Insulin Bootcamp: Dosing, Monitoring, Titrating, and Care Coordination

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Disclosures

• **Stuart Haines** – declares that he has no financial or other conflicts-of-interest related to the content of this presentation.

• **Joshua Neumiller** – declares that he has no financial or other conflicts-of-interest related to the content of this presentation.
CPE Information

- Target Audience: Pharmacists
- ACPE#: 0202-0000-19-056-L01-P
- Activity Type: Application-based
Supporter

This activity is supported by independent educational grants from Novo Nordisk.
Pharmacist Learning Objectives

At the completion of this application-based activity, participants will be able to:

• Compare the characteristics of new insulin products available in the market.
• Demonstrate how to safely titrate and switch insulin products.
• Describe strategies to minimize insulin-induced hypoglycemia, including patient education tools.
• Discuss management strategies that ensure the coordination of diabetes care among patients switching between healthcare settings.
Newer Insulin Treatment Options
Which of the following statements is **TRUE** about the newer insulin products approved by the FDA in the past 5 years?

A. All of the newer products are available in pre-filled pen devices.

B. None of the newer products are available in pre-mixed combinations with other insulins.

C. All of the newer products are considered “ultra-long acting” insulins and can be dosed once daily.

D. All of the newer products improve glycemic control more effectively than “traditional” insulin products.
## Available Insulin Products

<table>
<thead>
<tr>
<th>Type</th>
<th>Basal Insulins</th>
<th>Prandial Insulins</th>
<th>Premixed Insulins</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human</strong></td>
<td>• NPH U100</td>
<td>• Regular human insulin U100</td>
<td>• Regular human insulin 70/30</td>
</tr>
<tr>
<td></td>
<td>• Regular human insulin U500 (pen)</td>
<td>• Regular human insulin U500 (pen)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Insulin inhalation powder</td>
<td></td>
</tr>
<tr>
<td><strong>Analog</strong></td>
<td>• Detemir U100</td>
<td>• Aspart U100</td>
<td>• Aspart protamine + aspart (70/30)</td>
</tr>
<tr>
<td></td>
<td>• Glargine U100</td>
<td>• Aspart U100 (Fiasp®)</td>
<td>• Lispro protamine + lispro 75/25</td>
</tr>
<tr>
<td></td>
<td>• Glargine equiv U100</td>
<td>• Lispro U100</td>
<td>• Lispro protamine + lispro 50/50</td>
</tr>
<tr>
<td></td>
<td>• Glargine U300</td>
<td>• Lispro U200</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Degludec U100</td>
<td>• Glulisine U100</td>
<td>• Insulin degludec + insulin aspart (70/30)</td>
</tr>
<tr>
<td></td>
<td>• Degludec U200</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

See Drugs@FDA: FDA Approved Drug Products; www.accessdata.fda.gov/Scripts/cder/drugsatfda/; Accessed October 1, 2018.
## Available Delivery Methods for Newer Insulins

<table>
<thead>
<tr>
<th>Rapid Acting Insulin Analogs</th>
<th>Vials</th>
<th>Prefilled Pens</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-100 Aspart (Fiasp®)</td>
<td>✔</td>
<td>✔ FlexTouch® Pen</td>
</tr>
<tr>
<td>U-200 Lispro</td>
<td>✔</td>
<td>✔ KwikPen®</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long-Acting Insulin Analogs</th>
<th>Vials</th>
<th>Prefilled Pens</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-100 Detemir</td>
<td>✔</td>
<td>✔ FlexTouch® Pen</td>
</tr>
<tr>
<td>U-100 Glargine</td>
<td>✔</td>
<td>✔ SoloStar® Pen</td>
</tr>
<tr>
<td>U-100 Glargine Equivalent</td>
<td>✗</td>
<td>✔ KwikPen®</td>
</tr>
<tr>
<td>U-100 Degludec</td>
<td>✗</td>
<td>✔ FlexTouch® Pen</td>
</tr>
<tr>
<td>U-200 Degludec</td>
<td>✗</td>
<td>✔ FlexTouch® Pen</td>
</tr>
</tbody>
</table>
| U-300 Glargine                        | ✗     | ✔ SoloStar® Pen  
                                       |       | ✔ Max SoloStar® Pen |

See Drugs@FDA: FDA Approved Drug Products; www.accessdata.fda.gov/Scripts/cder/drugsatfda/; Accessed November 1, 2018.
Pharmacokinetic Profile of Currently Available Insulins

Flood TM. J Fam Pract. 2007; 56(suppl 1):S1-S12.
## Insulin Glargine U-300: Clinical Evidence

