Comparison of GLP-1 Agonists

full update August 2024

This chart compares GLP-1 agonists (including the "twincretin" tirzepatide) in regard to A1c reduction, weight loss, dosing, tolerability, clinical outcomes (e.g., cardiac or kidney benefit), how supplied, cost, and storage. For a review of class **adverse effects**, see **footnote f**.

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Dulaglutide (*Trulicity*) A1c: -1.09% (mean across trials)[1] Weight loss: 0.73 kg (mean across trials)[1]	Single dose pen (autoinjector): 0.75, 1.5, 3 (US), 4.5 mg (US) US: $977.42 Canada: ~$250 (1.5 mg/week) Store at 2ºC to 8ºC, or room temp (≤30ºC) for ≤14 days.	**Initial**: 0.75 mg once weekly. **Max**: may increase to 1.5 mg once weekly, then by 1.5 mg weekly every four weeks to a max of 4.5 mg once weekly. **Comparative dose**: see footnote g. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤1.5 mg.[15]	• Added to standard DM treatment in patients with CV disease or risk factors, over ~5.4 years reduced the composite of nonfatal MI, nonfatal stroke, and death from CV or unknown causes (NNT = 71).[4] For individual outcomes, only nonfatal stroke was significantly reduced. • Reduced a composite of new macroalbuminuria, 30% decrease in eGFR, or need for dialysis/transplant (NNT= 40), driven by prevention of macroalbuminuria (exploratory analysis).[5] • Discontinuation due to adverse GI effects (1.5 mg): ~1 in 15 patients[3]
Exenatide (*Byetta* [US]) A1c: -0.7% (10 mcg BID monotherapy)[a,c] Weight loss: -1.5 kg (10 mcg BID monotherapy)[a,c]	Sixty (60)-dose pen: 5, 10 mcg (needles not included) US: $849.95 Store at 2ºC to 8ºC. In-use pens can be stored at ≤25ºC for up to 30 days.	**Initial**: 5 mcg BID within 60 min before the two main meals (≥6 hours apart). **Max**: may increase to 10 mcg BID after four weeks. **Comparative dose**: see footnote g. **Missed dose**: skip missed dose **Kidney impairment**: Not recommended if CrCl <30 mL/min. Use 10 mcg BID with caution if CrCl 30 to 50 mL/min. Use caution in kidney transplant.	• Discontinuation due to adverse GI effects (10 mcg BID): ~1 in 24 patients[3]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Exenatide (*Bydureon BCise* [US]) A1c: -0.64% (adults); -0.71% (pediatrics)[a,c] Weight loss: 0.92 kg (from baseline)[c]	Single dose pen (autoinjector): 2 mg US: $827.45 Store at 2°C to 8°C, or room temp (≤30°C) for ≤4 weeks.	For patients 10 years and older: 2 mg once every seven days **Comparative dose**: see footnote g. **Kidney impairment**: Not recommended if eGFR <45 mL/min/1.73 m^2. Use caution in kidney transplant. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.	• Once-weekly exenatide added to standard DM therapy in patients with or without CV disease had a neutral CV effect, but was associated with a reduction in death from any cause compared to placebo (NNT = 341).[6] • Discontinuation due to adverse GI effects: ~1 in 22 patients.[3] • Highest rate of injection site reactions among once-weekly GLP-1s.[3] • Required mixing immediately before injection.
Liraglutide (*Saxenda*) Indicated for weight loss. Weight loss: 3.7 to 5.2 kg (3 mg once daily x 56 weeks)[a,c]	Dial-a-dose pen: 18 mg/3 mL (pen needles not included) US: $1,349.02 Canada: ~$450 Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤30 days.	For patients 12 years and older: 3 mg **once daily** (start with 0.6 mg once daily, increase dose weekly by 0.6 mg to goal of 3 mg once daily). For adults, discontinue after 16 weeks if <4% (after 12 weeks if ≤5% [Canada]) weight loss achieved. **Comparative dose**: see footnote g. **Missed dose**: Skip the missed dose. If more than three days have elapsed since the last dose, retitrate starting with 0.6 mg once daily (US).	• See *Victoza*, below for information on clinical outcomes in type 2 DM. • ~44% to 62% of patients met weight loss goal (≥5%) at 56 weeks compared to 16% to 34% with placebo. • Discontinuation due to adverse effects: ~1 in 11 patients.[c]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Liraglutide[d] (*Victoza*) A1c: -1.04% (adults); -1.06 (pediatrics)[1,a,c] Weight loss: 1.33 kg[1]	Dial-a-dose pen: 18 mg/3 mL (needles not included) US: $815.27 Canada: $336.10 Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤30 days.	For patients 10 years and older: **Initial**: 0.6 mg once daily for one week, then 1.2 mg once daily. (Pediatric patients may achieve control with 0.6 mg once daily.) **Max**: may increase to 1.8 mg once daily after one week. **Comparative dose**: see footnote g. **Missed dose**: Skip the missed dose. If more than three days have elapsed since the last dose, retitrate starting with 0.6 mg once daily (US).	