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Guide to Therapeutic Interchange of Insulin Products for Safe and Effective Transitions in Diabetes Management

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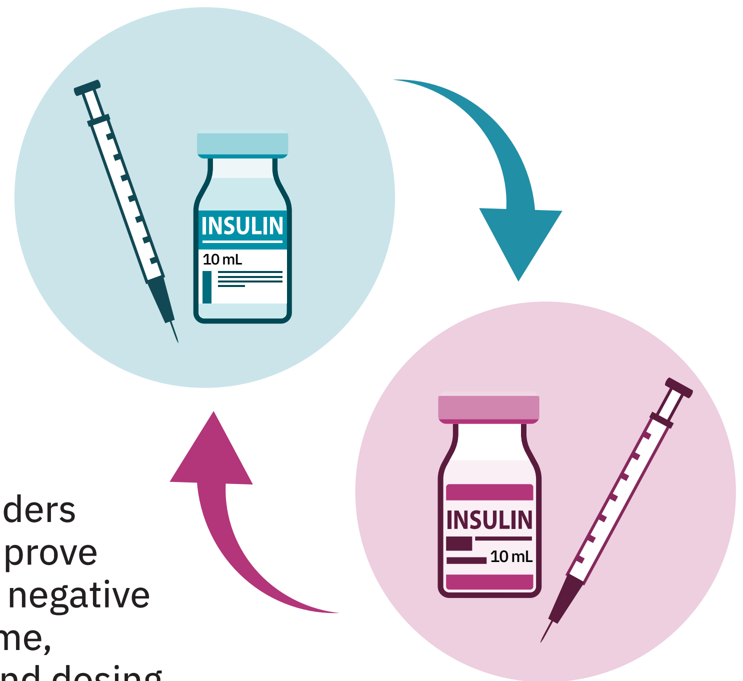


Making a prescription change from one insulin to another can improve diabetes management and adherence to care. In some cases, it may reduce costs for patients or be required by insurance.

Simple and clear strategies to help providers change between insulin products can improve patient comfort and decrease the risk of negative outcomes during this potentially risky time, such as hyperglycemia, hypoglycemia, and dosing mistakes.

Insulin formulations vary in pharmacokinetics, dosing intervals, and administration techniques, which may present barriers for some patients based on individual/personal factors. Transitions often require adjustments to both the dose and timing of administration, as well as changes to glucose testing and clinical recommendations for patients.

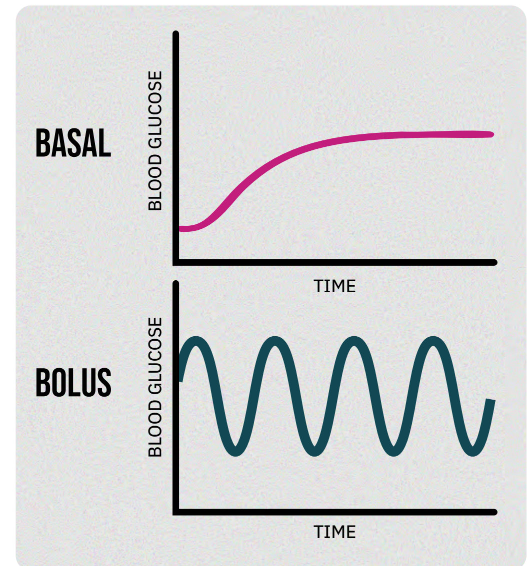
Types of Insulins and Considerations for Interchange[1-4]

Basal Insulins

Basal insulins serve as a base to control glucose levels overnight and between meals.