<table>
<thead>
<tr>
<th>Outcome</th>
<th>EDITION-1 T2D, A1C 7%-10%, ≥42 units/day of glargine or NPH + mealtime insulin ± metformin</th>
<th>EDITION-2 T2D, A1C 7%-10%, ≥42 units/day of glargine or NPH + OADs</th>
<th>EDITION-3 T2D, A1C 7%-11%, Insulin naive using OADs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in A1C from baseline (%)</td>
<td>U-300  -0.83</td>
<td>U-300 -0.57</td>
<td>U-300 -1.42</td>
</tr>
<tr>
<td></td>
<td>U-100 -0.83</td>
<td>U-100 -0.56</td>
<td>U-100 -1.46</td>
</tr>
<tr>
<td>Change in weight from baseline (kg)</td>
<td>U-300 +0.9</td>
<td>U-300 +0.08*</td>
<td>U-300 +0.49</td>
</tr>
<tr>
<td></td>
<td>U-100 +0.9</td>
<td>U-100 +0.66</td>
<td>U-100 +0.71</td>
</tr>
<tr>
<td>Daily basal insulin dose at end of study (units)</td>
<td>U-300 103*</td>
<td>U-300 91*</td>
<td>U-300 59.4*</td>
</tr>
<tr>
<td></td>
<td>U-100 94</td>
<td>U-100 82</td>
<td>U-100 52</td>
</tr>
<tr>
<td>Confirmed or severe nocturnal hypoglycemia events (%)</td>
<td>U-300 36*</td>
<td>U-300 30.5*</td>
<td>U-300 18*</td>
</tr>
<tr>
<td></td>
<td>U-100 46</td>
<td>U-100 41.6</td>
<td>U-100 24</td>
</tr>
</tbody>
</table>

Noninferiority criteria met.  
*P<0.05

Bolli GB. Diabetes Obes Metab. 2015;17:386-94.
## Insulin Degludec: Clinical Evidence

<table>
<thead>
<tr>
<th>Clinical Trial (Duration)</th>
<th>Background Therapy</th>
<th>Comparator Arms</th>
<th>Change in A1C (%)</th>
<th>End of Trial Insulin Dose (units/kg)</th>
<th>Hypoglycemia (episodes per pt-year)</th>
<th>Confirmed or Severe Nocturnal Hypoglycemia (per pt-year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinman (52 weeks)</td>
<td>Metformin (insulin naive)</td>
<td>IDeg U-100</td>
<td>-1.06</td>
<td>0.59</td>
<td>1.52</td>
<td>0.25*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glargine U-100</td>
<td>-1.19</td>
<td>0.60</td>
<td>1.85</td>
<td>0.39</td>
</tr>
<tr>
<td>Garber (52 weeks)</td>
<td>Insulin ± OADs</td>
<td>IDeg U-100</td>
<td>-1.1</td>
<td>0.75*</td>
<td>11.1*</td>
<td>1.4*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glargine U-100</td>
<td>-1.2</td>
<td>0.69</td>
<td>13.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Gough (26 weeks)</td>
<td>Metformin ± DPP-4 inhibitor (insulin naive)</td>
<td>IDeg U-200</td>
<td>-1.22</td>
<td>0.53*</td>
<td>1.22</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glargine U-100</td>
<td>-1.42</td>
<td>0.60</td>
<td>1.42</td>
<td>0.28</td>
</tr>
</tbody>
</table>


Noninferiority criteria met.  
*P<0.05.
New Prandial Insulin – Ultra-Rapid Acting

• Insulin aspart (Fiasp®)
• Contains excipients nicotinamide and arginine
• Faster onset of exposure vs insulin aspart (Novolog®) (20.7 vs 31.6 min to reach 50% of max concentration)
• In patients with type 1 diabetes:
  • 50% greater glucose-lowering effect in the first 30 min after dose vs insulin aspart
  • Significantly greater mean change in plasma glucose 2 hrs after a standard meal vs current aspart (72.36 vs 54.54 mg/dL)
• Clinical outcomes – similar reductions in A1c and rates of hypoglycemia

New Prandial Insulin – Inhaled Insulin Powder

- Single-use cartridges of 4, 8, and 12 units
- Shorter time to peak (12-15 min) vs. subcutaneous insulins
- Shorter duration of action (2.5-3 hours) vs. subcutaneous insulins
- The inhaler may be used for 15 days
- The insulin powder cartridges must be stored in the refrigerator and used within 3 to 10 days after they are removed from the refrigerator
- Do not use in patients with chronic lung disease or active lung cancer
- Not recommended for active or recent smokers

See Drugs@FDA: FDA Approved Drug Products; www.accessdata.fda.gov/Scripts/cder/drugsatfda/; October 1, 2018
When Even More Insulin is Needed ...