• Added to standard care in patients with type 2 DM with CV disease or at high CV risk over ~4 years reduced:[7] o death from CV causes, nonfatal MI, or nonfatal stroke, NNT = 53; death from CV causes, NNT = 77; death from any cause, NNT = 71. o new macroalbuminuria or doubling of SCr plus eGFR ≤45 mL/min/1.73 m^2, need for dialysis/transplant, or death from kidney causes (NNT =67), driven by prevention of macroalbuminuria (NNT = 83). o Did not reduce the individual rates of MI, nonfatal stroke, or HF-related hospitalizations. • Discontinuation due to adverse GI effects (1.8 mg): ~1 in 18 patients[3]
Semaglutide (*Ozempic*) A1c: -1.4% (1 mg weekly as monotherapy)[a,c] Weight loss (1 mg): 3.5 kg[a,c] *Continued…*	Multi-dose pen: 0.25 or 0.5 mg (four 0.25 mg doses or two 0.5 mg doses), 1 mg (4 doses), 2 mg (4 doses [US]) (includes needles) US: $1,291.36 Canada: ~$235 (1 mg/week) Store at 2°C to 8°C. In-use pens can be stored at room temp (≤30°C) for ≤56 days.	**Initial**: 0.25 mg once weekly for four weeks, then 0.5 mg once weekly, **Max**: may increase to 1 mg once weekly after four weeks. After four weeks on the 1 mg dose, may increase to 2 mg once weekly. **Comparative dose**: see footnote g. **Missed dose**: if <48 hours remain until the next scheduled dose, skip the missed dose. If >48 remain, administer the missed dose. If two or more consecutive doses are missed, consider starting with 0.25 mg once weekly.[c] Some experts would restart with 1 mg if one or two doses are missed, 0.5 mg if three or four doses are missed, or 0.25 mg if ≥5 doses are missed.[15]	• In type 2 DM patients with CV disease, CKD, or CV risk factors, reduced the combined endpoint of CV death, nonfatal MI, or nonfatal stroke (NNT = 44 for ~ 2 years). For individual outcomes, only nonfatal stroke was significant. A composite of new onset macroalbuminuria or doubling of SCr plus eGFR ≤45 mL/min/1.73 m^2, need for dialysis/transplant, or death from kidney causes was reduced (NNT = 44), driven by prevention of macroalbuminuria.[8] • In type 2 DM with CKD, reduced a composite of major kidney events (kidney failure, ≥50% reduction in eGFR, kidney or CV death) (NNT = 20 over 3 years). Kidney function declined more slowly, and the risks of major CV events and all-cause mortality were reduced.[21]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Ozempic, continued			• Discontinuation due to adverse GI effects (1 mg): ~1 in 10 patients[3]
Semaglutide (*Rybelsus*) A1c: -1.1% (as monotherapy, 14 mg/day)[a,c] Weight loss (14 mg): 3.8 kg[a,c]	3 mg, 7 mg, or 14 mg tablets. US: 968.52 Canada: 233.38	**Initial**: 3 mg once daily at least 30 minutes before the first food, beverage, or other oral medications of the day, with ≤120 mL of water (~half a glass). After 30 days, increase the dose to 7 mg once daily. **Max**: After 30 days on the 7 mg dose, may increase to 14 mg once daily. **Comparative dose**: patients taking *Rybelsus* 14 mg may switch to *Ozempic* 0.5 mg. Patients on *Ozempic* 0.5 mg can be switched to *Rybelsus* 7 mg or 14 mg (US). Also see footnote g. **Missed dose**: skip the missed dose	• ORAL semaglutide in patients with type 2 DM and CV disease, CKD, or CV risk factors had a neutral CV effect.[9] • Discontinuation due to adverse GI effects: ~1 in 15 patients[c]
Semaglutide (*Wegovy*) Indicated for weight loss. Weight loss: ~10.6 to 12.7 kg (2.4 mg once weekly at one year)[13,14]	Single-dose pen (autoinjector): 0.25, 0.5, 1, 1.7, 2.4 mg. US: $1,349.02 Canada: $419.73 Store at 2°C to 8°C. Can be stored at room temp (≤30°C) for ≤28 days.	For patients 12 years and older: 0.25 mg once weekly, increased every four weeks to 0.5 mg, 1 mg, 1.7 mg, then 2.4 mg once weekly. Canada: consider stopping if the patient is not showing progress after 12 weeks on the maintenance dose. **Comparative dose**: see footnote g. **Missed dose**: if <48 hours remain until the next scheduled dose, skip the missed dose. If >48 hours remain, administer the missed dose. If two or more consecutive doses are missed, consider restarting with 0.25 mg once weekly.[c] Some experts would restart with 1 mg if one or two doses are missed, 0.5 mg if three or four doses are missed, and 0.25 mg if ≥5doses are missed.[15]	• Reduces CV risk (prevents 1 event for every 67 patients treated for ~ 3 years.[10] • 67% to 85% of patients met weight loss goal (≥5%) at 52 weeks compared to 30% to 48% with placebo.[13,14] • Discontinuation due to adverse effects: ~ 1 in 15 patients[c]

