

Insulin

Along with human insulin analogs, recombinant DNA human insulins are the most widely used insulins in this country. Through genetic engineering, bacteria or yeast are transformed into little “factories” that produce synthetic human insulin.



THERE ARE THREE MAIN CHARACTERISTICS of insulin. **Onset** is the length of time before insulin reaches the bloodstream and begins lowering blood glucose; **peak time** is the time during which insulin is at its maximum strength in terms of lowering blood glucose levels; and **duration** is how long the insulin continues to lower blood glucose. There are also several different types (remember, everyone has a unique response to insulin, so the times mentioned here are approximate):

Rapid-acting insulins, such as insulin lispro (Humalog), insulin aspart (NovoLog), and insulin glulisine (Apidra), begin to work about 15 minutes or less after they are injected, peak in about an hour, and continue to work for 2 to 4 hours. (Be sure to check the package inserts on rapid-acting insulins for product-specific directions, because they vary slightly.) In fact, you should never delay eating after using insulin lispro, insulin aspart, or insulin glulisine.

Because these insulins leave the bloodstream quickly, there is less chance of hypoglycemia (low blood glucose) several hours after the meal. All are very similar in their activity, but you should not use them interchangeably unless advised to do so by your doctor.

After-meal use of rapid-acting insulins may be of some benefit to young children, because their caloric intake is often difficult to predict before meals. After-meal use can also benefit those who have delayed stomach emptying (gastroparesis).

Regular or short-acting insulin (human) usually reaches the bloodstream within 30 minutes after injection. It peaks anywhere from 2 to 3 hours after injection, and is effective for about 3 to 6 hours. Typically, the higher the dose of regular insulin, the longer its duration of action.

Intermediate-acting insulin (human) generally reaches the bloodstream about 2 to 4 hours after it is injected. It peaks 4 to 12 hours later, and is effective for about 12 to 18 hours. NPH is the only intermediate-acting insulin currently marketed, and it is often used in combination with regular insulin.

Long-acting insulins such as insulin glargine (Lantus) and insulin detemir (Levemir) have continuous, “peakless” action that mimics natural basal (background) insulin secretion. Although it provides a long-lasting effect, insulin glargine’s onset is between 2 and 4 hours, and its duration of action is approximately 24 hours. Insulin glargine is clinically proven to reduce low blood glucose, especially during the night. It must not be mixed with any other type of insulin. Insulin glargine can be injected any time during the day, as long as it is taken around the same time each day. It should not be administered intravenously. Insulin detemir is a long-acting insulin that can last up to 24 hours, though its duration of action is thought to be less than that of insulin glargine.

Many people use both rapid- or short-acting insulins and insulin glargine or insulin detemir in an effort to mimic the body’s natural insulin secretion. Because the long-acting insulins glargine and detemir do not provide a peak to cover meals, injections of rapid-acting or short-acting regular insulin must be

given before all meals to provide bolus coverage for food intake. Both types of insulin are clear in appearance. If you are on this type of dual insulin therapy, it is very important that you choose the correct insulin from the correct vial. (One distinguishing factor is that insulin glargine vials are taller and narrower than those of other insulins.)

Premixed insulins may be convenient for those who mix NPH and regular into one syringe. Often, the insulin is premixed in a prefilled pen, a portable and accurate means of administering insulin, replacing the traditional vial and syringe.

The most typical mixture is 70 percent NPH and 30 percent regular. A mixture of 75 percent insulin lispro protamine and 25 percent insulin lispro, known on the market as the Humalog Mix 75/25, combines intermediate-acting insulin and rapid-acting mealtime insulin. Humalog 50/50 and Humulin 50/50 are additional mixtures that are available. Likewise, a mixture of 70 percent insulin aspart protamine and 30 percent insulin aspart (NovoLog Mix 70/30) is available.

Premixed insulin can be helpful for people who have poor eyesight or dexterity. Insulin pens may also be useful for people with these issues.

