New Strategies for the Management of Diabetes: The Emerging Role of Concentrated Insulins

Presented as a Live Webinar
Wednesday, September 21, 2016
1:00 p.m. – 2:00 p.m. ET

On-demand Activity
Live webinar recorded and archived to be watched at your convenience
Available after November 1, 2016

www.onepenonepatient.org/webinar

Planned by ASHP Advantage
Supported by an educational grant from Novo Nordisk Inc.

© 2016 American Society of Health-System Pharmacists
Activity Overview

This educational activity will review the benefits of early initiation of insulin on outcomes for patients with diabetes mellitus. The benefits and limitations of the newer concentrated insulin products will be reviewed, and strategies for ensuring their safe use and administration will be discussed.

Learning Objectives

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

- Review the benefits of early initiation of insulin therapy on long-term patient outcomes.
- Describe the benefits and limitations of the newer concentrated insulins.
- Explain strategies for ensuring the safe use and administration of the newer concentrated insulins.

Continuing Education Accreditation

ASHP is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

This activity provides 1.0 hour (0.1 CEU – no partial credit) of continuing pharmacy education credit (ACPE activity #0204-0000-16-459-H01-P for the live activity and ACPE activity #0204-0000-16-459-L01-P for the on-demand activity).

Participants will process CPE credit online at http://elearning.ashp.org/my-activities. CPE credit will be reported directly to CPE Monitor. Per ACPE, CPE credit must be claimed no later than 60 days from the date of the live activity or completion of a home-study activity.
Activity Faculty

Mark F. Lutz, Pharm.D., CPPS
Drug Information Specialist
Beaumont Hospital
Royal Oak, Michigan

Mark F. Lutz, Pharm.D., CPPS, is Drug Information Specialist at Beaumont Hospital in Royal Oak, Michigan. At this site, he serves as preceptor for the drug information and medication safety rotations in the postgraduate year 1 (PGY1) residency. He is also preceptor for the medication safety learning experience for the PGY2 residencies in pharmacy administration and critical care. In addition, Dr. Lutz serves as adjunct faculty for three colleges of pharmacy in Michigan: University of Michigan, Ferris State University, and Wayne State University.

Dr. Lutz earned his Doctor of Pharmacy degree from University of Michigan College of Pharmacy in Ann Arbor and completed an ASHP-accredited PGY1 residency at William Beaumont Hospital. He is a board-certified professional in patient safety through the Certification Board for Professionals in Patient Safety.

Within the Beaumont Health System, Dr. Lutz is involved in several committees and initiatives related to his practice interests of medication safety, drug formulary management, and decision support. He has taken a lead role in the multidisciplinary evaluation of inpatient insulin pen safety, implementation of system safety improvements, and insulin formulary changes. At Beaumont, he also is a patient safety first responder on the patient safety response team.

Dr. Lutz participated in several capacities for the ASHP quality improvement initiative, “Strategies for Ensuring the Safe Use of Insulin Pens in the Hospital,” including assisting in online resource development, conducting webinars, and serving as a distance mentor for hospitals in five states. He is a member of ASHP, Michigan Pharmacists Association, and Michigan Society of Health-System Pharmacists (MSHP). He was honored as the 2015 MSHP Pharmacist of the Year.
Julie M. Sease, Pharm.D., BCPS, BCACP, CDE, FCCP
Associate Dean for Academic Affairs
Professor of Pharmacy Practice
Presbyterian College School of Pharmacy
Clinton, South Carolina

Julie M. Sease, Pharm.D., BCPS, BCACP, CDE, FCCP, is Associate Dean for Academic Affairs and Professor of Pharmacy Practice at Presbyterian College School of Pharmacy in Clinton, South Carolina.

Dr. Sease earned her Doctor of Pharmacy degree from the University of South Carolina College of Pharmacy and completed a primary care pharmacy practice residency at William Jennings Bryan Dorn VA Medical Center (VAMC), both in Columbia, South Carolina. She is a board-certified pharmacotherapy specialist, board-certified ambulatory care pharmacist, and certified diabetes educator.