Drug/ A1c decrease/ Weight loss	**Availability Cost[b] Storage[c]**	**Dosing (subcutaneous injection in ADULTS unless otherwise specified)[c]**	**Comments (e.g., clinical outcomes, tolerability)**
Tirzepatide[e] (*Mounjaro*) A1c: -2.1%[1,a] Weight loss: 6.18 kg (as monotherapy, 15 mg/week).[a,c]	Single-dose vial or pen (autoinjector [US]): 2.5, 5, 7.5, 10, 12.5 (US), 15 mg (US) (vial does not includes needles or syringe) US: $1,069.08 Canada: ~$97 (10 mg vial) Store at 2ºC to 8ºC. Can be stored at room temp (≤30ºC) for ≤21 days.	**Initial**: 2.5 mg once weekly for four weeks, then 5 mg once weekly. **Max**: may increase by 2.5 mg/week every four weeks to a max of 15 mg once weekly. **Comparative dose**: see footnote g. **Missed dose:** If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤5 mg once weekly.[15]	• May delay oral contraceptive absorption. Advise switching to a non-oral contraceptive or adding a barrier contraceptive for four weeks after initiation or a dosage increase.[c] • Discontinuation due to adverse GI effects (15 mg): ~1 in 16 patients.[c]
Tirzepatide[e] (*Zepbound* [US]) Indicated for weight loss. Weight loss: ~18.8 kg (15 mg once weekly at week 72)[12,a]	Single-dose vial or pen: 2.5, 5, 7.5, 10, 12.5, 15 mg (vials do not include syringe or needle) US: $1,059.87 Store at 2ºC to 8ºC. Can be stored at room temp (≤30ºC) for ≤21 days.	Start with 2.5 mg once weekly, increase dose every 4 weeks to 5 mg, 7.5 mg, 10 mg, 12.5 mg, then 15 mg. **Comparative dose**: see footnote g. **Missed dose**: If <72 hours remain until the next scheduled dose, skip the missed dose. If ≥72 hours remain, administer the missed dose.[c] If ≥3 doses are missed, consider restarting with ≤5 mg once weekly.[15]	• May delay oral contraceptive absorption. Advise switching to a non-oral contraceptive or adding a barrier contraceptive for four weeks after initiation or a dosage increase.[c] • Discontinuation due to adverse effects: ~ 1 in 15 patients[c] • Though no specific guidance is available, stopping after 12 weeks if <5% weight loss achieved is reasonable based on guidelines.[11] • 85% to 91% of patients met weight loss goal (≥5%) at 72 weeks compared to 35% with placebo.[12]

Abbreviations: BID = twice daily; CKD = chronic kidney disease; CV = cardiovascular; DM: diabetes mellitus; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; HF = heart failure; MI = myocardial infarction; NNT = number needed to treat; SCr = serum creatinine

a. Diabetes indication: mean A1c and weight reduction compared to placebo, as an add-on to other diabetes medication (unless monotherapy is specified). Weight loss indication: mean weight loss with lifestyle changes and/or diet. Weight loss is the amount above that seen with placebo. Weight loss varies based on lifestyle modification, baseline weight, etc.
b. Wholesale acquisition cost (US) per month of maximum dose (or dose specified). US medication pricing by Elsevier, accessed July 2024. Canadian cost is wholesale. Prices for products that are dosed weekly represent a 28-day supply. Prices for products that are dosed daily represent a 30-day supply.
c. **US product information used in creation of this chart**: *Trulicity* (December 2022), *Byetta* (December 2022), *Bydureon BCise* (May 2023), *Saxenda* (April 2023), *Victoza* (July 2023), *Ozempic* (September 2023), *Rybelsus* (January 2024), *Wegovy* (March 2024), *Mounjaro* (July 2023), *Zepbound* (March 2024). **Canadian product monographs used in creation of this chart**: *Trulicity* (July 2024), *Saxenda* (April 2024), *Victoza* (March 2024), *Ozempic* (March 2024), *Rybelsus* (February 2024), *Wegovy* (March 2024), *Mounjaro* (July 2024)
d. **Liraglutide** is available in combination with insulin degludec (*Xultophy*).
e. **Tirzepatide** is a GLP-1 agonist and glucose-dependent insulinotropic polypeptide (GIP) agonist (i.e., a "twincretin").
f. **Adverse effects**:[c] (Note that in the US, these medications must be dispensed with a **Medication Guide**.)
    - GI side effects are common during dose escalation (e.g., nausea, vomiting, diarrhea). Resulting volume depletion may lead to acute kidney injury. GLP-1 agonists have been associated with bowel obstruction.[17] Educate patients about the potential for ileus.[20]
        - These GI side effects, and delayed gastric emptying, entail special considerations in surgical patients. See our chart, *Perioperative Management of Diabetes*.
    - These drugs carry warnings about gallbladder disease (low risk) and pancreatitis (association unclear).[3,19,20,c] Stop if pancreatitis is suspected, and do not restart if pancreatitis is confirmed. There have been reports of pancreatic cancer in patients using GLP-1 agonists, but current evidence does not support causality.[19]
    - These drugs are contraindicated in patients with a personal or family history of medullary thyroid cancer or patients with multiple endocrine neoplasia type 2. They cause thyroid C-cell tumors in mice.
    - Rapid improvement in glycemic control is associated with diabetic retinopathy complications.
    - Risk of hypoglycemia is low as monotherapy.
    - Monitor for depression and suicidal ideation in patients taking these drugs for weight loss. Discontinue if symptoms develop.
    - Don't combine with other GLP-1 agonists. Generally, avoid use in patients taking a dipeptidylpeptidase-4 inhibitor (e.g., saxagliptin), as combining these two classes of medications is unlikely to improve weight loss or glycemic control and is not cost-effective.[18]
g. **Comparative dosing based on glycemic efficacy**.[15] Consider a lower starting dose if GI tolerability is a priority.[16]
    - exenatide 5 mcg BID ~liraglutide 0.6 mg/week ~semaglutide 3 mg orally once daily
    - dulaglutide 0.75 mg/week ~ exenatide 10 mcg BID ~ liraglutide 1.2 mg/week ~ semaglutide 0.25 mg/week ~ semaglutide 7 mg orally once daily
    - dulaglutide 1.5 mg/week ~ exenatide 2 mg/week ~ liraglutide 1.8 mg/week ~ semaglutide 0.5 mg/week ~ semaglutide 14 mg orally once daily ~ tirzepatide 2.5 mg/week
    - dulaglutide 4.5 mg/week ~ semaglutide 1 mg/week
    - semaglutide 2 mg/week ~ tirzepatide 5 mg/week