• U-500 Regular Human Insulin
• Useful when single dose of insulin exceeds 100 units or when total daily insulin requirements > 200 units
• Smaller volume allows for larger doses
• Onset similar to regular insulin (30-60 minutes) but duration similar to NPH insulin (8-12 hours)
• Typically administered 2 or 3 times daily
• Total daily insulin requirements may be lower
• Now available in a 3mL disposable pen – significantly reduces the risk of dosing errors

Fixed-Ratio Basal Insulin Plus GLP-1 Receptor Agonist

• **Insulin Glargine/Lixisenatide (Soliqua®)**
  - **Initiation:**
    - If taking < 30 units basal insulin: 15 units glargine U-100 (5 μg lixisenatide)
    - If taking 30 to 60 units basal insulin: 30 units glargine U-100 (10 μg lixisenatide)
  - **Titration:** 2 to 4 units (insulin glargine U-100 component) once weekly
  - **Max dose:** 60 units insulin glargine U-100/20 μg lixisenatide

• **Insulin Degludec/Liraglutide (Xultophy®)**
  - **Initiation:** 16 units insulin degludec (0.58 mg liraglutide) once daily
  - **Titration:** 2 units (insulin degludec) every 3 to 4 days
  - **Max dose:** 50 units insulin degludec/1.8 mg liraglutide

Insulin glargine/lixisenatide Prescribing Information. http://products.sanofi.us/Soliqua100-33/Soliqua100-33.pdf
CASE STUDIES
Assessment Question #2

LW is a 58 year old Asian female with type 2 DM on two oral medications. Last A1c = 8.4%. She is 5’ 1” tall and weighs 62 kg. Last week, she was started on insulin glargine U-100 and instructed to take 10 units sub-Q HS. The patient reports fasting BG readings the past 3 mornings of 136 mg/dL, 148 mg/dL, and 127 mg/dL. Reports no symptoms of hypoglycemia. Which of the following is the next BEST step?

A. Move the insulin dose to morning
B. Decrease insulin dose by 2 units
C. Increase insulin dose by 2 units
D. Continue current insulin dose for 2 weeks before changing dose
Case #1

You work in a community-based diabetes education program

LK is a 63 year old African American man

**HPI:** Referred by primary care provider (PCP) to initiate insulin therapy and for diabetes education. His A1C has been persistently above 9% for the last 12 months despite adherence to a 3-drug oral regimen.

The PCP encourages LK to lose weight and exercise. LK is worried about starting insulin. His mother had diabetes and was using insulin before she passed away.
Case #1

Past Medical History:
Type 2 diabetes x 7 years
Dyslipidemia x 9 years
Hypertension x 21 years
Obesity
Case #1

Medications:
Metformin 1000mg PO twice daily
Glyburide 10mg PO once daily
Pioglitazone 45mg PO once daily
Irbesartan 150mg PO daily
Amlodipine 10mg PO daily
Rosuvastatin 20mg PO daily
Aspirin 81mg PO daily
Social & Family Hx:
• Resides with wife; has 2 grown children
• Wants to retire in the next 12-18 months
• Weight stable for the past year; wants to lose weight
• Previously smoked 1 ppd; quit 10 years ago; has never used illicit drugs
• Does not drink alcohol
• Father died from “old age”; mother died from a stroke
• Has high deductible insurance plan – must pay first $2500 out-of-pocket
Case #1

Glucose Control History:
• A1C 9.2% - measured at PCP visit 2 months ago
• SMBG most days before breakfast
  • Fasting 30-day average = 191 mg/dL
• Does not recall ever experiencing hypoglycemia; has only vague notions about what the symptoms are and how to treat it
Case #1

Vital Signs:
BP = 128/66  
Pulse = 80, regular
Weight = 224 lbs  
Height = 5’ 11”
BMI = 31.5  
Temp = 98.7

Labs (drawn this morning - fasting):
Glucose = 181  
A1C = 9.4%
BUN = 19  
SCr = 1.3  
eGFR > 60 ml/min
Na = 139  
K = 4.9
Tchol = 153  
LDL = 72  
HDL = 41  
Trig = 201
Pharmacists’ Patient Care Process

- Collect
- Assess
- Plan
- Implement
- Follow-up: Monitor and Evaluate

Image Used with Permission from JCPP. Available at: [https://jcpp.net/patient-care-process/](https://jcpp.net/patient-care-process/)
1) **COLLECT!** What information (available in the case) is most critical to assessing this patient’s health status and medication-related needs? What additional information is needed in order to assess this patient?

2) **ASSESS!** What is your assessment of glycemic control and other health-related needs? What insulin products are appropriate options and should be discussed with this patient?