- **Long-acting insulins,** including glargine U-100 and detemir, provide a flatter, more predictable insulin profile compared to intermediate-acting options. Glargine U-100 and detemir typically last 20 to 24 hours and may require once- or twice-daily dosing, depending on patient needs. When interchanging between these agents, patients may need a dose reduction to prevent hypoglycemia, specifically when switching from twice-daily detemir to once-daily glargine U-100.
- **Ultra-long-acting insulins,** such as glargine U-300 and degludec, can provide extended coverage for up to 36 to 42 hours. These formulations offer a small benefit in the risk of nocturnal hypoglycemia and provide flexibility in the timing of daily doses. When transitioning between a long-acting agent and an ultra-long-acting agent, providers generally can switch at a 1:1 conversion; however, a higher dose of glargine U-300 may be needed to achieve the same effect compared to glargine U-100. In some instances, specifically pediatrics, a 20% reduction may be needed when switching between a long-acting insulin and degludec or from twice daily basal insulin to glargine U300 (see Table 1).[1-4]
- **Intermediate-acting insulin,** also known as neutral protamine hagedorn (NPH) insulin, has an onset of action of 1 to 2 hours, peaks between 4 and 12 hours, and lasts 12 to 18 hours. It is typically used for patients who require a low-cost option and can be used as part of a twice-daily regimen in place of other basal insulins. NPH insulin does have a pronounced peak, which increases the risk of hypoglycemia, especially in patients with unpredictable meal schedules. When converting from NPH insulin to long-acting insulin, it is recommended to start with 80% of the total daily NPH insulin dose as long-acting insulin to reduce the risk of hypoglycemia due to the loss of NPH insulin's peak.

Figure 1. Impact of Basal and Bolus Insulins on Blood Glucose Over Time



Bolus and Premix Insulins

Bolus and premix insulins are typically administered before meals to manage postprandial glucose spikes, acting quickly with a short duration of effect.

- **Rapid-acting insulins**, such as insulin lispro, aspart, and glulisine, have an onset of approximately 10 to 30 minutes, peak within 30 minutes to 3 hours, and last about 4 hours. These insulins are ideal for patients using basal/bolus regimens who require control of postprandial glucose levels. Ideally, these insulins should be taken 15 minutes before meals. While rapid-acting, ultra-rapid, and short-acting insulins can often be interchanged at a 1:1 dose ratio, the key difference is in the timing of administration. When switching between types of insulin, providers should maintain the same dose initially and adjust the timing as described below..
- **Ultra-rapid-acting insulins**, such as lispro-aabc or faster aspart, have a slightly faster onset and shorter duration than insulin lispro or aspart and manage postprandial glucose excursions better than rapid-acting insulins. Ultra-rapid insulins should be taken at the start of the meal and may offer an advantage for those with unpredictable intake or schedules.
- **Short-acting insulin**, also known as regular insulin, has a slower onset of 30 to 60 minutes, peaks in 2 to 4 hours, and lasts 5 to 8 hours. It is best suited for cost-sensitive patients as it is less expensive compared to analog rapid insulins. It requires earlier pre-meal dosing (best if given 30 minutes pre-meal) due to its longer onset of action, which may be risky for some patients, especially if meals are skipped or delayed.
- **Premixed insulins** (e.g., 70/30, 75/25, and 50/50 combinations) combine intermediate-acting and short- or rapid-acting insulins in fixed ratios to simplify basal and mealtime coverage (e.g., 70% NPH insulin with 30% short-acting insulin). Though these formulations may be convenient, they offer less dosing flexibility. Additionally, there are challenges in switching between premixed formulations, which stem from differences in insulin ratios, timing, and peak effects, which can result in altered glycemic control if not carefully managed.
- **U-500 regular insulin** is a concentrated formulation used in patients with severe insulin resistance and high total daily insulin requirements, typically above 200 units per day. Unlike U-100 regular insulin, U-500 regular insulin has both basal and bolus properties due to its prolonged action. This formulation reduces injection volume, which can improve absorption in patients who require high doses. However, its potency and duration require careful patient selection, training, and monitoring to prevent hypoglycemia. Transitioning to U-500 from a U-100 basal/bolus regimen involves calculating the total daily dose of U-100 insulin and administering 80% to 100% of that as U-500 divided into two or three daily injections. Due to its complexity, it is important to consider referral to endocrinology or clinical pharmacists for the management of patients who require U-500 regular insulin.

