Back to Insulin Basics: Solidifying Strategies to Overcome Barriers and Improve the Insulin Initiation Experience

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FACULTY

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View bio at www.ashpadvantage.com/startinsulin

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Curtis L. Triplitt, Pharm.D., CDCES
• Speaker for AstraZeneca, Eli Lilly and Company, Janssen Pharmaceuticals, Inc., and Novo Nordisk
Learning Objectives

• Compare the clinical profiles of currently available insulin products with respect to dosing, variability, volume, and safety.
• Review best practices for initiating insulin therapies.
• Explain the concept of psychological insulin resistance.
• Review patient and healthcare provider barriers to overcoming therapeutic inertia.

Diabetes Epidemic

• Over 30 million Americans have Diabetes Mellitus
• 84 million have prediabetes and are at risk of progression to diabetes mellitus
• Diabetes is the leading cause of working-age blindness and amputations
• Estimated to cost $327 billion in 2017

www.diabetes.org accessed January 10, 2020
Natural History of Type 2 Diabetes

- Onset
- Diagnosis
- Years from diagnosis
- Insulin resistance
- Insulin secretion
- Postprandial glucose
- Fasting glucose
- Microvascular complications
- Macrovascular complications
- Pre-diabetes
- Type 2 diabetes


The Challenge of Glycemic Control

HbA1c Levels (2007-2010 Population With Diagnosed Diabetes)*

- "Under Control" 53%
- 7% > HbA1c < 7.9% 25%
- > 8% 22%

*Data derived from National Health and Nutrition Examination Survey; includes T1D and T2D.


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When is Insulin Appropriate?

- A1C >10% or blood glucose levels >300mg/dL
- Any time glycemic control is inadequate on other therapies
- Type 1 DM is suspected
- Ongoing metabolic catabolism
  - Weight loss
  - Ketosis
  - Very high triglycerides
- Pregnancy


Insulin Initiation: Therapeutic Inertia is Common

81,573 people with type 2 diabetes in the U.K. Clinical Practice Research Datalink Identified between January 2004 and December 2006, with follow-up until April 2011.

- On 2 oral agents and A1C >7% >7 years to start insulin!
- On 2 oral agents and A1C >8% >6 years to start insulin!
- % therapy intensified correctly titrated over time period?
  Only 6-25%

Khunti K et al. *Diabetes Care*. 2013;36:3411-17
Key Barriers to Insulin Therapy

**Patient Barriers**
- Patient reluctance
- Sense of failure
- Loss of independence
- Belief that insulin is ineffective
- Fear of injections
- Fear of hypoglycemia
- Concerns about weight gain

**Provider Barriers**
- Therapeutic inertia
- Lack of insulin training, time, and/or support
- Fear of hypoglycemia
- Concerns about weight gain

What Can We Do?
Increase Our Knowledge About Insulin

**Improve Patient Ability to Start/Continue Insulin:**
1. How to Overcome Psychological Insulin Resistance
2. Educational principles for insulin
   - How to instruct on injections

**Know:**
1. Insulin availability and cost
2. Relevant differences between insulins
3. Clinically appropriate initiation/titration
PK Profile of Currently Available Insulins

PK = pharmacokinetic; NPH = neutral protamine Hagedorn.


Understanding the Insulin Therapy Components


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### Insulin Regimens: Learning the Lingo

- **Basal only (most common starting point)**
  - 1 injection (at bedtime or every 24 hours)
  - Added to oral agents
- **Basal Plus (usually 2-3 injections)**
  - Basal insulin injection
  - Adding one rapid-acting analog or inhaled insulin sequentially starting with largest meal; if inadequate control, then add 2nd rapid-acting injection to 2nd largest meal
- **Basal bolus (usually 4-5 injections)**
  - Basal insulin injection (once a day or split twice a day)
  - Rapid-acting insulin before each meal
- **Premixed**
  - 2 injections

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### Type 2 DM: Building an Insulin Regimen