3) **PLAN!** Among the appropriate options, what insulin product would you recommend? Should the other antidiabetic medications be continued?

4) **IMPLEMENT!** How would you initiate therapy? (Initial dose, dose titration)

5) **FOLLOW-UP!** What subjective and objective data should be collected during follow-up patient encounters to determine effectiveness and safety? How would you ensure a safe transition back to his PCP?
DEBRIEF
Practical Considerations

• Is this the best insulin for this patient?
  • What are the appropriate treatment options for this patient?
  • Potential benefits over alternatives
  • Potential adverse effects and long term risks
• Will the patient be able to use this medication appropriately?
  • Drug administration technique
  • Initiating therapy and titrating the dose
  • Monitoring therapy
• Will the patient have access to this medication?
  • Cost issues
  • Formulary considerations
Barriers to Insulin Therapy
Injection Education

• Inform patient of resources (e.g., tutorial videos)
• Educate and demonstrate process using demo pens and needles
• Have patient perform first injection in office
Insulin Pen vs. Vial/Syringe

• In 23 out of 24 studies patients preferred pen due to ease of use
• Patients report better perceived clinical efficacy
• Patients felt more confident in ability to maintain glycemic control

Address fear of needles and provide accurate education to minimize adverse effects

- Use the smallest needle (4mm)
- Do not inject through clothing
- Count to 10 before withdrawing needle
- Rotate sites (at least 1 cm)
## Basal Insulin Pens: Practical Comparisons

<table>
<thead>
<tr>
<th></th>
<th>Units per pen</th>
<th>Max units per injection</th>
<th>Storage at room temp (days)</th>
<th># of days a pen lasts if taking 40 units/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPH</td>
<td>300</td>
<td>60</td>
<td>14</td>
<td>7.5</td>
</tr>
<tr>
<td>Detemir (Levemir®)</td>
<td>300</td>
<td>80</td>
<td>42</td>
<td>7.5</td>
</tr>
<tr>
<td>Glargine U-100 (Lantus®)</td>
<td>300</td>
<td>80</td>
<td>28</td>
<td>7.5</td>
</tr>
<tr>
<td>Glargine U-100 (Basaglar®)</td>
<td>300</td>
<td>80</td>
<td>28</td>
<td>7.5</td>
</tr>
<tr>
<td>Glargine U-300 (Toujeo®)</td>
<td>450</td>
<td>80</td>
<td>42</td>
<td>11.25</td>
</tr>
<tr>
<td></td>
<td>900</td>
<td>160</td>
<td>42</td>
<td>22.5</td>
</tr>
<tr>
<td>Degludec U-100 (Tresiba®)</td>
<td>300</td>
<td>80</td>
<td>56</td>
<td>7.5</td>
</tr>
<tr>
<td>Degludec U-200 (Tresiba®)</td>
<td>600</td>
<td>160</td>
<td>56</td>
<td>15</td>
</tr>
</tbody>
</table>
# Prandial Insulin Pens: Practical Comparisons

<table>
<thead>
<tr>
<th>Prandial Insulin Pens</th>
<th>Units per pen</th>
<th>Max units per injection</th>
<th>Storage at room temp</th>
<th># of days a pen lasts if taking 60 units/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Aspart (Novolog®)</td>
<td>300</td>
<td>80</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>Lispro U-100 (Humalog®)</td>
<td>300</td>
<td>60</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>Lispro U-200 (Humalog®)</td>
<td>600</td>
<td>60</td>
<td>28</td>
<td>10</td>
</tr>
<tr>
<td>Glulisine (Apidra®)</td>
<td>300</td>
<td>80</td>
<td>28</td>
<td>5</td>
</tr>
</tbody>
</table>
ADA/EASD Position Statement
Starting and Adjusting Basal Insulin

**Start**
With 10 units/day or 0.1–0.2 units/kg/day

**Adjust**
Use an evidence-based titration algorithm, i.e., ↑ by 2 units every 3 days to reach FPG target

**For Hypo**
Determine cause; consider reducing dose by 10%–20%

Using Antihyperglycemic Agents with Insulin

• Continued use of metformin, GLP1-RA, and SGLT2 inhibitors can mitigate weight gain and may reduce the risk of hypoglycemia
• BIDS (Bedtime insulin daytime sulfonylurea) using NPH insulin resulted in less weight gain and lower risk of hypoglycemia when compared to intensive insulin therapy but not when compared to basal insulin alone
• Thiazolidinediones (TZDs) plus insulin can result in very significant weight gain and increased risk of hypoglycemia
• In most cases, reducing medication burden and cost should be a goal — so eliminating sulfonylureas, DPP-4 inhibitors, TZDs, and meglitinides would be appropriate