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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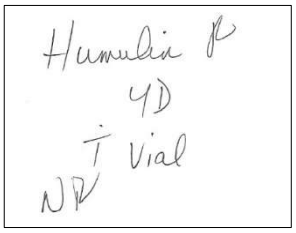
Technician Tutorial:
Dispensing Insulin and Other Injectable Diabetes Meds

Insulin is a hormone secreted by the pancreas. It helps the body use glucose (sugar) as an energy source by acting like a "key" that allows glucose to enter the body's tissues. People with diabetes either produce very little or no insulin (type 1) or don't use available insulin properly or make enough insulin (type 2). Without the right amounts or proper functioning of insulin, glucose builds up in the blood and organs, causing tissue damage or death. Although type 2 diabetes can often be managed with oral meds, many patients with type 2 diabetes and all patients with type 1 diabetes will require injections of insulin. For more details on oral diabetes meds, review our charts, *Drugs for Type 2 Diabetes* (US) and *Stepwise Treatment of Type 2 Diabetes* (Canada).

There are several insulin products on the market. One way to classify them is by how quickly they take effect and how long effects last. For example, short-acting (e.g., regular insulin [*Humulin R*]) and rapid-acting insulins (e.g., insulin aspart [*NovoLog* (US), *NovoRapid* (Canada)]) act relatively quickly and the effect is relatively short. On the other hand, long-acting insulin, such as insulin glargine (*Lantus*, etc) or insulin detemir (*Levemir*), has a longer time to onset and effects last much longer. Sometimes people will need to use two different types of insulin, such as a long-acting one to cover them throughout the day and a short-acting one to cover them after meals. You can find more details in our chart, *Comparison of Insulins* (US subscribers; Canadian subscribers).

There are also other injectable drugs used to treat diabetes besides insulin. They include exenatide (*Byetta*), exenatide extended release (*Bydureon BCise* [US]), liraglutide (*Victoza*), lixisenatide (*Adlyxin* [US], *Adlyxine* [Canada]), dulaglutide (*Trulicity*), and semaglutide (*Ozempic*). These "GLP-1 agonists" increase the body's natural secretion of insulin and are commonly used to treat type 2 diabetes. Other examples of injectable diabetes meds include tirzepatide (*Mounjaro* [US]), a "GLP-1/GIP agonist," and pramlintide (*Symlin* [US]), an amylin analog. These meds mimic hormones in the gut that help reduce blood sugar levels.

Pharmacy technicians need to be familiar with the different types of insulin and other injectable diabetes medications to help prevent mix-ups with these products.



Eileen is a 55-year-old female who is dropping off an Rx for Humulin *insulin. You notice an abbreviation that looks like "ud," which you understand it to mean, "use as directed." However, you realize this abbreviation could also look like "4 days" or "40." You also see a letter that could either be an "N" or an "R" after the drug name. This could lead to incorrect interpretation of the Rx as* Humulin N *instead of* Humulin R*, or vice versa. There's also no concentration on the order, so it's unclear if the patient should get* Humulin R *U-100 or* Humulin R *U-500. You check with your pharmacist for clarification.*

When are patients prescribed GLP-1 agonists or insulin?

Patients will often need to take more than one type of diabetes medication to reach their diabetes treatment goals. Patients with type 2 diabetes are usually started on the oral medication metformin, with one or two additional oral medications added as needed to reach their blood sugar goal. GLP-1 agonists are typically reserved for patients with type 2 diabetes who require two or more diabetes medications to control their blood

sugar, or A1C (the average of blood glucose levels over the past three months). GLP-1 agonists are often tried before moving to insulin and like the oral diabetes meds, they may be used with insulin.