**At Bedtime (NPH)**
- **Convenient**
- **Minimizes # of injections/day**
- **Improves fasting blood glucose and glycemic control in majority of patients**
- **Similar glycemic control with less hypoglycemia versus more complex insulin regimens**

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### Currently Available* Insulins

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Time to Onset (hr)</th>
<th>Time to Peak Action (hr)</th>
<th>Duration of Action (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid-acting insulin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspart, Lispro (U-100, U-200),</td>
<td>≤ 0.25</td>
<td>0.5-1.5</td>
<td>4-6</td>
</tr>
<tr>
<td>Glulisine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspart with niacinamide</td>
<td>≤ 0.2</td>
<td>0.5-1.5</td>
<td>4-6</td>
</tr>
<tr>
<td>Insulin human (inhaled)</td>
<td>≤ 0.2</td>
<td>0.75</td>
<td>1.5-4</td>
</tr>
<tr>
<td><strong>Short-Acting insulin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin human regular (U-100)</td>
<td>0.5</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td><strong>Insulin human regular (U-500)</strong></td>
<td>0.25</td>
<td>4</td>
<td>13-24</td>
</tr>
<tr>
<td><strong>Intermediate-Acting insulin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human insulin isophane (NPH)</td>
<td>2-4</td>
<td>4-10</td>
<td>12-18</td>
</tr>
<tr>
<td><strong>Long-Acting Insulins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detemir</td>
<td>3-4</td>
<td>6-8 (though relatively flat)</td>
<td>Up to 24</td>
</tr>
<tr>
<td>Glargine (U-100)</td>
<td>2-4</td>
<td>flat</td>
<td>20-24</td>
</tr>
<tr>
<td><strong>Ultra-long Acting insulins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glargine (U-300)</td>
<td>6</td>
<td>flat</td>
<td>up to 36</td>
</tr>
<tr>
<td>Degludec (U-100, U-200)</td>
<td>1</td>
<td>flat</td>
<td>&gt;42</td>
</tr>
</tbody>
</table>

*Patient-specific onset, peak, and duration may vary from times listed in table. *Premix products not depicted

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### Starting Basal Insulin

**Every 24 hour long-acting insulin OR**

Bedtime intermediate-acting insulin

**Daily dose:** 10 units or 0.1-0.2 units/kg/day

- **Check FPG daily**

  - Increase dose by 2-3 units every 2-3 days until FPG at desired goal
  - **Check FPG daily**

  - In the event of hypoglycemia or FPG level <70 mg/dL:
    - Reduce insulin dose by 4 units, or by 10-20%

- **Check FPG daily**

  - **Treat to Target**

    | FPG over last 2-3 days | Basal Insulin Adjustment |
    |------------------------|--------------------------|
    | >180 mg/dL             | +8 units                 |
    | 140-180                | +6 units                 |
    | 120-140                | +4 units                 |
    | 100-120                | +2 units                 |
    | Below goal             | -2 to -4 units           |

**FPG = fasting plasma glucose**

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United States Diabetes Organizations: Algorithms for Insulin Use to Achieve Glycemic Control

American Diabetes Association:
Pharmacologic Approaches to Glycemic Treatment

American Association of Clinical Endocrinologists/American College of Endocrinology:
Comprehensive Type 2 Diabetes Management Algorithm

National Diabetes Organizations: Glucagon Like Peptide-1 Receptor Agonist (GLP-1RA) Prior to Basal Insulin?