Upon completion of her residency, Dr. Sease joined the faculty of her alma mater, which later became the South Carolina College of Pharmacy, and practiced in the primary care clinics of Dorn VAMC. Since joining the faculty of Presbyterian College School of Pharmacy, she developed a clinical practice site delivering diabetes and anticoagulation management at Good Shepherd Free Medical Clinic in Clinton, then provided clinical services at Montgomery Center for Family Medicine in Greenwood, South Carolina.

Dr. Sease is a member of American Association of Colleges of Pharmacy, American Association of Diabetes Educators (AADE), American College of Clinical Pharmacy (ACCP), and ASHP, and she currently serves on the AADE annual meeting planning committee. She was elected a fellow of ACCP in 2014. With expertise in ambulatory care, Dr. Sease often lectures on the topics of diabetes, dyslipidemia, anticoagulation, chronic obstructive pulmonary disease, hypertension, and various gastrointestinal disorders. She has authored numerous journal articles and book chapters, and she regularly writes responses for Medscape Pharmacists Ask the Expert.
Disclosure Statement

In accordance with the Accreditation Council for Continuing Medical Education’s Standards for Commercial Support and the Accreditation Council for Pharmacy Education’s Standards for Commercial Support, ASHP requires that all individuals involved in the development of activity content disclose their relevant financial relationships. A person has a relevant financial relationship if the individual or his or her spouse/partner has a financial relationship (e.g. employee, consultant, research grant recipient, speakers bureau, or stockholder) in any amount occurring in the last 12 months with a commercial interest whose products or services may be discussed in the educational activity content over which the individual has control. The existence of these relationships is provided for the information of participants and should not be assumed to have an adverse impact on the content.

All faculty and planners for ASHP Advantage education activities are qualified and selected by ASHP and required to disclose any relevant financial relationships with commercial interests. ASHP identifies and resolves conflicts of interest prior to an individual’s participation in development of content for an educational activity. Anyone who refuses to disclose relevant financial relationships must be disqualified from any involvement with a continuing pharmacy education activity.

- Mark F. Lutz, Pharm.D., CPPS, declares that he has no relationships pertinent to this activity.
- Julie M. Sease, Pharm.D., BCPS, BCACP, CDE, FCCP, declares that she has no relationships pertinent to this activity.
- All other planners report no financial relationships relevant to this activity.

Additional Educational Activities and Resources

- Strategies for Ensuring the Safe Use of Insulin Pens in the Hospital
  - www.onepenonepatient.org
  - Tool kit: Sample policies and procedures, assessment tools, and educational resources
  - Resource center: Compilation of guidelines, articles, and useful websites
- Individualization of Insulin Therapy for Type 2 Diabetes Mellitus: What You Need to Know
  - www.ashpadvantage.com/go/type2
  - Series of live and on-demand activities
    - On-demand activity, “Individualizing Insulin Therapy for Type 2 Diabetes Mellitus (1 hour CPE)
    - Discussion Guide (coming Fall 2016)
    - Midday Symposium and Webinar, “Individualizing Insulin Therapy for Type 2 Diabetes Mellitus: Clinical Case Vignettes,” on December 5, 2016
    - Ask the Experts webinar on March 23, 2017
    - e-newsletters and Engaging the Experts interviews (coming 2017)
Learning Objectives

At the conclusion of this knowledge-based educational activity, participants should be able to
- Review the benefits of early initiation of insulin therapy on long-term patient outcomes
- Describe the benefits and limitations of the newer concentrated insulins
- Explain strategies for ensuring the safe use and administration of the newer concentrated insulins

Benefits of Early Insulin Initiation

- Overcoming glucotoxicity
  - β-cell rest
  - Preservation of β-cell mass and function
- Improved insulin sensitivity
- Anti-inflammatory and antioxidant properties that may protect against endothelial dysfunction
- Long-term protection for end organs regardless of future treatment or glycemic control

Disclosures

- Julie M. Sease, Pharm.D., BCPS, BCACP, CDE, FCCP, declares that she has no relationships pertinent to this activity.
- Mark F. Lutz, Pharm.D., CPPS, declares that he has no relationships pertinent to this activity.
- All other planners report no financial relationships relevant to this activity.