### GLP-1 RAs + Basal Insulin vs Basal-Bolus Insulin Meta-analysis

#### Δ A1c

<table>
<thead>
<tr>
<th>Study</th>
<th>Weighted Mean Difference (95% CI)</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diamant et al (2014)</td>
<td>-0.03 (-0.17 to 0.11)</td>
<td>32.25</td>
</tr>
<tr>
<td>Rosenstock et al (2014)</td>
<td>-0.16 (-0.33 to 0.01)</td>
<td>22.50</td>
</tr>
<tr>
<td>Shao et al (2014)</td>
<td>-0.11 (-0.23 to 0.01)</td>
<td>45.25</td>
</tr>
<tr>
<td>Overall (I²=0.0%, P=0.470)</td>
<td>-0.10 (-0.17 to -0.02)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

#### Hypoglycemia Risk

<table>
<thead>
<tr>
<th>Study</th>
<th>Relative Risk (95% CI)</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diamant et al (2014)</td>
<td>0.70 (0.55 to 0.90)</td>
<td>50.42</td>
</tr>
<tr>
<td>Rosenstock et al (2014)</td>
<td>0.65 (0.50 to 0.83)</td>
<td>49.21</td>
</tr>
<tr>
<td>Shao et al (2014)</td>
<td>0.14 (0.01 to 2.65)</td>
<td>0.37</td>
</tr>
<tr>
<td>Overall (I²=0.0%, P=0.526)</td>
<td>0.67 (0.56 to 0.80)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

#### ΔBody Weight

<table>
<thead>
<tr>
<th>Study</th>
<th>Weighted Mean Difference (95% CI)</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diamant et al (2014)</td>
<td>-4.60 (-5.33 to -3.87)</td>
<td>33.66</td>
</tr>
<tr>
<td>Rosenstock et al (2014)</td>
<td>-1.50 (-2.06 to -0.94)</td>
<td>33.81</td>
</tr>
<tr>
<td>Overall (I²=98.7%, P&lt;0.0001)</td>
<td>-5.66 (-9.80 to -1.51)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

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CASE STUDY #2
JW is a 28 year old man with type 1 diabetes who uses insulin lispro and insulin glargine U-100 via vial and syringe. He is at A1C goal (6.2%), but experiences frequent hypoglycemia (4-5 events per week). JW reports symptoms of hypoglycemia when his blood glucose is <60 mg/dL. Based on this information, which of the following would be the BEST first course of action?

A. Congratulate JW on his A1C of 6.2% and make no changes at this time
B. Convert JW to an ultra-long acting basal insulin analog
C. Immediately start JW on an insulin pump and CGM
D. Raise JW’s glycemic targets in the short term to avoid hypoglycemia
Case #2

SW is a 38 year old Caucasian female with type 1 diabetes mellitus (T1D)

**HPI:** SW has been referred to the pharmacotherapy clinic by her new PCP for evaluation of her current insulin regimen. She has been experiencing large fluctuations in blood glucose, including frequent hypoglycemic events (5-6 per week).

SW recently moved to the area and established care with her new PCP for the first time 1 week ago. She has been referred to an endocrinology practice, but the earliest she can be seen is 4 months from now.
Case #2

Past Medical History:
Type 1 diabetes x 12 years
Migraines
Case #2

Medications:
Insulin detemir (pen) 14 units twice daily
Insulin aspart (pen) 1:12 + 1/40 >100 mg/dL w/meals
Sumatriptan 100 mg PRN migraine; may repeat after 2 hours if needed
Case #2

Social & Family Hx:

• Lives with husband of 15 years and 3 active children (7, 11 and 14 years of age)
• Works part time as a school nurse
• Reports gaining ~10 lbs over the last year
• Has never smoked
• Drinks 1-2 alcoholic beverages rarely (5-6 x per year) in social settings
• Has good insurance coverage with low medication copays
Case #2

Glucose Control History:

- A1C = 7.8% (drawn 6 days ago)
- SMBG before meals and at bedtime (often forgets to check before meals)
  - Overall average = 182 mg/dL
  - Fasting average = 212 mg/dL
  - Pre-lunch average = 115 mg/dL
  - Pre-dinner average = 92 mg/dL
  - Bedtime average = 219 mg/dL
  - Range over previous 7 days = 42 – 292 mg/dL
- Hypoglycemia occurring 5-6 times per week; most occur in the afternoons/evening a few hours after lunch or dinner and also overnight
- Hypoglycemia symptoms typically don’t present until glucose level is < 60 mg/dL
- SW reports sometimes forgetting her evening dose of basal insulin due to being busy with child activities; she sometimes doubles up on her morning insulin detemir to compensate
Case #2

Vital Signs:
BP = 122/82
Weight = 172 lbs
BMI = 31.2
Pulse = 66, regular
Height = 5’ 4”
Temp = 98.4

Labs (drawn 6 days ago - fasting):
Glucose = 182
A1c = 7.8%
BUN = 15
SCr = 1.0
eGFR > 60 ml/min
Na = 142
K = 4.1
Tchol = 159
LDL = 90
HDL = 52
Trig = 86
Case #2 - Questions

1) COLLECT! What information (available in the case) is most critical to assessing this patient’s health status and medication-related needs? What additional information is needed in order to assess this patient?