- Cardiovascular (CV) Outcome Trials:
  - Potential CV benefits with GLP-1 RA’s
  - LEADER, SUSTAIN-6, REWIND, EXSCEL trials
  - Potential renal benefits
- Similar A1C reductions to basal insulin initiation
- If on optimized basal insulin, similar A1C reductions to mealtime insulin
- Less hypoglycemia versus basal insulin
- Weight loss in majority of patients
- Cost can be similar if newer agents are used

- When to Recommend Insulin First?
  - A1C is high (>10-11%)
  - Catabolism is present, which may indicate insulin deficiency
    - weight loss, ketosis, ongoing polyuria and/or polydipsia
  - Type 1 DM is suspected
American Diabetes Association 2019* Injectable Therapy Recommendations

- *2019 algorithm presented
- 2020 guidelines similar, but 2019 provides more “guidance” such as:
  1. Initiation
  2. Titration
  3. Combination

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The image contains a diagram titled "Algorithm for Adding/Intensifying Insulin" and "American Diabetes Association 2019 Injectable Therapy Recommendations (p 2)". The diagram outlines strategies for insulin management, including dose adjustments and glycemic control goals.

The text mentions key terms such as PPG (postprandial glucose), DSMES (Diabetes Self Management Education and Support), TDD (total daily dose of insulin), SGLT2i (sodium glucose cotransporter-2 inhibitor), and DPP4i (dipeptidyl peptidase-4 inhibitor). The text references "Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes - 2019. Diabetes Care. 2019;42(Suppl 1):S90-S102."
Comparing the New Generation of Basal Insulins

Insulin Degludec and Insulin Glargine (U-300)

• Smaller depot surface area reduces rate of absorption
  – Half-life ~ 23 hours
  – Steady state in 4 days
  – Duration of action ≤ 36 hours

• Only available in pens
• U-300 insulin glargine pen is white with green label
  – 300 U/mL, 1.5 mL pen, Max 80 units/injection, Dose 1 unit increments
• U-300 insulin glargine MAX pen is white with green STRIPES on the label
  – 300 U/mL, 3 mL pen, Max 160 units/injection, Dose 2 unit increments

U-100, U-200 Insulin Degludec

- Prolonged action due to dihexamer and multihexamer formations and albumin binding
  - Duration of action >42 hours
  - Half-life ~24 hours
  - Steady state in 2-3 days

- Only available in pens
- U-100 degludec pen is blue with green label
  - 100 units/mL, 3mL, Max 80 units per injection, Dose 1 unit increment
  - U-200 degludec pen is blue with green STRIPES on label
  - 200 units/mL, 3mL, Max dose per injection is 160 units, 2 unit increments

Cardiovascular Safety of New Generation Basal Insulins

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DEVOTE Study Design

- n=7637 patients with T2DM at high risk of CV events
  - Age ≥50 years with with CVD or renal disease
  - Age ≥60 years with ≥1 CV risk factor

- Randomization
  - U-100 insulin degludec: n=3818
  - U-100 insulin glargine: n=3819

- Noninferiority study: prespecified margin <1.3 for upper bound of 95% CI of the HR for the primary endpoint; superiority tested if noninferiority criterion met
  - Primary endpoint: composite of CV death, nonfatal MI, or nonfatal stroke
  - Key secondary endpoints
    - Adjudicated severe hypoglycemia
    - Composite of CV death, nonfatal MI, nonfatal stroke, or hospitalization for unstable angina
    - All-cause death


Cardiovascular Outcomes: Insulin Degludec vs. Glargine

DEVOTE CVOT Outcomes

<table>
<thead>
<tr>
<th>Hazard rate (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite endpoint* Non-inferiority</td>
<td>0.91 (0.78-1.06)</td>
</tr>
<tr>
<td>Expanded composite endpoint†</td>
<td>0.92 (0.80-1.05)</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.91 (0.76-1.11)</td>
</tr>
<tr>
<td>Noncardiovascular death</td>
<td>0.84 (0.60-1.16)</td>
</tr>
<tr>
<td>CV death</td>
<td>0.96 (0.76-1.21)</td>
</tr>
<tr>
<td>CV death excluding undetermined cause of death</td>
<td>0.91 (0.69-1.20)</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td>0.85 (0.68-1.06)</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>0.90 (0.65-1.23)</td>
</tr>
<tr>
<td>Unstable angina hospitalization</td>
<td>0.95 (0.68-1.31)</td>
</tr>
</tbody>
</table>