The Role of Concentrated Insulins in Diabetes Management

- Insulin, the mainstay of diabetes management
- Type 1 diabetes mellitus (T1DM)
  - Rapid β-cell destruction, insulin deficit
  - Basal plus rapid-acting insulin creates imperfect substitute for endogenous insulin production
- Type 2 diabetes mellitus (T2DM)
  - Insulin resistance
  - Progressive β-cell dysfunction, relative insulin deficit
  - Eventual insulin requirement in many (failure of oral hypoglycemic therapy)
  - Initial insulin requirement in some (critical β-cell failure and glucotoxicity)


Traditional (“U-100”) Basal Insulins

<table>
<thead>
<tr>
<th>Duration Classification</th>
<th>Insulin</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate-acting</td>
<td>NPH</td>
<td>2-4 hr</td>
<td>4-10 hr</td>
<td>Up to 20 hr</td>
</tr>
<tr>
<td>Long-acting</td>
<td>Insulin glargine</td>
<td>1-3 hr</td>
<td>None</td>
<td>24+ hr</td>
</tr>
<tr>
<td></td>
<td>Insulin detemir</td>
<td>1-3 hr</td>
<td>Variable</td>
<td>Dose dependent: 0.1 units/kg: 6 hr 0.2 units/kg: 12 hr 0.4 units/kg: 20 hr 0.8 units/kg: 22-24 hr</td>
</tr>
<tr>
<td></td>
<td>Insulin degludec</td>
<td>1-3 hr</td>
<td>None</td>
<td>24+ hr</td>
</tr>
</tbody>
</table>


Basal Insulin Dosing

- Typical starting dose for insulin naïve:
  - 10 units daily
  - 0.1-0.2 units/kg daily
- Higher insulin resistance = increased doses:
  - 2 units/kg or greater
- As dose of insulin increases, the volume of insulin increases:
  - Unpredictable absorption
  - Increased pain and discomfort
  - Leakage

The Need for Concentrated Insulins

- Increased T2DM
- Insulin resistance increase
- Insulin secretion decline
- Increased insulin dose requirement

Traditional vs. Concentrated Basal Insulins

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional</td>
<td></td>
</tr>
<tr>
<td>NPH (Novolin N, Humulin N)</td>
<td>100 units/mL</td>
</tr>
<tr>
<td>Insulin glargine (Lantus, Basaglar)</td>
<td>100 units/mL</td>
</tr>
<tr>
<td>Insulin degludec (Tresiba)</td>
<td>100 units/mL</td>
</tr>
<tr>
<td>Insulin detemir (Levemir)</td>
<td>100 units/mL</td>
</tr>
<tr>
<td>Concentrated</td>
<td></td>
</tr>
<tr>
<td>Regular (Humulin R U-500)</td>
<td>500 units/mL</td>
</tr>
<tr>
<td>Insulin glargine (Toujeo)</td>
<td>300 units/mL</td>
</tr>
<tr>
<td>Insulin degludec (Tresiba)</td>
<td>200 units/mL</td>
</tr>
</tbody>
</table>

Early insulin initiation in patients with type 2 diabetes has which of the following possible effects?

a. Increases rate of β-cell destruction
b. Decreases insulin sensitivity
c. Potentiates endothelial dysfunction
d. Protects against end-organ damage

