The New Age of Insulin:
Exploring the Latest Trends in Insulin Therapy

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Disclosure

Conflicts of Interest and Financial Relationships Disclosures:

Susan Cornell, PharmD, CDE, FAPhA, FAADEx
• Advanced Practitioner Advisory Board and Speaker’s Bureau:
  • Sanofi, Novo Nordisk.

Objectives

At the conclusion of this knowledge-based educational activity, participants will be able to:

1. Discuss the current trends in the pathophysiology and progressive nature of diabetes.
2. Describe implications for the use of different insulin products in the diabetes management and care plan.
3. Compare the pharmacokinetic and pharmacodynamic parameters of insulin formulations and delivery methods.
Why is Glucose Control Important?

• 60% of people with type 2 diabetes have at least one complication because of diabetes

• Complications are often present at time of diagnosis
**β-cell Decline in Prediabetes and T2DM**

- Normal glucose tolerance
- Impaired glucose tolerance
- Type 2 diabetes

IR = insulin resistance


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**The Ominous Octet:**

Circa 2008

Hyperglycemia

- Brain
- Peripheral tissue (muscle)
- Liver
- GI tract (stomach/small intestine)
- Pancreas (β-cell)
- Pancreas (α-cell)
- Fat cells (adipose tissue)


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**Treatment Approach to T2DM**

- **Dietary changes**
  - Reduce consumption of calories
  - Reduce consumption of simple carbohydrates

- **Increase physical activity**

- **Medications**
  - Improve or replace insulin secretion
  - Reduce insulin resistance
  - Reduce glucagon secretion
  - Reduce hepatic glucose production
  - Increase urinary glucose excretion

Glucose-Lowering Comparison

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Used in Pre-Diabetes</th>
<th>Target Insulin Resistance</th>
<th>Target Glucose Reduction (FPG)</th>
<th>A1C Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>No</td>
<td>No</td>
<td>Both</td>
<td>1.5 - 2.0</td>
</tr>
<tr>
<td>Metformin</td>
<td>Yes</td>
<td>Maybe?</td>
<td>FPG</td>
<td>0.5 - 1.5</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>No</td>
<td>No</td>
<td>PPG</td>
<td>0.5 - 2.0</td>
</tr>
<tr>
<td>Ags</td>
<td>Yes</td>
<td>No</td>
<td>FPG</td>
<td>0.5 - 1.5</td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
<td>No</td>
<td>No</td>
<td>PPG</td>
<td>0.5 - 0.7</td>
</tr>
<tr>
<td>Wire and agonists</td>
<td>No</td>
<td>No</td>
<td>PPG</td>
<td>0.4</td>
</tr>
<tr>
<td>SGLT-2 inhibitors</td>
<td>No</td>
<td>Maybe?</td>
<td>FPG</td>
<td>0.7 - 2.0</td>
</tr>
<tr>
<td>SGLT-1 agonists</td>
<td>Yes</td>
<td>No</td>
<td>Short acting – PPG</td>
<td>0.8 - 1.5</td>
</tr>
<tr>
<td>Amylase analogs</td>
<td>No</td>
<td>No</td>
<td>PPG</td>
<td>0.4</td>
</tr>
<tr>
<td>Insulin</td>
<td>No</td>
<td>Yes (to a degree)</td>
<td>Regal – FPG</td>
<td>2 as much as needed</td>
</tr>
</tbody>
</table>

AGIs = alpha-glucosidase inhibitors; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; FPG = fasting plasma glucose; PPG = postprandial glucose; SGLT-2 = sodium-glucose cotransporter-2.

Insulin “fixes 5 defects”

Hyperglycemia

- Pancreas β-cell
- Pancreas α-cell
- Liver
- GI tract (stomach/small intestine)
- Fat cells (adipose tissue)
- Brain
- Kidney

GLP-1RA “fixes” 6 defects

Hyperglycemia

- Pancreas β-cell
- Pancreas α-cell
- Liver
- GI tract (stomach/small intestine)
- Fat cells (adipose tissue)
- Brain
- Kidney

Insulin Resistance

- Major defect in individuals with type 2 diabetes
- Reduced biological response to insulin
- Closely associated with obesity
- Associated with cardiovascular risk
- Type 1 diabetes patients can be insulin resistant as well
Insulin Therapy for Insulin Resistance

- Insulin, insulin, and yet more insulin!
- Causes weight gain and fluid retention
- Increased risk of hypoglycemia
- Expensive at high volumes (especially the pens)
- Multiple injections per day often needed
- Pumps not practical with high-volume insulin usage