Median follow-up: 1.99 years

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Insulin Glargine (U-300) vs. Insulin Glargine (U-100): Meta-analysis of Phase III Trials

<table>
<thead>
<tr>
<th></th>
<th>Baseline to Month 6</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Glargine U-300 (n=1247)</td>
<td>Glargine U-100 (n=1249)</td>
</tr>
<tr>
<td>A1c (%) LA mean</td>
<td>-1.02</td>
<td>-1.02</td>
</tr>
<tr>
<td>Weight (kg), LS mean</td>
<td>0.51</td>
<td>0.79</td>
</tr>
<tr>
<td>Any nocturnal hypoglycemia*</td>
<td>2.1</td>
<td>3.06</td>
</tr>
<tr>
<td>Confirmed BG &lt;70 mg/dL or severe hypoglycemia any time of day*</td>
<td>15.22</td>
<td>17.77</td>
</tr>
<tr>
<td>Severe hypoglycemia any time of day*</td>
<td>0.11</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* = events per participant-year, RR = relative risk, CI = confidence interval, LS = least squares, BG = blood glucose.

Degludec vs. Glargine (U-100): Meta-analysis

Insulin Degludec (U-100) vs. Insulin Glargine (U-100)
5 type 2 DM studies and 2 Type 1 DM studies

<table>
<thead>
<tr>
<th></th>
<th>Degludec vs. Glargine</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attain FPG target of 90mg/dl without Nocturnal Hypoglycemia</td>
<td>Odds Ratio 1.82</td>
<td>1.49-2.22</td>
</tr>
<tr>
<td>Nocturnal confirmed* hypoglycemia</td>
<td>Rate Ratio 0.68</td>
<td>0.57-0.82</td>
</tr>
</tbody>
</table>

* confirmed= 12AM to 6AM. PG <56mg/dL

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Flexible vs Fixed Dosing U-300 Glargine*

6-Month Treatment Period (main study)
6-Month Extension Period (main study)

U-300 once daily every 24 ± 3 h

“Flexible”

U-300 once daily every 24 h

“Fixed”

6 months (randomization, sub-study)
9 months (end of sub-study)

HbA1C (%)
6.0
6.5
7.0
7.5
8.0

EDAITION 1
EDAITION 2

P=NS
P=NS

Documented, Symptomatic Hypoglycemia (<70mg/dl)

Subjects (%)
0
20
40
60
80
100

Nocturnal
Total Hypo

P=NS

*Edition 1 Sub-study, n=108. Edition 2 Sub-study, n=86


Flexible vs. Fixed Insulin Degludec Dosing: BEGIN FLEX Trial

- **Trial design:** 26-week, randomized, open-label, parallel-group, treat-to-target trial in patients with type 2 diabetes
- **Primary outcome:** non-inferiority of flexible* insulin degludec dosing (8-40 hour intervals between doses) compared with glargine

*FLEX*= changing dosing interval: 36-40 hours between injections then 8-12 hours between injections throughout study


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### BEGIN FLEX- A1C Outcomes

#### A1C

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>CHANGE 26 weeks</th>
<th>P value</th>
<th>At 26 weeks</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glargine Daily</td>
<td>8.4%</td>
<td>-1.26</td>
<td>P=NS</td>
<td>43.9%</td>
<td>P=NS</td>
</tr>
<tr>
<td>Degludec Daily</td>
<td>8.4%</td>
<td>-1.07</td>
<td></td>
<td>40.8%</td>
<td></td>
</tr>
<tr>
<td>Degludec FLEX</td>
<td>8.5%</td>
<td>-1.28</td>
<td></td>
<td>38.9%</td>
<td></td>
</tr>
</tbody>
</table>