Strength

All insulins come dissolved or suspended in liquids, but the solutions have different strengths. The most commonly used strength in the United States is U-100. That means it has 100 units of insulin per milliliter of fluid. U-500 insulin is five times more concentrated than U-100 insulin and is used infrequently.

If you are traveling, it’s essential

that you purchase the correct strength of insulin. And because different syringes are used for different insulin strengths, it’s essential that your syringe match your insulin.

Mixing Insulins

Often people will be instructed to take a given amount of rapid-acting and a given amount of another type of insulin. NPH insulins mix easily with regular, insulin aspart, insulin lispro, and insulin glulisine. Mixtures containing insulin aspart, insulin lispro, or insulin glulisine should be injected immediately after mixing. These insulins should be mixed with NPH only under the guidance of your doctor. Insulin glargine and insulin detemir are not to be mixed with other insulins.

Additives

All insulins have added ingredients. These prevent bacteria from growing and help maintain a neutral balance between acids and bases. In addition, intermediate- and long-acting insulins contain ingredients that prolong their actions. In rare cases, the additives can bring on an allergic reaction.

Consumer Advice

Your pharmacy. In selecting a pharmacy, consider one that is close to you and open when you want to shop. Use a store where a pharmacist is available and will take an interest in your medical needs, be available to answer questions, and tell you what problems to watch for.

Shipping. If you order insulin by mail, consider the effect of shipping during hot summer months in the

INSULINS COMMONLY USED IN THE UNITED STATES (As of Oct. 1, 2007)

Generic Name	Brand Name	Form	Manufacturer	Cloudy or Clear
RAPID-ACTING				
insulin glulisine	Apidra*	analog	Sanofi-Aventis	clear
insulin lispro	Humalog*	analog	Eli Lilly and Company	clear
insulin aspart	NovoLog*	analog	Novo Nordisk, Inc.	clear
REGULAR				
regular	Humulin R	human	Eli Lilly and Company	clear
regular	Novolin R*, ReliOn (Wal-Mart)	human	Novo Nordisk, Inc.	clear
INTERMEDIATE-ACTING				
NPH	Humulin N*	human	Eli Lilly and Company	cloudy
NPH	Novolin N*, ReliOn (Wal-Mart)	human	Novo Nordisk, Inc.	cloudy
LONG-ACTING				
insulin detemir	Levemir*	analog	Novo Nordisk, Inc.	clear
insulin glargine	Lantus*	analog	Sanofi-Aventis	clear
MIXTURES				
70% NPH/30% regular	Humulin 70/30*	human	Eli Lilly and Company	cloudy
70% NPH/30% regular	Novolin 70/30*†, ReliOn (Wal-Mart)	human	Novo Nordisk, Inc.	cloudy
50% lispro protamine, 50% insulin lispro	Humalog Mix 50/50*	analog	Eli Lilly and Company	cloudy
75% lispro protamine (NPL)/25% lispro	Humalog Mix 75/25*	analog	Eli Lilly and Company	cloudy
70% aspart protamine/30% aspart	NovoLog Mix 70/30*†	analog	Novo Nordisk, Inc.	cloudy

*Available in prefilled, disposable pens or cartridges for reusable pens. (Insulin pens are listed on pages RG22 and RG23.) †Note difference between Novolin 70/30 (70% NPH/30% regular) and NovoLog Mix 70/30 (70% aspart-protamine/30% aspart).

HUMAN & ANALOG INSULIN: TIME OF ACTION

Insulin	Onset	Peak (hours)	Duration (hours)
lispro, aspart, glulisine	<15 minutes	1–2	3–4
regular	30 minutes–1 hour	2–3	3–6
detemir	1–2 hours	relatively flat	up to 24
glargine	1–2 hours	no pronounced peak	24
NPH	2–4 hours	4–10	10–16

South or freezing winter months in the North. Ask the distributor how the bottles will be kept cool and inspect them carefully when they arrive. If you use a local pharmacy,

look for one that makes deliveries. This can be helpful when you are ill or busy.