Insulin is the mainstay of therapy for people with type 1 diabetes since their bodies can't make insulin. Insulin is also used for some people with type 2 diabetes, usually those who aren't controlled on a combination of oral or non-insulin injectable medications.

Why is insulin considered a high-alert medication?

Insulin is considered high alert because errors can cause serious patient harm, even death. Patients need very specific doses of insulin to keep their blood sugar within range. If patients take too much insulin, it could lead to hypoglycemia, which is dangerously low blood sugar. Symptoms of low blood sugar can include shakiness, dizziness, sweating, blurred vision, confusion, nausea, and in severe cases, brain damage, coma, or death. On the other hand, if patients don't get enough insulin, they may develop hyperglycemia, which is dangerously high blood sugar that can cause increased thirst, frequent urination, blurred vision, and in more severe cases, kidney failure, nerve damage, vision loss, or the potentially deadly medical emergency, diabetic ketoacidosis (DKA).

Examples of insulin errors include confusion between insulin products and/or concentrations and mistaking dangerous abbreviations. For example, "U" for "units" can be mistaken for a number "4" or a zero, resulting in an overdose. Be vigilant when dispensing insulin and refer Rxs that seem inappropriate to your pharmacist. Also be extremely careful when dispensing U-500 insulin. This medication has been singled out as especially risky since dispensing U-500 instead of U-100 could lead a patient to get five times the intended dose. You can learn more about safety considerations with high-alert meds by taking our CE, *High-Alert Medication Safety*. For strategies to help prevent insulin errors, review our checklist, *Tips to Improve Insulin Safety*.

What should be done when inputting Rxs for injectable diabetes meds into the computer?

Choose the correct product. Some brands of insulin, such as *Lantus* and *Humalog* U-100, come as both a vial and pen. Pay attention to different formulations of the same med and be sure to select the right one, such as with *Byetta* and *Bydureon BCise*. Both contain exenatide, but *Byetta* is dosed twice daily and *Bydureon BCise* is dosed once per week since it's extended release. Also be careful not to incorrectly substitute among insulin products that are not interchangeable. For instance, in some US states you may be able to automatically substitute the interchangeable biosimilar insulin glargine-yfgn U-100 (*Semglee*) for *Lantus*. However, *Basaglar*, another form of insulin glargine U-100, is not a generic for or interchangeable with *Lantus* in the US. In Canada, some provinces consider *Basalgar* a biosimilar of *Lantus* and may allow substitution but check with your pharmacist if you aren't sure. Additionally, orders written for "insulin aspart" could be for *Novolog* (*NovoRapid* in Canada) or *Fiasp*. And orders for "insulin lispro" could be for *Admelog*, *Humalog*, or *Lyumjev* (US). Don't automatically switch between any of these products because they're not equivalent.

Watch out for look-alike/sound-alike drug names. *Humulin* and *Humalog* mix-ups are common. *Levemir* and *Lantus* can also be confused. *Lantus* has even been confused with *Humalog* even though they look and sound different. Also watch for look-alike/sound-alike errors with generic names of GLP-1 agonists, since they all end in "tide" – dulaglutide, liraglutide, lixisenatide, etc. And be careful not to confuse the oral GLP-1 agonist semaglutide (*Rybelsus*) with the injectable version (*Ozempic*). Keep in mind *Rybelsus* is taken daily while *Ozempic* is injected weekly. Watch for mix-ups with the injectable GLP-1 agonists that are approved for weight loss, such as *Wegovy* (US) which contains semaglutide and *Saxenda* which contains liraglutide. These should not be substituted for the products approved for diabetes (e.g., *Ozempic* [semaglutide], *Victoza* [liraglutide]) since they have different dosing and uses. For instance, the doses for weight loss are typically higher than the doses for diabetes.

Confusion can also arise with diabetes meds that start with "T," including *Tradjenta* (*Trajenta* in Canada), *Trulicity*, *Toujeo SoloStar* (*Toujeo DoubleStar* in Canada), and *Tresiba*.

Double-check the concentration and strength. For instance, orders written for "insulin glargine" could be for U-100 *Basaglar*, *Lantus*, or *Semglee*, or U-300 *Toujeo SoloStar* or *Toujeo Max SoloStar* (*Toujeo DoubleStar* in Canada). And insulin degludec (*Tresiba*) comes in U-100 and U-200 versions while regular insulin comes in U-100 and U-500 versions (*Humulin R* U-500 [US], *Entuzity Kwikpen* [Canada]). Dispensing the wrong concentration could lead to the patient having dangerously high or low blood sugar. If you get an Rx without a concentration, clarify this with a pharmacist so the correct product is dispensed. Watch for GLP-1 agonists that come in several strengths. These doses often need to be titrated up slowly to limit stomach side effects, such as nausea or vomiting. For instance, dulaglutide comes in four strengths: 0.75, 1.5, 3, and 4.5 mg (it comes in two strengths in Canada: 0.75 and 1.5 mg). And the GLP-1/GIP agonist tirzepatide (US only) comes in six strengths: 2.5, 5, 7.5, 10, 12.5, and 15 mg.