#### A1C: Attain <7%


### Head-to-Head Trials:

**Insulin Degludec vs. U-300 Insulin Glargine**

<table>
<thead>
<tr>
<th></th>
<th>Insulin?</th>
<th>CV Safety</th>
<th>Randomized</th>
<th>Real-World</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEVOTE</td>
<td>U300 IG U100 ID</td>
<td>✔</td>
<td></td>
<td></td>
<td>Novo</td>
</tr>
<tr>
<td>BRIGHT</td>
<td>U300 IG U100 ID</td>
<td>✔</td>
<td></td>
<td></td>
<td>Sanofi</td>
</tr>
<tr>
<td>DELIVER Naive D</td>
<td>U300 IG ID (strength not stated)</td>
<td>✔</td>
<td>✔</td>
<td>Sanofi</td>
<td></td>
</tr>
<tr>
<td>CONCLUDE</td>
<td>U300 IG U200 ID</td>
<td>✔</td>
<td></td>
<td></td>
<td>Novo</td>
</tr>
<tr>
<td>CONFIRM</td>
<td>U300 IG U100 or U200 ID</td>
<td>✔</td>
<td>✔</td>
<td>Novo</td>
<td></td>
</tr>
</tbody>
</table>

U-300 IG= U-300 insulin glargine; U-100 or U-200 ID= insulin degludec


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## Insulin Degludec vs. Insulin Glargine (U-300)

<table>
<thead>
<tr>
<th></th>
<th>Duration (weeks)</th>
<th>A1C (%)</th>
<th>ALL Hypo (95% CI)</th>
<th>Nocturnal Hypo (95% CI)</th>
<th>Severe Hypo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRIGHT</td>
<td>24</td>
<td>-1.64</td>
<td>0.88 (0.66-1.17)</td>
<td>0.99 (0.74-1.32)</td>
<td>1 episode</td>
</tr>
<tr>
<td>CONCLUDE</td>
<td>88</td>
<td>DEG -0.1%</td>
<td>0.88 (0.73-1.06)</td>
<td>0.63 (0.48-0.84)</td>
<td>0.2 (0.7-0.57)</td>
</tr>
<tr>
<td>DELIVER Naive D</td>
<td>24</td>
<td>-1.67</td>
<td>0.94 (0.54-1.37)</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>CONFIRM</td>
<td>24</td>
<td>-1.22</td>
<td>0.64 (0.47-0.88)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hypo=hypoglycemia; Glar: insulin glargine; Deg: insulin degludec


## Hypoglycemia: Insulin Degludec versus Glargine

### DEVOTE CVOT Safety Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe hypoglycemia*</td>
<td>0.60 (0.48-0.76)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Unconsciousness or coma</td>
<td>0.81 (0.55-1.19)</td>
<td>0.28</td>
</tr>
<tr>
<td>Seizure</td>
<td>1.02 (0.38-2.73)</td>
<td>0.97</td>
</tr>
<tr>
<td>Nocturnal severe hypoglycemia</td>
<td>0.47 (0.31-0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥1 severe hypoglycemia event</td>
<td>0.73 (0.60-0.89)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Episode requiring assistance from another person to actively administer carbohydrate or glucagon or take other corrective actions. CI, confidence interval.

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Severe Hypoglycemia Increases Risk of CV Death

DEVOTE CVOT Outcomes

<table>
<thead>
<tr>
<th>DAYS FROM SEVERE HYPOGLYCEMIA EVENT</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANY TIME</td>
<td>2.51 (1.79-3.5)</td>
</tr>
<tr>
<td>365</td>
<td>2.78 (1.92-4.04)</td>
</tr>
<tr>
<td>180</td>
<td>3.31 (1.99-4.90)</td>
</tr>
<tr>
<td>90</td>
<td>3.28 (1.85-5.83)</td>
</tr>
<tr>
<td>15</td>
<td>4.2 (1.35-13.09)</td>
</tr>
</tbody>
</table>

Higher Risk of CV Death after Severe Hypo

*Episode requiring assistance from another person to actively administer carbohydrate or glucagon or take other corrective actions.
CI=confidence interval


How Can We Best Help Our Patients Understand This Complex Information?
What Patients Need to Know