Check labels. Don't just ask for "NPH"; look at the full brand name,

strength, and kind. You might bring a used bottle with you to make sure you get the same insulin you got

text continued on page RG14

LESS COMMONLY USED INSULINS

Generic Name	Brand Name	Form	Manufacturer
regular	Humulin R, U-500*	human	Eli Lilly and Company
50% NPH/50% regular	Humulin 50/50	human	Eli Lilly and Company

*Humulin R, U-500 is used in patients who are extremely insulin resistant. Otherwise in the United States, insulin is standardized to U-100 (100 units per cc).

OTHER INJECTABLE DRUGS

Drug Name (generic)	Manufacturer	Comments
Byetta (exenatide)	Amylin Pharmaceuticals, Inc., and Eli Lilly and Company	For use only by those with type 2 diabetes who are taking metformin, a sulfonylurea, a thiazolidinedione, a combination of metformin and a sulfonylurea, or a combination of metformin and a thiazolidinedione, but have not achieved adequate glycemic control. Enhances insulin secretion in the presence of high blood glucose and may suppress appetite. Available in 5- and 10-microgram pens. When to take: twice daily within 60 minutes before the morning and evening meals. Side effects: nausea and vomiting. Risk of hypoglycemia is increased when administered in combination with a sulfonylurea. May need to reduce sulfonylurea dose.
Symlin (pramlintide acetate)	Amylin Pharmaceuticals, Inc., and Eli Lilly and Company	For use only by those with type 2 or type 1 diabetes who take mealtime insulin. It helps suppress appetite and lower high blood glucose after meals. When to take: Take before a meal that has at least 250 calories or ≥ 30 g of carbohydrates. Cannot be mixed with insulin, so it must be taken as a separate injection. When starting Symlin, it is recommended to reduce mealtime insulin by half and follow the Symlin dose escalation instructions. Side effects: nausea and insulin-induced hypoglycemia.

text continued from page RG13

before. Before you pay, check the label to make sure you have the correct insulin and the correct directions.

Expiration date. Make sure you will be using all the insulin you are buying before its expiration date. Your pharmacist can help you select the right size vial.

Quantity purchases. Buying more than one bottle of insulin at a time can be cheaper than buying it by the bottle. But keep expiration dates in mind.

Keep alert. Rarely, insulin lots must be recalled, and you will need to check the control number of your bottles against that of the recalled lot.

Price. It pays to shop around for your insulin. Prices can vary by several dollars a bottle depending on where it's sold. (Note: Don't switch brands or types of insulin

without your doctor's advice.) However, it is important to get all of your prescriptions at one pharmacy to ensure that there is one central source for all your medications.

Storage and Safety

Although manufacturers recommend storing your insulin in the refrigerator, injecting cold insulin can sometimes be painful. To counter that, many providers recommend storing the bottle of insulin you are using at room temperature. Check product labels for how long an insulin vial or cartridge should be used after the seal is punctured. This will vary depending on the type of insulin and whether it's packaged in a vial or pen/cartridge system.

If you buy more than one bottle

at a time—a possible money-saver—store the extra bottles in the refrigerator. Then, take out the bottle ahead of time so it is ready for your next injection. Never store insulin in the freezer, direct sunlight, or the glove compartment of a car.

Before you use any insulin, check the expiration date. Don't use any insulin beyond that date. And examine the bottle closely to make sure it looks normal before you draw the insulin into the syringe. If you use regular, insulin aspart, insulin lispro, insulin glargine, insulin glulisine, or insulin detemir, make sure it is clear. Check for particles or discoloration of the insulin. If you find any of these in your insulin, do not use it, and return the unopened bottle to the pharmacy for exchange or refund. ▲