Watch for duplicate therapy. Many patients will use more than one type of insulin, such as a shorter-acting insulin (regular, lispro, aspart, etc) with meals and a longer-acting insulin (glargine, detemir, degludec, etc) once (or sometimes twice) a day. However, duplicate therapy issues come into play when the patient has prescriptions for two or more of the same type of insulin. For example, if a patient has prescriptions for both *Lantus* and *Levemir*, you should bring this to the attention of the pharmacist. Also, there are some products that are combinations of a long-acting insulin and GLP-1 agonist (e.g., *Soliqua* [insulin glargine/lixisenatide], *Xultophy* [insulin degludec/liraglutide]). Be sure that patients taking these meds are no longer getting prescriptions filled for the individual components. Duplicate therapy alerts will also come up when a patient is switching from one type of insulin or GLP-1 agonist to another. Get the pharmacist involved to review these. Pharmacists need to counsel the patient to make sure they know the proper technique for using the new product, are aware of new doses, etc.

Enter complete dosing instructions. Insulin prescriptions may have complex instructions. Check notes on e-Rxs for extra instructions from the prescriber. Pay special attention when entering dosing instructions for these Rxs into the computer. Make sure the Rx label reads exactly as written on the prescription. Additional label space may be required for detailed instructions.

Be aware that a prescriber might write the Rx instructions for insulin as "use as directed," with changes communicated directly to the patient. (Insurers frown upon "use as directed," and the pharmacist will often need to clarify instructions with the prescriber.) Patients may be instructed by the prescriber on how to vary the dose of their short-acting or rapid-acting insulin depending on what they eat at each meal. You may also see Rxs written for "SS" or "sliding scale" insulin. This is more common in hospitals or nursing homes. A sliding scale means the insulin dose varies depending on the patient's blood sugar.

The pharmacist calls the prescriber and clarifies that Eileen's Rx is for Humulin R *U-100. The pharmacist also gets more detailed instructions than the "use as directed" sig on the Rx. Eileen will need to use 15 units of insulin with each meal.*

Enter an accurate quantity to be dispensed. One insulin vial typically contains 10 mL. (Some come in 3 mL institutional sizes, for hospital use.) For reimbursement purposes, Rx quantities for liquids are usually entered in mL, not vials or packages. For instance, entering a quantity of "1" when dispensing one insulin vial may lead to inadequate reimbursement. This may be communicated as "1 mL," instead of the full 10 mL contained in one vial.

For pens that come in multipacks, such as *Victoza*, enter the total number of mL in the box or carton instead of the number of pens or the number of mL in one pen. For example, a five-pack of insulin pens that contain 3 mL of drug in each pen will require a dispense quantity of 15 mL.

Enter an accurate days' supply. When specific dosing instructions are included, a days' supply can be calculated. Divide the total number of units per vial, pen, or box by the total units injected daily.

Example:
If a patient uses 100 units of *Lantus* per day, how long will one 10 mL vial of 100 units/mL last?
100 units/mL x 10 mL/vial = 1,000 units/vial; 1,000 units/vial x 1 day/100 units = 10 days.

When specific dosing instructions are NOT on the Rx, the pharmacist may need to clarify with the prescriber's office. You can also ask the patient how they've been advised to take the med to determine how long it should last. Submitting an incorrect days' supply for reimbursement can cause third-party problems. Insurance companies will often reject a claim with a "refill too soon" message if a claim is transmitted before the previous prescription's days' supply has passed. For example, if a prescription is entered for a 30-day supply, insurance will not pay for a refill if the patient runs out in just 14 days. Also, billing incorrectly can lead to audits or chargebacks.

Keep storage and stability in mind when entering days' supply for injectable diabetes med Rxs. These meds typically have to be discarded after a specific number of days once in use. In the above example, what if the patient were taking 20 units of *Lantus* per day instead of 100 units? This would be calculated as a days' supply of 50. However, any in-use *Lantus* vials should be discarded after 28 days. As such, this Rx should be entered into the computer as being for one 10 mL vial and a 28-day supply.

Also be alert for patients requiring multiple insulin vials for a one-month supply. In the example above, if the Rx quantity is written for a 30-day supply, three vials would need to be dispensed (100 units/day x 30 days = 3,000 units, requiring three 10 mL vials).

Humulin R *U-100 is available in a 10 mL vial with a concentration of 100 units/mL. When filling Eileen's prescription, you enter the quantity dispensed as 10 mL and calculate that if Eileen eats three meals a day, she is expected to use about 45 units of* Humulin R *U-100 each day. You enter a days' supply of 22 days (100 units/mL x 10 mL = 1,000 units/vial x 1 day/45 units = 22 days/vial), which is within the product's stability of 31 days once in use.*

Follow company policy when billing pen devices. It's important to be aware that in the US, the FDA-approved labeling for insulin pens states to dispense in the original sealed carton. This helps ensure patients get the "Patient Information" and "Instructions for Use" with each box. In the past, pharmacies may have broken a box to dispense just enough insulin to meet payer quantity limits. However, this practice puts pharmacies at risk of audit if they do not dispense a full box. This can pose a challenge depending on how much insulin a patient is using. For example, assume a patient is using 30 units of insulin per day and gets a prescription for an insulin pen that comes in a package of five 100 units/mL pens containing 3 mL each. The full box would be entered into the computer with a quantity of 15 mL (5 pens x 3 mL) and the days' supply would be entered as 50 days (300 units/pen x 1 day/30 units = 10 days/pen; 5 pens x 10 days/pen = 50 days). However, many insurance companies have days' supply limits, and in this example, 50 days will likely exceed them.