Human Insulin Regular U-500

- Human insulin (recombinant DNA origin):
  - 20-mL vials; 10,000 units/vial
  - 3-mL KwikPen; 1,500 units/pen
- Reduced hexamer formation leads to faster dissociation and absorption:
  - Peak: 30 minutes (administer 30 minutes prior to meals)
  - Duration: ~7 hours (BID or TID dosing)
  - T1/2: 4 hours
- Appropriate for patients requiring > 200 units of insulin/day

U-500 Initiation Trial

- Design: 24-week, open-label, randomized trial
- Purpose: To compare BID and TID U-500 insulin for replacement of high-dose U-100 insulin
- Population:
  - T2DM (~15 years duration) with A1c ≥7.5% and ≤12.0% (mean 8.7%)
  - 200-600 units of U-100 insulin a day (mean 287.5 units/day)
  - Body mass index ≥25 kg/m² (mean 41.9 kg/m²)
  - 18-75 years of age (mean 55.4 years)
U-500 Initiation Trial: Hemoglobin A1c (A1c) Reduction

- Baseline 8.7%
  - BID: -1.3% (7.4%)
  - TID: -1.2% (7.5%)
- Difference in least squares mean A1c change from baseline was -0.1% (95% CI -0.33% to 0.12%)
  - Clinical equivalence established (noninferiority margin 0.4%)

Adverse Effects to Expect:
Weight gain: 4.9 kg
Hypoglycemia: ~ 0.5 episodes/person/week


U-500 Initiation Trial: How to Titrate U-500

<table>
<thead>
<tr>
<th>TID</th>
<th>BID</th>
<th>SMBG Value to Base Adjustment From</th>
<th>SMBG Value to Base Adjustment From</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-breakfast</td>
<td>Pre-lunch</td>
</tr>
<tr>
<td>BID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/50</td>
<td>+5%</td>
<td>Max Daily Increase: 30%</td>
<td>Max Daily Increase: 20%</td>
</tr>
<tr>
<td>70-130</td>
<td>No change</td>
<td>Adjustments based on 3-day mean except lows (only 1 required); 3 AM checks when increase in last 48 hr</td>
<td></td>
</tr>
<tr>
<td>131-180</td>
<td>+10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>181-200</td>
<td>+15%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;200</td>
<td>+15%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RB is a 65-year-old woman with T2DM who uses a U-500 insulin pen to inject U-500. She is currently receiving 250 units before breakfast and 175 units before dinner. Her A1c is 9.2%, and her self-monitored blood glucose (SMBG) log shows average pre-breakfast readings of 210 and average pre-lunch readings of 180. Which of the following describes the most appropriate adjustment plan for RB’s U-500 at this time?

a. Increase morning dose by 10%, increase evening dose by 15%
b. Increase morning dose by 15%, increase evening dose by 10%
c. Increase morning dose by 5%, increase evening dose by 15%
d. Increase morning dose by 15%, increase evening dose by 5%

Insulin Degludec

- Long-acting human insulin analog
  - 200 units/mL (U-200)
  - 3-mL FlexTouch pens; 600 units/pen
- Multihexamer chain formation following injection, zinc depletes and individual hexamers dissociate into monomers allowing degludec to be absorbed into the blood
  - Peak: None
  - Duration: 42 hours (daily dosing any time of day)
  - T1/2: 25 hours

Insulin Degludec: BEGIN LOW VOLUME Trial

- Design: 26-week, open label, treat to target trial
- Purpose: To compare the safety and efficacy of insulin degludec 200 units/mL with insulin glargine 100 units/mL
- Population
  - 457 insulin naive patients with T2DM
  - Mean body mass index: 32.4 kg/m²
  - Concomitant treatment with metformin +/- dipeptidyl peptidase-4 inhibitor

BEGIN LOW VOLUME Trial: Results

- A1c (baseline 8.3%)
  - Insulin degludec: 200 units/mL: -1.3% (7%)
  - Insulin glargine 100 units/mL: -1.3% (7%)
- Hypoglycemia
  - Insulin degludec: 1.22 episodes/patient-year (0.18 nocturnal)
  - Insulin glargine: 1.42 episodes/patient-year (0.28 nocturnal)
- Weight gain
  - Insulin degludec: 1.9 kg
  - Insulin glargine: 1.5 kg
- Mean daily dose 11% lower with degludec