- Insulin
  - Storage and expiration
- Preparation of insulin product
  - Syringe and vial?
  - Pen device?
- Choosing syringes or pen needles
- How to properly use the device
- How to dispose of the device

Basal Insulin Delivery Options

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Concentration</th>
<th>Vial</th>
<th>Pen</th>
<th>Max Dose per pen injection</th>
<th>Relative Cost “AWP”</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPH</td>
<td>U-100</td>
<td>X</td>
<td>X</td>
<td>60</td>
<td>$</td>
</tr>
<tr>
<td>Glargine</td>
<td>U-100</td>
<td>X</td>
<td>X</td>
<td>80</td>
<td>$$</td>
</tr>
<tr>
<td>Glargine</td>
<td>U-300</td>
<td>X</td>
<td></td>
<td>160 “MAX pen”</td>
<td>$$</td>
</tr>
<tr>
<td>Detemir</td>
<td>U-100</td>
<td>X</td>
<td>X</td>
<td>80</td>
<td>$$$</td>
</tr>
<tr>
<td>Degludec</td>
<td>U-100</td>
<td>X</td>
<td>X</td>
<td>80</td>
<td>$$$$</td>
</tr>
<tr>
<td>Degludec</td>
<td>U-200</td>
<td>X</td>
<td></td>
<td>160</td>
<td>$$$$</td>
</tr>
<tr>
<td>Regular Human</td>
<td>U-500</td>
<td>X</td>
<td>X</td>
<td>300</td>
<td>$$</td>
</tr>
</tbody>
</table>

AWP = average wholesale price


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### Expiration of Products

<table>
<thead>
<tr>
<th>Products/Device</th>
<th>Refrigerated</th>
<th>Unrefrigerated</th>
<th>Once Used (opened)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin lispro, aspart, glulisine, glargine</td>
<td>Expiration Date</td>
<td>28 days</td>
<td>28 days</td>
</tr>
<tr>
<td><strong>Vials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin human R or N (Humulin)</td>
<td></td>
<td>31 days</td>
<td>31 days</td>
</tr>
<tr>
<td>Insulin human R or N (Novolin)</td>
<td>Expiration Date</td>
<td>42 days</td>
<td>42 days</td>
</tr>
<tr>
<td>Insulin human R (U-500)</td>
<td></td>
<td>40 days</td>
<td>40 days</td>
</tr>
<tr>
<td><strong>Pens</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin lispro, aspart, glulisine, Insulin glargine (U-100)</td>
<td>Expiration Date</td>
<td>28 days</td>
<td>Do not refrigerate 28 days</td>
</tr>
<tr>
<td>Insulin human R (U-500)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vials and pens</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin detemir</td>
<td>Expiration Date</td>
<td>42 days</td>
<td>Do not refrigerate 42 days</td>
</tr>
<tr>
<td>Insulin degludec (U-100 or U-200)</td>
<td></td>
<td>56 days</td>
<td>56 days</td>
</tr>
<tr>
<td>Insulin glargine (U-300)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Insulin Pen Injection Technique

- Dial dose of insulin on the pen
  - Air in insulin chamber? Remove first
  - Ensure proper dose appears in the “dosing window”
- Screw on pen needle (remove outer/inner cap)
- Smoothly insert pen needle flush to skin, use 90° angle
- Depress the button to release insulin into SC tissue
- Delay withdraw of needle for 5 to 10 seconds after dose is delivered
  - Ensures full dose is delivered
- Pen may leak if needle kept on pen
- Always have the patient demonstrate back their technique
Approximately 2-2.5 mm* (1.25-3.25 mm) regardless of gender, age, ethnicity, BMI

Short needle should work for majority of patients

*Mean skin thickness results with 95% confidence intervals combined at all 4 injection sites
BMI=body mass index

Absorption of regular insulin is consistent across Deep versus Superficial SC injection

Regular insulin is absorbed at similar rates at both sites, whether injected into deep or superficial subcutaneous tissue

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### Insulin Initiation: We Must Address Patients’ Concerns