High Doses of Insulin

- Concerns:
  - Hypoglycemia
  - Medication errors in dosing
  - Absorption issues
  - Patient insulin variability (pharmacokinetics and pharmacodynamics)
- Problems:
  - Over-basalization
  - Failure to treat the physiological defects
    - Insulin resistance
    - Decrease satiety

Thinking like a Pancreas
The Basal-Bolus Concept

• "Components" of Insulin Replacement
  • Basal insulin: 50% of daily needs
    • Controls nighttime and between-meal glucose at a nearly constant level
  • Bolus insulin: 50% of daily needs
    • Controls mealtime glucose
    • 10% to 20% of total daily insulin requirement at each meal
  • Correction dose (sensitivity factor)
    • Additional insulin needed (usually pre-meal)
      • Often to correct for fasting hyperglycemia

Pharmacokinetic Profile of Currently Available Insulins

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset (hr)</th>
<th>Peak (hr)</th>
<th>Duration (hr)</th>
<th>Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lispro U100 &amp; U200</td>
<td>within 15 min</td>
<td>0.5-1.5</td>
<td>3-5</td>
<td>Clear</td>
</tr>
<tr>
<td>Aspart U100</td>
<td>within 15 min</td>
<td>1-2</td>
<td>3-5</td>
<td>Clear</td>
</tr>
<tr>
<td>Glulisine</td>
<td>0.25-0.5</td>
<td>0.5-1</td>
<td>4</td>
<td>Clear</td>
</tr>
<tr>
<td>Regular U100</td>
<td>0.5-1</td>
<td>2-4</td>
<td>5-8</td>
<td>Clear</td>
</tr>
<tr>
<td>Aspart inhalable</td>
<td>within 5 min</td>
<td>20-40 minutes</td>
<td>3</td>
<td>Powder</td>
</tr>
<tr>
<td>Regular U-500</td>
<td>30 min</td>
<td>4</td>
<td>6-24 hr</td>
<td>Clear</td>
</tr>
<tr>
<td>NPH</td>
<td>2-4</td>
<td>4-24</td>
<td>Clear</td>
<td></td>
</tr>
<tr>
<td>Insulin Detemir</td>
<td>3-4</td>
<td>6-8</td>
<td>(though relatively flat) up to 20-24</td>
<td>Clear</td>
</tr>
<tr>
<td>Insulin Glargine U100</td>
<td>1.5 flat</td>
<td>24</td>
<td>Clear</td>
<td></td>
</tr>
<tr>
<td>Insulin Degludec U300</td>
<td>1.5 flat</td>
<td>26</td>
<td>Clear</td>
<td></td>
</tr>
<tr>
<td>Lispro Mix 50/50</td>
<td>0.25-0.5</td>
<td>0.5-3</td>
<td>14-24</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Lispro Mix 75/25</td>
<td>0.25-0.5</td>
<td>0.5-2.5</td>
<td>14-24</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Aspart Mix 70/30</td>
<td>0.1-0.2</td>
<td>1-4</td>
<td>18-24</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Degludec/aspart Mix 70/30</td>
<td>0.23 – 1.2</td>
<td>2.3</td>
<td>&gt;24</td>
<td>Cloudy</td>
</tr>
</tbody>
</table>

Note: Patient-specific onset, peak, duration may vary from times listed in table. Peak and duration are often very dose-dependent with shorter duration of actions with smaller doses and vice versa.
Insulin Strategies in T2DM

- Metformin + basal insulin
  - Fasting coverage
  - Hypoglycemic risk
  - GLargine, detemir, degludec – lower risk
  - Human insulin isophane (NPH) – higher risk
  - Weight gain/neutral

- Basal insulin + bolus insulin (with or without metformin)
  - Fasting and postprandial coverage
  - High hypoglycemic risk (mostly from bolus)
  - Regular, aspart, lispro, glulisine
  - Weight gain

- Basal insulin + GLP-1 agonist (with or without metformin)
  - Fasting and postprandial coverage
  - Low hypoglycemic risk (glargine, detemir, degludec)
  - Weight neutral/loss

**Approach To Starting and Adjusting Insulin in T2D**

### Initiate Basal Insulin

Usually with metformin +/- other noninsulin agent

- Start: 10 units/day or 0.1-0.2 units/kg/day
- Adjust: 10-15% or 2-4 units once/twice weekly to reach FBG target
- For hypo: identify/fix cause; can decrease dose by 10-20% or 4 units.