Which of the following statements comparing the effects of insulin degludec U-200 with insulin glargine U-100 is correct?

a. Improved A1c control with degludec
b. Smaller daily dose required with glargine
c. More weight gain with degludec
d. Lower rates of hypoglycemia with glargine

Insulin Glargine (U-300)

- Long-acting human insulin analog
  - 300 units/mL (U-300)
  - 1.5-mL SoloStar pens; 450 units/pen
- Acidic solution neutralized after subcutaneous injection forming a depot from which glargine is slowly released
  - Peak: None
  - Duration: >30 hours (daily dosing any time of day)
  - T1/2: 18-19 hours

Insulin Glargine (U-300): A1c Reduction

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Patient Population</th>
<th>A1c Baseline</th>
<th>A1c Reduction (Comparator)</th>
<th>A1c Reduction (Glargine U-300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glargine U-100p</td>
<td>T1DM, poor control</td>
<td>8.1%</td>
<td>-0.4%</td>
<td>-0.4%</td>
</tr>
<tr>
<td>Glargine U-100p</td>
<td>T2DM, poor control, basal insulin +/- metformin</td>
<td>8.2%</td>
<td>-0.8%</td>
<td>-0.8%</td>
</tr>
<tr>
<td>Glargine U-100p</td>
<td>T2DM, poor control, basal insulin plus metformin, DPP-4 inhibitor, T2D</td>
<td>8.2%</td>
<td>-0.56%</td>
<td>-0.57%</td>
</tr>
<tr>
<td>Glargine U-100p</td>
<td>T2DM, poor control; oral antidiabetic agents alone</td>
<td>8.5%</td>
<td>-1.5%</td>
<td>-1.5%</td>
</tr>
</tbody>
</table>

Trend: Higher TDD with U-300 than U-100 insulin glargine 11-15% T2DM and 17.5% T1DM

DPP-4 = dipeptidyl peptidase 4, T2D = type 2 diabetes

See page 15 for enlarged view
Insulin Glargine U-300: Adverse Effects

- Weight gain compared with U-100
  - -0.6 kg (T1DM)
  - +0.2 kg (T2DM)
- Hypoglycemia
  - Any time of day
    - U-300: 15.22 events per participant-year
    - U-100: 17.73 events per participant-year
      - RR 0.86; 95% CI 0.77-0.97
  - Nocturnal
    - U-300: 2.1 events (annualized rate)
    - U-100: 3.06 events (annualized rate)
      - RR 0.69; 95% CI 0.57-0.84

RR = relative risk, CI = confidence interval

Which of the following accurately describes how insulin glargine U-300 compares with insulin glargine U-100?

a. Less hypoglycemia
b. Lower total daily dose requirement
c. Higher rates of A1c goal achievement
d. Comparable weight loss in patients with T2DM

Insulin Glargine U-300: Dosing Points

- New start
  - Weight (kg) x 0.2 = TDD (units) of U-300 (T2DM)
  - 1/3 to 1/2 TDD with TDD = 0.2 to 0.4 units/kg (T1DM)
- Dose conversion from basal insulin: 1 to 1
- Dose conversion from twice-daily NPH: 80% of total daily NPH dose
- Titrated every 3-4 days
  - Based on fasting glucose
  - Titrated over 12 weeks in EDITION trials

Ensuring Safe Use of Concentrated Insulins in the Inpatient Setting

Concentrated Insulins: Formulary Management

- Pen and vial
  - Insulin regular (U-500)
- Pen only
  - Insulin degludec (U-200)
  - Insulin lispro (U-200)
  - Insulin glargine (U-300)

Formulary Decisions
- Efficacy
- Safety
- Cost

© 2016 American Society of Health-System Pharmacists
Insulin Pen Use Safety Recap:

<table>
<thead>
<tr>
<th>Safety Requirement</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct administration technique</td>
<td>Avoid hypoglycemia or hyperglycemia due to improper dose delivery</td>
</tr>
<tr>
<td>Pen used in one patient only, not shared, even when pen needle is changed</td>
<td>Evidence for biological contamination, Misuse in healthcare settings, Bloodborne infection transmission risk (HIV, hepatitis b, hepatitis C)</td>
</tr>
</tbody>
</table>


Insulin Pen Safety: Where to Start, Where to Improve!