- Are there other treatment options the patient could try first?
- Does insulin mean my diabetes is getting worse?
- I’m scared of needle pain
  - I don’t want to get “hooked on the needle”
- I’m worried about developing low blood glucose levels

**These are logical concerns!**

### Overcoming Psychological Insulin Resistance

- Use motivational interviewing skills
  - “So what you are telling me is...”
- Avoid using insulin as a “threat”
  - Use insulin as the **solution**
  - Discuss it openly
  - Avoid gestures/facial expression that it is a bad thing
  - Promise a reassessment after a “limited” time trial
- Recommend insulin pens and higher gauge, shorter pen needles
- Demonstrate how to use the device, then have patient teach back device and injection technique in the office/pharmacy
- Manage expectations
  - Tell patient that injection is less painful than finger stick
  - Most patients do not feel pain with higher gauge, short needles
- Teach patient to recognize and treat hypoglycemia

# “Q&A” About Diabetes and Insulin

<table>
<thead>
<tr>
<th>Provider</th>
<th>To Patient</th>
<th>For Patient-Outcome “What’s in it for me?”</th>
</tr>
</thead>
</table>
| Diabetes is progressive and over time the ability to make insulin can be diminished | What are your fears or concerns if insulin would be necessary? | - This may mean you feel less fatigue  
- You may have more energy  
- You will be at lower risk of some serious complications |

| I can’t do this. | What concerns about taking/potentially taking insulin are the most difficult for you? | Taking insulin is a series of steps, we can work together until the steps come together |

---

## Concern Answers

<table>
<thead>
<tr>
<th>Concern</th>
<th>Answers</th>
</tr>
</thead>
<tbody>
<tr>
<td>What have you heard about insulin?</td>
<td>Did [<em><strong><strong>] die from a low sugar reaction? It is likely insulin was started too late and that [</strong></strong></em>] had high blood sugars for a very long time, which puts people at risk for a lot of serious complications. Keeping your blood sugar at goal can decrease your risks of having these complications</td>
</tr>
<tr>
<td>This stuff can kill you! My [_____] started insulin, and was dead three years later</td>
<td>Insulin may cause a low blood sugar reaction. Testing your blood sugar at home is important, especially if you think you are having the signs/symptoms of low blood glucose (REVIEW: Testing, Hypoglycemia)</td>
</tr>
</tbody>
</table>

---

“Q&A” About Diabetes and Insulin

<table>
<thead>
<tr>
<th>Concern</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>I’m afraid of needles</td>
<td>Most people have a fear of needles, that’s normal, but just to be clear, insulin isn’t addictive.</td>
</tr>
<tr>
<td>“I don’t want to get hooked on the needle”</td>
<td>Are there addiction concerns with you or a family member I should be aware of? Let’s try an injection together and see how you do.</td>
</tr>
<tr>
<td>So if I get better, can I stop insulin?</td>
<td>Well let’s try it for a couple of weeks and see where we are at...many people have to continue with insulin, but we will take it one week at a time.</td>
</tr>
<tr>
<td>This is so overwhelming</td>
<td>Yes, it is a lot of new information. Are there questions we can answer now that may help get you started?</td>
</tr>
<tr>
<td>I can’t remember all those steps at once!</td>
<td>You don’t have to remember everything at once. Let’s try a step at a time....</td>
</tr>
</tbody>
</table>


Key Takeaways

- Inadequate glycemic control is common
- Timely initiation and titration of insulin helps the majority of patients achieve A1C goals
  - Therapeutic inertia is common with initiation and titration of insulin
- Understand the needs of your patient when starting basal insulin products
  - Cost?
  - Ease of use?
  - Avoidance of hypoglycemia?
  - Allaying common fears?
Newer basal insulin choices with advantageous pharmacokinetics may improve ease of use and minimize hypoglycemia.

- Conduct a motivational interview “Q&A” with your patient to improve the insulin initiation experience.

**Key Takeaways**

**Select References**