Add 1 rapid-acting insulin injection before largest meal

- Start: 4 units, 0.01 units/kg, or 10% basal dose
- Adjust: if A1c < 8%, can ↓ basal by same amount
- For hypo: identify/fix cause; can ↓ dose by 2-4 units or 10-20%

Change to premixed insulin twice daily (before breakfast and supper)

- Start: divide current basal dose into 2/3 AM & 1/3 PM or 1/2 AM & 1/2 PM
- Adjust: ↑ dose by 1-2 units or 10-15% once/twice weekly until reach SMBG target
- For hypo: identify/fix cause; can ↓ dose by 2-4 units or 10-20%

### Add GLP-1RA

- If not tolerated or A1c target not reached, change to 2 injections insulin regimen.

### If A1c not controlled - Consider

- Add ≥ 2 rapid-acting insulin injections before meals (basal-bolus)

### Concentrated & “Low Volume” Insulin
The Evolution of Insulin

Bovine insulin (1922)
Lente & ultralente (1951)
Lispro (1996)
Glulisine (2004)
NPH (1950)
rDNA (1982)
Aspart, glargine (2000)
Detemir (2005)

Polling Question #1

Which insulin is not a true basal insulin?

1. Insulin detemir U-100
2. Insulin glargine U-100
3. NPH U-100
4. Regular insulin U-500

“Concentrated and/or Low Volume” Insulins

• Basal
  • Insulin degludec (U-100, U-200)
  • Insulin glargine (U-300)

• Bolus
  • Insulin lispro (U-200)

• Bolus that thinks it’s a basal
  • Insulin human regular (U-500 pen)
Pharmacokinetic Profile of Currently Available “Basal” Insulins

Plasma Insulin Levels

“Basal” Insulin Comparison

<table>
<thead>
<tr>
<th>Insulin - Basal</th>
<th>Onset (hr)</th>
<th>Peak (hr)</th>
<th>Duration (hr)</th>
<th>Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular U-500</td>
<td>30 min</td>
<td>1-4</td>
<td>up to 24 hr</td>
<td>Clear</td>
</tr>
<tr>
<td>mix - Basal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>1-2</td>
<td>4-10</td>
<td>(though relatively flat) up to 16-20</td>
<td>Clear</td>
</tr>
<tr>
<td>Insulin Detemir</td>
<td>3-4</td>
<td>6-8</td>
<td>(though relatively flat) up to 16-20</td>
<td>Clear</td>
</tr>
<tr>
<td>Insulin Glargine U100</td>
<td>1.5 flat</td>
<td>20-24</td>
<td>Clear</td>
<td></td>
</tr>
<tr>
<td>Insulin Glargine U300</td>
<td>1.5 flat</td>
<td>20-24</td>
<td>Clear</td>
<td></td>
</tr>
<tr>
<td>Insulin Degludec U100 &amp; U200</td>
<td>0.5 – 1 flat</td>
<td>&gt;30</td>
<td>Clear</td>
<td></td>
</tr>
</tbody>
</table>

Note: Patient specific onset, peak, duration may vary from times listed in table. Peak and duration are often very dose dependent with shorter duration of actions with smaller doses and vice versa.

Candidates for Concentrated/ Low Volume Insulin

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rationale</th>
<th>Product to Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocturnal hypoglycemia</td>
<td>Needs peak-less (flat) basal insulin profile</td>
<td>Degludec U-100, U-200 Glargine U-300</td>
</tr>
<tr>
<td>Insulin resistance (severe with high insulin requirements; e.g. &gt;200 units TDD)</td>
<td>Temporary &quot;flat&quot; for insulin resistance</td>
<td>Regular U-500</td>
</tr>
<tr>
<td>High basal insulin needs (&gt; 80 units per injection)</td>
<td>High dose requires 2+ basal injections/day</td>
<td>Degludec U-200 Glargine U-300</td>
</tr>
<tr>
<td>High bolus insulin needs (&gt; 20 units per day)</td>
<td>Reduces the number of pen changes per month</td>
<td>Lispro U-200</td>
</tr>
</tbody>
</table>

TDD = total daily dose

Adapted from Smith J, Rx Consultant 2/16
Safety Concerns with “Newer” Insulins

- Familiarity with new products
- Understanding of pharmacokinetic and pharmacodynamic nuances
- Knowledge on dose adjustments and conversions
- “Lack” of interchangeability