Table 1. Converting Between Insulins[1-4]

Conversion Type	Steps	Example (Patient TDD = 60 units)	Clinical Considerations
Rapid-acting insulin/ short-acting insulin	1. Calculate TDD. 2. Use 80% of TDD to initiate short-acting insulin 3. Split dose into 3 meals/day.	▪ 80% of 60 units of rapid-acting insulin = 48 units of short-acting insulin. ▪ Give 16 units pre-meal x 3 meals.	▪ Rapid-acting to rapid-acting insulin is interchanged in a 1:1 ratio. ▪ Rapid-acting to short-acting insulin is interchanged with a 20% dose reduction. ▪ There may be an additional adjustment to the dose based on meal carbohydrate content and/or pre-meal glucose, as instructed by the provider.
Long- or ultra-long-acting insulin	1. Calculate TDD. 2. Use 80% of TDD to initiate new long-acting insulin.	▪ 80% of 60 units = 48 units of new insulin.	▪ Consider interchange from long-acting insulin to degludec or twice daily long-acting insulin to glargine U-300 with a 20% dose reduction. ▪ If using >80 unit/day of glargine U-300 or degludec, consider interchange to glargine U-100 with a 20% dose reduction, split into 2 equal doses two times a day. ▪ Interchange once daily long-acting insulin to glargine U-300 at a 1:1 ratio. A dose increase may be needed.
Basal/bolus insulin to premixed insulin (e.g., 70/30)	1. Calculate TDD (basal + bolus). 2. Use 80% of TDD to initiate premixed insulin. 3. Split dose: 2/3 AM, 1/3 PM.	▪ 80% of 60 units = 48 units pre-mixed insulin. ▪ Give 32 units AM, 16 units PM of 70/30 insulin.	▪ Simplifies regimen (e.g., fewer injections). ▪ Good for patients with structured meals, lower health literacy, or cognitive impairment. ▪ Risk of hypoglycemia if meals are skipped or delayed.
Premixed insulin to basal/bolus insulin (e.g., 70/30 or 75/25 or 50/50)	1. Calculate the current TDD of premixed insulin. 2. Estimate basal dose = 50% of TDD. 3. Divide the remaining 50% into rapid-acting insulin before meals.	▪ 50% of 60 units = 30 units basal insulin (e.g., glargine once daily). ▪ 10 units rapid-acting insulin (e.g., lispro) premeal x 3 meals.	▪ Allows for flexible mealtime dosing. ▪ Ideal for motivated patients who can count carbs, have variable eating patterns, or require tighter glucose control. ▪ Requires frequent monitoring and patient engagement.

TDD = total daily dose

Clinical and Practical Considerations for Interchange[4-6]

Prior to implementing a change, clinicians must understand the pharmacokinetic and pharmacodynamic differences between insulins so they can choose appropriate dose conversions and advise patients on glucose testing intervals, as well as changes to meals or carbohydrate load.

When considering interchange and dose conversion, it is important to consider patient-specific needs. These include risk factors such as food insecurity, housing instability, and lack of access to refrigeration or storage. Additionally, it is essential to consider any visual, physical, or cognitive impairments the patient may have, as well as their occupation and the overall feasibility of administering insulin and conducting tests at different times throughout the day.

Insurance coverage and cost sharing are also important considerations. While a particular product may offer ease in administration, low-cost generic alternatives may provide better long-term management and affordability. Patient preferences and concerns regarding insulin devices, dosing, and testing intervals should also be considered.

Communicating insulin changes should be approached in a patient-centered manner, assessing health literacy and using multiple modalities to assist in the transmission of information in the patient's preferred language. Using simple written plans as well as the teach-back method, and providing education to family members, can improve adherence and reduce risks. Pharmacists can assist both clinicians and patients in planning for an insulin interchange, educating patients, and titrating the new insulin to appropriate dosages. Short-term follow-up with a member of the clinical team should be planned after initiating an insulin interchange.

Additional Cardi-OH Resources

- Addressing Common Barriers to Insulin Initiation and Use
  cardi-oh.org/resources/addressing-common-barriers-to-insulin-initiation-and-use
- Shared Decision Making and Diabetes Care
  cardi-oh.org/resources/shared-decision-making-and-diabetes-care
- Minimizing Hypoglycemia Risk to Improve Cardiovascular Health
  cardi-oh.org/resources/minimizing-hypoglycemia-risk-to-improve-cardiovascular-health
- Modified ADA Diabetes Algorithm: Pharmacologic Treatment
  cardi-oh.org/resources/modified-ada-diabetes-algorithm-pharmacologic-treatment
- Outpatient Diabetes Management for Primary Care Providers: Medications Intensification and Algorithm
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