Always follow your company's policy on how to handle these situations and consider some general best practices. For example, always first bill an accurate days' supply based on the prescribed quantity. If plan limits are exceeded, call the payer's help desk to request an override. If no override is available, clearly document the payer's guidance on the Rx hard copy and in the computer. For example, note insurance limits, actual days' supply, and whether to adjust days' supply. Talk to your pharmacist about including the actual days' supply in the Rx sig, such as, "1 box should last 50 days." Put a flag in the patient profile to indicate that this Rx shouldn't be refilled earlier than the date which reflects the actual days' supply. Don't enroll these Rxs in automatic refill programs, as this could be considered fraud due to overbilling.

Get the pharmacist involved if insulin is too expensive. They may be able to get the patient switched to a more affordable product. For example, regular insulin, NPH, or 70/30 insulin may cost less than other types of insulin and can lower blood sugar similarly to other types of insulin. Generic versions may also help patients save money. For instance, authorized generics for *Humalog* U-100 (insulin lispro), *NovoLog* (insulin aspart), and *NovoLog Mix 70/30* (insulin aspart protamine/insulin aspart) are available in the US. These authorized generics may be less expensive than the brand and they lower blood glucose the same amount as the brand. Also pay attention to late refills for insulin prescriptions or return-to-stocks; this could be a sign that patients are rationing to save money.

How should I prepare and label injectable diabetes meds for dispensing?

Take steps to ensure correct product selection from the shelf. There are several different types of injectable GLP-1 agonists and insulins available, and they are all kept in the fridge. To prevent mix-ups when selecting a product from the fridge, use separate bins or shelf alerts to distinguish products that look similar. Keep concentrated insulins (e.g., U-200, U-300, U-500) in a separate place to avoid accidentally dispensing one of these in place of U-100. For more tips on how to properly store medications in the refrigerator, check out our tech tutorial, *Keep it Cool: Storing Meds in the Fridge or Freezer*.

When you remove the insulin from the fridge for Eileen's Rx, you take care not to confuse Humulin R *with* Humulin N *(an intermediate-acting insulin),* Humalog *(a rapid-acting insulin), or a* Humulin *70/30 or* Humalog *50/50 or 75/25 mixture. You also make sure you have U-100 and not the higher strength U-500.*

Don't cover up important information when labeling products. Don't cover the product name, storage information, expiration date, and NDC code (DIN in Canada) that may be printed on the box. If more than one vial or package of pens is needed to fill a prescription, print duplicate labels.

Use auxiliary labels to let patients know how long their medication is good. Injectable GLP-1 agonists and insulin are only good for a specific time period once in use. This beyond-use date is much shorter than the expiration date printed on the package. An auxiliary label with a "Use by" date is helpful for the patient, as well as a "Refrigerate" label to remind patients to keep the med in the fridge until they start using it. Information on beyond-use dates may be found on product packaging or product inserts.

Note that most insulins and other injectable meds that come in pens should not be placed back in the refrigerator once in use. At this point, they should usually be stored at room temperature. Storing them in the fridge can cause some pens to malfunction and leak.

Although Humulin R *U-100 requires refrigeration in the pharmacy, it can be kept at room temperature for up to 31 days once in use. You place an auxiliary label indicating this on Eileen's prescription.*

Label insulin pens for individual patients in the hospital setting. Keep in mind the mantra "one pen, one patient" when dispensing insulin pens in the hospital. Make sure a patient-specific label is attached to the pen itself and not just to the cap or the bag it is delivered in to help prevent mix-ups between patients. Even if the needle on a pen is changed, there is still a risk for cross contamination between patients. Nurses should never use one patient's pen to administer insulin to another patient.

Store filled Rxs in the fridge. Workflow for storage and retrieval of refrigerated Rxs varies among pharmacies. Many pharmacies place an Rx label receipt stapled to a bag in an alphabetized bin near the cash register but store the refrigerated medication in a "patient pickup" bin in the refrigerator. Make sure to use a "Refrigerate" sticker or another reminder on the Rx label receipt and bag with this method, to ensure medication is retrieved from the refrigerator when the patient pays for the Rx. Other pharmacies may have a

separate storage area in the refrigerator for labeled and bagged prescriptions ready to be picked up. Follow your pharmacy's procedure to ensure proper storage.

Once the pharmacist has checked Eileen's prescription, you put the labeled insulin in a designated "patient pick up" section of the refrigerator. Then you place a "Refrigerate" sticker on the Rx label receipt and bag before putting it in the will-call section of the pharmacy.

What should be considered when dispensing insulin syringes and pen needles?

Most insulin syringes and pen needles can be purchased without a prescription; however, a prescription is required for third-party coverage. Depending on local laws or store policy, insulin syringes may require a prescription, or only be dispensed along with insulin. Enter the insulin prescription in the computer before prescriptions for syringes or other diabetes supplies. Some third-party payers reject coverage for diabetes supplies until the insulin prescription has been entered because they need to detect an "active" insulin prescription to justify the diabetes supplies.