Rationale for Concentrated Insulin Use

- When daily insulin requirements are in excess of 200 units/day, the volume of U-100 injected insulin may become an issue
- Physically too large for a single subcutaneous administration
- Multiple injections are required to deliver a single dose
- Increased injections may lead to compliance issues and poor glycemic control
- Discomfort
- Unpredictable absorption (rate-limiting step in insulin activity)

Insulin Human Regular U-500

- Insulin characteristics
  - Five times as concentrated as U-100 insulin
  - Decreased injection volume (vs. U-100)
  - Solely for severely insulin-resistant patients
  - Total daily dose exceeding 200 units/day
- Pharmacokinetics/pharmacodynamics
  - Mean onset of action 15 minutes
  - Mean duration of action 21 hours (range 13-24 hours)
  - Each individual patient varies in their response depending on:
    - Site of injection
    - Exercise patterns
    - Other variables
- Clinical pearls
  - Time to onset: similar to U-100 regular insulin
  - Duration of effect: similar to NPH insulin
  - Consider it a “mixed short/intermediate” type insulin
**PK and PD profiles for U-500 vs U-100 Human Insulin**

- Human Regular U-500 Insulin
  - 50-Unit Dose
  - 100-Unit Dose

- Human Regular U-100 Insulin
  - 50-Unit Dose
  - 100-Unit Dose

**Human Regular U-500**

- Now available in an insulin pen:
  - 1500 units/pen
  - Maximum 300 units/injection
  - No “dose conversions” needed
  - Dials in increments of 5 units

- Still available in vial form (20 mL)
  - New syringe dedicated for U-500 approved July 2016
  - Use with U-500 insulin only

**Regular U-100 to U-500 Dosing**

- Converting from any U-100 insulin to U-500 human regular insulin:
  - A1C ≤ 8%: empiric reductions in total daily dose (TDD) of 10-20% have been recommended
  - A1C ≥ 10%: empiric increases in TDD of 10-20% can be considered

- Distributing the Total Daily Dose (TDD):
  - Recommendations vary from 2-3 doses per day
    - Algorithm available
  - Administer 30 minutes before meals due to the relatively short onset of action
Regular U-500 to U-100 Dosing

• No recommendations are currently available on how to convert from Regular U-500 to basal-bolus U100 dosing
  • Can differ based on delivery device used
    • Pen vs. U-100 insulin syringe or TB syringe
  • Clinical expertise warranted

Concentrated Glargine (U-300)

• Smaller depot surface area
• Reduced rate of absorption
• Relatively flat and prolonged PK/PD profiles
  • Half-life ~23 hours
  • Steady state in 4 days
  • Duration of action ≤ 36 hours
• Available only in a pen
  • 450 units/pen (1.5 mL)
  • Maximum 80 units/injection
  • 3 pens per box

PK and PD of U-300 Insulin Gliargine
vs U-100 Insulin Gliargine

U-300 glargine displays a more even and prolonged PK/PD profile compared with U-100 glargine, offering blood glucose control beyond 24 hours

LLOQ = lower limit of quantification; GIR = glucose infusion rate.

US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/drugsatfda/
Glargine U-100 to U-300 Dosing

• Changing from once daily long-acting:
  • Initial dose can be same U-100 insulin glargine
    • Expect that a higher daily dose of U-300 insulin glargine will be needed to maintain the same level of glycemic control
  • Changing from BID NPH insulin:
    • Initial dose is 80% of the total daily NPH dosage

Glargine U-300 to U-100 Dosing

• When converting from U-300 to U-100
  • A 20% reduction is recommended to minimize hypoglycemic risk with the U-100 insulin product

Insulin Degludec (U-100 & U-200)

• “Ultra long acting” insulin
• Relatively flat and prolonged PK/PD profiles
  – Duration of action ~42 hours (at least)
  – Half-life ~25 hours
  – Steady state in 3 to 4 days
  – Less patient insulin variability
• Flexible dosing schedule
• Available only in a pen
  – U-200: 600 units/pen (3 mL), max 160 units/injection
  • Dial in increments of 2 units!
  – U-100: 300 units/pen (3 mL), max 80 units/injection

US Food and Drug Administration. www.accessdata.fda.gov/scripts/cder/drugsatfda/
Basal Insulin Degludec

Flat, stable profile of both 100 unit/mL and 200 unit/mL formulations

Mean 24-Hour GIR Profile of the Two Insulin Degludec Formulations at Steady State

GIR = glucose infusion rate.