2) ASSESS! What is your assessment of glycemic control and other health-related needs? What concerns, if any, do you have about the patient’s current insulin regimen?

3) PLAN! Based on your assessment of this case, what changes would you consider making to her insulin regimen? How would you address this patient’s episodes of hypoglycemia?

4) IMPLEMENT! What steps would you take to adjust this patient’s insulin therapy?

5) FOLLOW-UP! What subjective and objective data should be collected during follow-up patient encounters to determine effectiveness and safety?
DEBRIEF
Hypoglycemia

• Plasma glucose concentration < 70 mg/dL
• More common in type 1 diabetes
• Threshold for symptoms varies
  • Hypoglycemia unawareness
    • Inducible
    • Reversible
• Risks
  • Increased risk of CV events and mortality
  • Increased risk of falls in the elderly
  • Increased risk of accidental injury (e.g., driving accidents)
  • Increased risk of hospitalization
Strategies to Avoid Hypoglycemia

- Prevention
- Detection
- Treatment
Strategies to Prevent Hypoglycemia

**Type 1 Diabetes**

- Drug selection
  - Ideal PK/PD of insulin products
- Drug dosing/administration
  - Timing of injections
  - Flexible dosing regimens
- Technology
  - Subcutaneous continuous insulin infusion (CSII)
  - Continuous glucose monitoring (CGM)
- Patient Education

**Type 2 Diabetes**

- Drug selection
  - Avoid high risk medications
- Drug dosing and administration
- Patient Education
Hypoglycemia Detection

• Counsel patients about appropriate blood glucose monitoring
  • Use of glucose meter
  • Interpretation of results

• Counsel on symptoms of hypoglycemia
  • Hunger
  • Headache
  • Fatigue
  • Confusion
  • Dizziness
  • Sweating
  • Tremulousness
Hypoglycemia Unawareness: Prevention is Key

• Individuals at risk for hypoglycemia should be asked about symptomatic and asymptomatic hypoglycemia at each encounter
• Hypoglycemia unawareness or ≥ 1 episode of severe hypoglycemia should trigger reevaluation of the treatment regimen
• Insulin-treated patients with hypoglycemia unawareness should be advised to raise glycemic targets to avoid hypoglycemia for at least several weeks

American Diabetes Association. Diabetes Care 2019;41(Suppl. 1).
Hypoglycemia Treatment

• The 15/15 Rule
  1. Check your blood glucose. If <70 mg/dL, eat or drink 15 grams of quick-acting carbs
  2. Wait 15 minutes
  3. Re-check your blood glucose
  4. If <70 mg/dL – repeat carb and recheck in 15 minutes
  5. If >70 mg/dL – consume a snack or meal within 60 minutes

• Glucagon
Reasons for Switching Insulin Products

• **Medical Switching**
  - Regimen complexity considerations
  - Adherence
  - Hypoglycemia
  - Glycemic control
  - Dosing limitations (large insulin doses/injection)

• **Non-Medical Switching**
  - Formulary restrictions/changes
  - Cost
  - Care transitions

Pharmacokinetic Profile of Currently Available Insulins

- Ultra-Rapid and Rapid (aspart, lispro, glulisine, insulin human [inhaled])
- Short (regular U-100)
- Mixed short/intermediate (regular U-500)
- Intermediate (NPH)
- Long (detemir)
- Long (U-100 glargine)
- Ultra-long
- Glargine U-300
- Degludec U-100 & U-200

Time (hr)

0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36

Plasma Insulin Levels

Flood TM. J Fam Pract. 2007; 56(suppl 1):S1-S12.
Ultra-Long Acting Insulins

Potential Benefits of Use

- Longer duration of action (true once-daily basal insulins)
- Flexibility with administration timing
- Less volume per injection (concentrated products)
- Potential for less glycemic variability
- Potential for less hypoglycemia

Who May Benefit?