Insulin syringes are marked in **units**, not mL like other syringes. Most insulin syringes are designed to be used with insulin vials containing U-100 insulin. Insulin syringes differ in the total amount of insulin they can hold (e.g., 100 units [1 mL], 50 units [0.5 mL], 30 units [0.3 mL]). They come with a needle attached. The needle "gauge" tells you how fine, or thin, the needle is. The larger the gauge, the thinner the needle. For example, 31-gauge needles are thinner than 28-gauge needles. Thinner needles may be more comfortable for the patient, but they also bend more easily. Needles also differ by length. Some common needle lengths are 1/2 inch (12.7 mm) and 5/16 inch (8 mm). Some patients prefer shorter needles for comfort. But shorter needles may not be long enough for overweight patients. Refer patients with injection pain to the pharmacist. They may need a shorter and/or thinner needle.

U-500 insulin vials must be used with U-500 syringes. These syringes help patients who use U-500 insulin avoid dangerous dosing errors that can happen if they draw up doses with syringes meant to measure U-100 insulin. U-500 syringes require a prescription and should only be used with U-500 insulin. Don't mix them up with U-100 syringes. U-500 syringes come in a green box with a green cap and say "U-500" in green on the barrel, to match the green cap and letters on the U-500 vial. As with U-500 insulin, store U-500 syringes apart from other stock, such as in a separate bin, or add an eye-catching label to the shelf tag.

Injectable pens require pen needles. When dispensing pens, choose the correct pen needle for the specific pen. Pen needles come in different sizes, similar to needles on insulin syringes. If you are unsure of which brand name or needle type a patient's pen requires, ask the pharmacist. You may also find this info in the "How Supplied" section of the prescribing information in the US, or the "Dosage Forms, Composition and Packaging" section of the product monograph in Canada. Process pens and pen needles as two separate prescriptions. Even though pen needles are OTC, most insurances cover them as long as the patient has a prescription for them. Patients should be discouraged from reusing their pen needles or leaving them on their pen. Reuse can increase the risk of injection pain and infection. Leaving them on can cause air bubbles, leaks, contamination, or clogging. Watch for patients who switch pen needle brands and let the pharmacist know. The way pen needles are used may differ between products.

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"Cheat Sheet" for Dispensing Insulin and Other Injectable Diabetes Meds

What are the different injectable diabetes meds available and how do they work?

Common types of injectable diabetes meds include various insulin products (*Lantus*, *Humalog*, *Novolin*, etc) and GLP-1 agonists (e.g., exenatide [*Byetta*], exenatide extended-release [*Bydureon BCise* (US)], liraglutide [*Victoza*], lixisenatide [*Adlyxin* (US), *Adlyxine* (Canada)], dulaglutide [*Trulicity*], semaglutide [*Ozempic*]). People with diabetes either produce very little or no insulin (type 1) or don't use available insulin properly (type 2). Insulin helps the body use glucose (sugar) for energy and prevents glucose buildup in the blood and organs. GLP-1 agonists increase the body's own natural secretion of insulin.

What should I be sure to do when dispensing injectable diabetes meds?

- Be alert for dangerous abbreviations on insulin Rxs; such as the use of "U" for units, which can be mistaken for the number "4" or a zero, resulting in an overdose.
- Choose the correct product when entering prescriptions and pulling meds from the fridge; there are many different kinds of insulins and other injectable diabetes meds available with similar names.
- Select the correct insulin concentration. Insulin can come in U-100, U-200, U-300, and U-500.
- Watch for duplicate therapy messages and ask the pharmacist to review them.
- Enter dosing instructions completely, and alert the pharmacist if instructions say to "use as directed;" this often needs to be clarified.
- Enter accurate quantities and days' supplies.
    - Quantities are typically calculated in mL for injectable diabetes meds, rather than the number of vials or packages.
    - When calculating insulin days' supply, divide the total number of units per vial, pen, or box by the total number of units the patient will inject daily.
- Get the pharmacist involved if patients cannot afford their medications or if you notice late refills.
- Don't cover important information when labeling packages (e.g., product name, storage info, expiration dates, or NDC/DIN codes).
- Print duplicate labels if dispensing more than one vial or package of pens.
- Apply a "Use by" auxiliary label so patients know how long their medication is good for while in use.
- Apply a "Refrigerate" auxiliary label to remind patients to keep the med in the fridge until they start using it.
- Follow your pharmacy's process for keeping the filled Rx stored in the fridge while waiting for it to be picked up by the patient.
- Ask patients if they have ever used the medication before, and get the pharmacist involved to counsel if they haven't, since administration of an injection can be tricky.

What should be considered when dispensing insulin syringes and pen needles?

- Enter prescriptions for the injectable med first, since some insurance companies won't cover syringes or pen needles until they see an "active" prescription for a med requiring these supplies.
- Dispense the correct needle gauge and length, and specific U-500 syringes to be used with U-500 insulin.
- Help discourage patients from reusing pen needles or leaving them on their pen.

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