insulin Units or greater, may need to use a concentrated regular insulin (U-500) instead. Prompt insulin zinc is given thirty to sixty minutes before a meal and/or a bedtime snack. 50, 190, 209, 210, 219

Maintenance: Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations. 50, 219

Gestational diabetes mellitus¾Subcutaneous, dosage must be determined by the physician, based on blood glucose concentrations and gestational duration. 218, 220

Diabetes mellitus, other, associated with certain conditions or syndromes¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 50

Note: Insulin requirements may change during illness or events causing psychological or physical stress. Dosage changes for patients receiving conventional therapy should be determined by the physician, based on each patient's needs and insulin sensitivity. Patients receiving intensive therapy may adjust individual doses to compensate for anticipated changes in diet or exercise but should consult a physician if the permitted adjustments are inadequate and/or glucose monitoring indicates the need for a permanent change in the daily dose. 50

Some patients experience a honeymoon phase after initial therapy and lose their requirement for insulin altogether or require much less for a limited period of time (several months to several years). 218, 221

Adolescents during puberty may require an increase in their total daily insulin dose. 50, 211, 218

Usual pediatric dose

Antidiabetic agent¾Subcutaneous, dosage must be determined by the physician, based on body weight and blood glucose concentrations. 1, 50

Strength(s) usually available

U.S.¾Not commercially available.

Canada¾Not commercially available. 161

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F). Protect from freezing. 11, 53

Stability:

Do not use if precipitate has become clumped or granular in appearance. 11

Auxiliary labeling:

· Shake gently. 11, 53

- Refrigerate. 11, 53

- Do not freeze. 11, 53

Note: Prompt Insulin Zinc Suspension USP is sometimes mixed with other insulin types as directed by the physician. 11