- People not receiving a full 24 hours of coverage with their current basal
- People with hectic/erratic schedules
- People who require large daily doses of insulin
- People experiencing nocturnal hypoglycemia with their current basal
Continuous Subcutaneous Insulin Infusion (CSII)

Potential Advantages:
• Improved glycemic control
• Precise dosage delivery
• Management of dawn phenomenon
• Increased flexibility in lifestyle
• Improved control during exercise
• Improved gastroparesis management
Continuous Glucose Monitoring (CGM)

Potential Advantages

• Improved glycemic control
  • Frequency of sensor use
• Reduced hypoglycemia
  • Low glucose suspend
  • Threshold alarms
    • Hypoglycemia unawareness

American Diabetes Association. Diabetes Care 2019;41(Suppl. 1).
CASE STUDY #3
Assessment Question #4

You are asked to help convert a patient from insulin glargine U-300 to insulin glargine U-100 upon admission to the hospital for an elective surgery. The patient is currently taking 50 units once daily of U-300. The patient reports his most recent A1C being 6.9%. What would be the most appropriate conversion strategy?

A. Start with 40 units of U-100 to avoid hypoglycemia  
B. Start with 40 units of U-100 to avoid hyperglycemia  
C. Start with 60 units of U-100 to avoid hypoglycemia  
D. Start with 60 units of U-100 to avoid hyperglycemia
Case #3

JW is a 61 year old Hispanic male with type 2 diabetes mellitus (T2D)

HPI: JW has been admitted to the hospital for an elective right total knee arthroplasty (TKA). Pharmacy has been asked to assist with conversion from his home insulin to the basal insulin on formulary (insulin glargine U100).

JW was converted to insulin glargine U300 several years ago.
Case #3

Past Medical History:
Type 2 diabetes x 16 years
Dyslipidemia
Hypertension
Osteoarthritis
Case #3

**Medications:**
- Insulin glargine U300 90 units daily in the AM
- Metformin 1,000 mg twice daily
- Sitagliptin 100 mg daily
- Atorvastatin 40 mg daily
- Lisinopril 10 mg daily
- Amlodipine 10 mg daily
- Acetaminophen 1,000 mg twice daily PRN
Case #3

Social & Family Hx:

- Lives with wife of 12 years
- Retired – former auto mechanic
- Previous smoker (30 pack-years), quit in 2005
- Does not drink alcohol
- Has good insurance coverage through his wife's employer
Glucose Control History:

- A1C 6.8% - measured at PCP visit 2 weeks ago
- SMBG every day upon waking
  - Fasting 30-day average = 112 mg/dL
- JW was experiencing nocturnal hypoglycemic events previously while taking a sulfonylurea, but has not experienced any lows since discontinuing the sulfonylurea
  - Review of glucose meter shows no values below 70 mg/dL
  - JW reports feeling “shaky” sometimes in the middle of the day if he forgets to eat lunch
Case #3

**Vital Signs:**
- BP = 126/68
- Pulse = 70, regular
- Weight = 213 lbs
- Height = 5’ 10”
- BMI = 30.6

**Labs (drawn at PCP visit 2 weeks ago - fasting):**
- Glucose = 118
- A1c = 6.8%
- BUN = 18
- SCr = 1.1
- eGFR > 60 ml/min
- Na = 138
- K = 4.7
- Tchol = 148
- LDL = 76
- HDL = 39
- Trig = 164
Case #3 - Questions

1) **COLLECT!** What information (available in the case) is most critical to assessing this patient’s health status and medication-related needs? What additional information is needed in order to assess this patient?

2) **ASSESS!** What is your assessment of glycemic control and other health-related needs? What are your primary concerns/considerations when making an insulin conversion for this patient?

3) **PLAN!** How would you adjust therapy for this patient during this care transition? What additional education or interventions would you consider?

4) **IMPLEMENT!** How would you approach a dose conversion from insulin glargine U-300 to insulin glargine U-100 in this patient?

5) **FOLLOW-UP!** After initial conversion to insulin glargine U-100, what additional follow-up would you recommend?
Critical Time Points for DSMES

1. At diagnosis
2. Annually for assessment of education, nutrition, and emotional needs
3. When new complicating factors (health conditions, physical limitations, emotional factors, or basic living needs) arise that influence self-management
4. When transitions occur

American Diabetes Association. Diabetes Care 2019;41(Suppl. 1).
Transitions to and from the Hospital

**Admission Considerations:**
- Perform A1C testing on all patients with diabetes or hyperglycemia admitted to the hospital if not performed in previous 3 months
  - Inpatient insulin use and discharge planning more effective if based on A1C at admission
- Diabetes self-knowledge assessed and DSME provided, as needed

**Discharge Considerations:**
- Risky time for all patients
- Discharge orders should consider self-care capabilities, diabetes type and severity, and effects of illness on blood glucose levels

American Diabetes Association. Diabetes Care 2019;41(Suppl. 1).
Reasons for Switching Insulin Products