Degludec U-200 Dosing

• Changing from once daily long-acting:
  • The dose is 1 to 1
    • Initial degludec dose can be same as the current U-100 insulin the patient is using
      • Glargine/detemir/degludec
  • Changing from BID NPH insulin:
    • The dose is 1 to 1:
      • Initial degludec (once daily) dose is same as the total daily NPH dosage

Degludec U-200 to U-100 Dosing

• When converting from U-200 to U-100
  • The dose is a 1 to 1 conversion
    • No change in the initial dose is necessary
Concentrated Basal Insulin Dosing
Conversion Comparison

<table>
<thead>
<tr>
<th>Glargine U-300</th>
<th>Degludec U-200</th>
<th>Humalog U-100</th>
</tr>
</thead>
<tbody>
<tr>
<td>True basal</td>
<td>True basal</td>
<td>Mixed basal/bolus</td>
</tr>
<tr>
<td>1 daily</td>
<td>1 daily</td>
<td>Multiple daily</td>
</tr>
<tr>
<td>injection</td>
<td>injection</td>
<td>injections of</td>
</tr>
<tr>
<td>2 daily</td>
<td>injection</td>
<td>basal-bolus</td>
</tr>
<tr>
<td>injection</td>
<td>injection</td>
<td>Total daily</td>
</tr>
<tr>
<td>80% of</td>
<td>80% of</td>
<td>dose divided</td>
</tr>
<tr>
<td>total daily</td>
<td>total daily</td>
<td>into 2 or 3</td>
</tr>
<tr>
<td>basal dose</td>
<td>basal dose</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>Maximum</td>
<td>Maximum</td>
</tr>
<tr>
<td>single-dose</td>
<td>single-dose</td>
<td>single-dose</td>
</tr>
<tr>
<td>injection</td>
<td>injection</td>
<td>injection</td>
</tr>
<tr>
<td>80 units</td>
<td>160 units</td>
<td>300 units</td>
</tr>
<tr>
<td>Dialed in 1-unit increments</td>
<td>Dialed in 2-unit increments</td>
<td>Dialed in 5-unit increments</td>
</tr>
<tr>
<td>450 units of insulin per pen</td>
<td>600 units of insulin per pen</td>
<td>1500 units of insulin per pen</td>
</tr>
<tr>
<td>Expect higher daily dose of glargine U-200 to maintain glycemic control</td>
<td>Monitor for hypoglycemia; administer with meals</td>
<td></td>
</tr>
</tbody>
</table>

Tresiba package insert, Toujeo package insert, Insulin regular U-500 package insert

Insulin lispro (U-200)

• No difference in kinetics from U-100 lispro
  • Half-life: 1 hour
  • Duration of action: ~3 hours
• Available only in a pen
  • 600 units/pen (3 mL)
  • Maximum 60 units/injection
  • 2 pens per box
• Addresses the problem of frequent pen turnover

Humalog U-200 Package insert

Patient Education

• Equipment and supplies needed to effectively manage insulin therapy at home:
  • Insulin
  • Syringes or pen needles
  • Blood glucose meter and strips
  • Lancets and lancing device
  • Glucagon emergency kit
  • Contact information of diabetes care provider(s)
What Patients Need to Know About Insulin AND Delivery Devices

- Storage and expiration
- When it should be refrigerated
- When it can be at room temperature
- When medication expires after first use
- How to prepare product for first use
- How to properly use the device
- How to dispose of the device

Product Expiration

<table>
<thead>
<tr>
<th>Products/Device</th>
<th>Refrigerated</th>
<th>Unrefrigerated</th>
<th>Once used (opened)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vials: Insulin lispro U-100, U-200, insulin aspart, insulin glulisine, insulin glargine</td>
<td>Expiration Date</td>
<td>28 days</td>
<td>28 days</td>
</tr>
<tr>
<td>Vial: Insulin human N</td>
<td>Expiration Date</td>
<td>31 days</td>
<td>31 days</td>
</tr>
<tr>
<td>Pens: Insulin lispro U-100, U-200, insulin aspart, insulin glulisine U-100, insulin glargine U-100</td>
<td>Expiration Date</td>
<td>28 days</td>
<td>Do not refrigerate (open, glargine, glulisine) 28 days</td>
</tr>
<tr>
<td>Vial &amp; pens: Insulin detemir</td>
<td>Expiration Date</td>
<td>42 days</td>
<td>42 days (pens should not be refrigerated)</td>
</tr>
<tr>
<td>Pens: Insulin degludec U-100, U-200</td>
<td>Expiration Date</td>
<td>56 days</td>
<td>56 days (pens should not be refrigerated)</td>
</tr>
<tr>
<td>Inhalers: Insulin human</td>
<td>—</td>
<td>Expiration Date</td>
<td>15 days for device</td>
</tr>
</tbody>
</table>


Patient Cases
JL is a 67-year-old retiree who was diagnosed with T2D 6 years ago. Three months ago, he had an A1C of 8.4%, with no changes to his diabetes therapy at that time. He presents today for a follow up visit.