- **Medical Switching**
  - Regimen complexity considerations
  - Adherence
  - Hypoglycemia
  - Glycemic control
  - Dosing limitations (large insulin doses/injection)

- **Non-Medical Switching**
  - Formulary restrictions/changes
  - Cost
  - Care transitions

### Conversion to Ultra-Long Insulin Products

#### Insulin Glargine U300

<table>
<thead>
<tr>
<th>Prior Treatment</th>
<th>Start With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once-daily basal insulin</td>
<td>1:1 conversion*</td>
</tr>
<tr>
<td>Twice-daily NPH</td>
<td>80% of total daily NPH dose</td>
</tr>
</tbody>
</table>

#### Insulin Degludec

<table>
<thead>
<tr>
<th>Prior Treatment</th>
<th>Start With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long- or intermediate-acting insulin</td>
<td>Same unit dose as the current total daily dose†</td>
</tr>
</tbody>
</table>

* For patients controlled on insulin glargine U100, expect a higher dose of U300 will be needed to maintain glycemic control.
† Start at 80% of total daily dose of long or intermediate-acting insulin to minimize hypoglycemia risk in pediatric patients.

Converting Between Basal Insulin Products

Glargine U100
- Start at same dose (10-18% higher dose likely required) → Glargine U300
- Start at same dose (lower dose may be required) → Degludec
- Start at same dose (higher dose may be required for patients switched to twice daily detemir) → Detemir

Glargine U300
- Start at 80% of U300 dose to minimize hypoglycemia risk → Glargine U100

Degludec
- Start at same dose – titrate based on clinical response → Glargine U300
- A change in dose may be required → Glargine U100

Detemir
- Start at same dose – titrate based on clinical response → Glargine U300
- A change in dose may be required → Glargine U100

Practical Recommendations for Insulin Product Switching

• Patient education on new pen device
• Clear patient instructions on new regimen – avoid medication administration errors
• Expect changes in glycemic control
• Consider potential empiric dose adjustments
• Expect the need for dose re-titration
• Increase monitoring
• Plan for sooner follow-up
Conclusions - Summary

• Many issues need to be carefully considered when using insulin therapy
  • Patient reluctance and clinical inertia
  • Initial treatment dose and delivery system
  • Timely titration of insulin doses
  • Safely switching between insulin products
  • Continuation of previously prescribed antidiabetic agents
  • Risk of hypoglycemia and weight gain

• Several new products make insulin delivery more convenient and may mitigate the risk of hypoglycemia and weight gain
Assessment Question #1

Which of the following statements is **TRUE** about the newer insulin products approved by the FDA in the past 5 years.

A. All of the newer products are available in pre-filled pen devices.
B. None of the newer products are available in pre-mixed combinations with other insulins.
C. All of the newer products are considered “ultra-long acting” insulins and can be dosed once daily.
D. All of the newer products improve glycemic control more effectively than “traditional” insulin products.
Assessment Question #2

LW is a 58 year old Asian female with type 2 DM on two oral medications. Last A1c = 8.4%. She is 5’ 1” tall and weighs 62 kg. Last week, she was started on insulin glargine U-100 and instructed to take 10 units sub-Q HS. The patient reports fasting BG readings the past 3 mornings of 136 mg/dL, 148 mg/dL, and 127 mg/dL. Reports no symptoms of hypoglycemia. Which of the following is the next **BEST** step?

A. Move the insulin dose to morning
B. Decrease insulin dose by 2 units
C. Increase insulin dose by 2 units
D. Continue current insulin dose for 2 weeks before changing dose
JW is a 28 year old man with type 1 diabetes who uses insulin lispro and insulin glargine U-100 via vial and syringe. He is at A1C goal (6.2%), but experiences frequent hypoglycemia (4-5 events per week). JW reports symptoms of hypoglycemia when his blood glucose is <60 mg/dL. Based on this information, which of the following would be the BEST first course of action?

A. Congratulate JW on his A1C of 6.2% and make no changes at this time
B. Convert JW to an ultra-long acting basal insulin analog
C. Immediately start JW on an insulin pump and CGM
D. Raise JW’s glycemic targets in the short term to avoid hypoglycemia
Assessment Question #4

You are asked to help convert a patient from insulin glargine U-300 to insulin glargine U-100 upon admission to the hospital for an elective surgery. The patient is currently taking 50 units once daily of U-300. The patient reports his most recent A1C being 6.9%. What would be the most appropriate conversion strategy?

A. Start with 40 units of U-100 to avoid hypoglycemia
B. Start with 40 units of U-100 to avoid hyperglycemia
C. Start with 60 units of U-100 to avoid hypoglycemia
D. Start with 60 units of U-100 to avoid hyperglycemia
Questions