Current Medications
- Metformin 1000 mg PO BID
- Lisinopril 20 mg PO daily
- Atorvastatin 40 mg PO daily
- Omeprazole 20mg PO daily

SMBG:
- Usually checks every morning
- FPG range 130-189 mg/dL

• Social History
- Nonsmoking with no illicit drug use
- Occasional alcohol use (~3 drinks per week)
- Self-reported inconsistent eating schedule
  - Usually eats breakfast and dinner
  - Often skips lunch
  - Largest meal of day is dinner
- Married with 2 grown children
- His wife does the cooking

Physical Exam, Vitals & Labs
- A1C – 8.4%
- Weight – 194 lbs.
- BMI – 28 kg/m²
- BP – 132/80 mmHg
- HR – 70 bpm
- Lipid panel – WNL
- SCr – 1.0 mg/dL
- eGFR – >100 mL/min/1.73 m²

Polling Question
JL is agreeable to starting basal insulin, as long as he only needs to “take 1 shot per day.” How many units of basal insulin would you start JL on?

1. 5 units
2. 10 units
3. 20 units
4. 30 units
Case #1: JL
Polling question

JL calls you 5 days later to ask if he should increase his insulin dose.

Degludec U-100: 10 units every morning

SMBG: He has been checking every morning

<table>
<thead>
<tr>
<th>Day</th>
<th>Value (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday</td>
<td>189</td>
</tr>
<tr>
<td>Tuesday</td>
<td>197</td>
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<tr>
<td>Wednesday</td>
<td>179</td>
</tr>
<tr>
<td>Thursday</td>
<td>172</td>
</tr>
<tr>
<td>Friday</td>
<td>170</td>
</tr>
</tbody>
</table>

What do you recommend?
1. Increase to 12 units every morning and call back in 1 week
2. Increase to 14 units every morning and call back in 1 week
3. Increase to 12 units every morning and call back in 1 month
4. No changes at this time, have JL call back in 1 month

Case #2: 59 year old with T2D

SR is a 59-year-old who was diagnosed with T2D 8 years ago. He presents to the ED today c/o a painful ulcer on his left foot.

Current Medications
- Insulin glargine U-300 (pen) 75 units once daily
- Insulin aspart (pen) 20-30 units per meal + Correction
- Lisinopril 10 mg daily
- Atorvastatin 10 mg daily

Patient reports:
- Checks BG every morning and usually checks before each meal
  - FPG range 110-170 mg/dL
  - Pre-meal range 100-240 mg/dL

Social History
- Non-smoking with no illicit drug use
- Occasional alcohol use (~2 drinks per week)
- Self-reported inconsistent eating schedule:
  - Usually skips breakfast
  - Lunch is the largest meal of the day (often fast food or restaurant)
  - Dinner is usually late (after 8pm)
- Divorced, lives alone. Has a niece that lives 1 mile away who checks in on him occasionally

Vitals & Labs at ED
- POC BG = 240 mg/dL
- Waiting A1C results
- Height = 5 feet 6 inches
- Weight = 280 lbs
- Body Mass Index (BMI) = 45 kg/m²
- Blood Pressure = 114/66 mm Hg
- Heart rate = 94 bpm

Previous labs (3 months ago)
- A1C = 8.4%
- Lipid panel = WNL
- SC = 1.0 mg/dL
- eGFR = >100 mL/min/1.73 m²
Case #1: SR
Polling Question
The hospital only has glargine U-100 on formulary. What dose would be appropriate to start SR on?

1. 45 units once daily
2. 60 units once daily
3. 75 units once daily
4. 90 units once daily

Clinical Pearls/Take-Aways
• Watch for over-basalization
  • High basal dose with no or little bolus insulin
• Continually increasing insulin doses does not reduce insulin resistance
• New, long-acting basal insulin analogs may provide benefit compared to "older" basal insulins
  • Flatter time-action profiles with less variability
  • Less hypoglycemia, particularly nocturnal hypoglycemia
• Patients need to know how to properly use insulin devices
  • Patient technique should be review at initiation and periodically thereafter