• Education
  – CPE webinar
• Resource center
  – External resources
  – Articles and guidelines
• Tool kit
  – Safety strategies
  – Sample documents
  – Outcome measures


Best Practices for Insulin Pen Use in the Hospital

• 12-member interprofessional expert panel
• Delphi technique
• Result
  – 35 best‐practice statements for safe use of insulin pens in hospitals
  – Actionable and feasible

Haines ST et al. AJHP. 2016; 73(suppl 5):S4‐16.

Insulin Pen Policy & Procedure: Defining Expectations

• Policy statement
  – Insulin pens are for single patient use only, and never shared, even if pen needle is changed
• Procedure
  – Preparation
    • By pharmacy
    • Patient‐specific labeling
  – Storage
    • Patient‐specific location
  – Administration
    • Patient identification
    • Correct technique
    • Prompt return to patient‐specific location
  – Disposal
    • Prompt, once discontinued or patient discharged


Strategies to Prevent Insulin Pen Sharing

• Tamper‐evident tape over cap/barrel
• Label securely affixed to barrel, with patient identifiers
• Patient‐specific storage location
• Incorporate barcode scanning technology
  – Right insulin
  – Pen for right patient


Barcoding Solutions: Right Pen, Right Patient

• Recommendations
  – Incorporate scan of manufacturer barcode during dispensing process
    • Verifies right insulin product
  – Affix label with patient‐specific barcode to pen barrel, covering manufacturer barcode
    • Nurse scan at bedside verifies pen is for right patient

© 2016 American Society of Health‐System Pharmacists
Insulin Pen Administration Technique

- How many steps?
- Define expectations
  - Policy and procedure
  - Staff education
- Monitor practice
  - Knowledge surveys
  - Direct observations

Monitoring Appropriate Pen Use

- Storage and labeling audits
  - Extra pens, unlabeled pens may indicate problem
- Barcode medication administration reports
  - Scanning compliance
  - “Wrong-pen” alerts…… what happened next?
  - Scanning incorrect pen?
  - Manual documentation without scanning correct pen?

Designing the System for Safety: Transitions of Care

- Educate and empower med history clinicians!

  Home medication list
  - Insulin glargine 22 units SQ at bedtime
  - Insulin lispro 6 units SQ three times daily with meals

- What is the patient taking?
  - Lantus (U-100 vial or pen) or Toujeo (U-300 pen)?
  - Humalog… (U-100 or U-200, vial or pen)?

- Recommendation
  - Provide detailed insulin product list (cards or online)

Use of Pens as a Multidose Vial: New Spin on Old Problem

- Use of pens as a multidose vial can introduce air and result in inaccurate dose delivery
  - Not advised unless emergency or pen malfunction

Use of Pens as a Multidose Vial: New Spin on Old Problem

- Outpatient report (ISMP)
  - Patient using insulin glargine U-100 vial & syringe switched to U-300 pen. Used leftover U-100 syringes to draw up “100 unit” dose from pen cartridge.
    - Result: 300 units given; hypoglycemia & hospitalization
- Inpatient concern
  - Nurse unfamiliar with pen use or without pen needles
  - Use “familiar” U-100 syringe to draw up dose?
- Recommendations
  - Supply pen needles, educate, reinforce, monitor
Insulin Regular (U-500): Then and Now

- 1952 - 2015
  - Vial and syringe, but what syringe?
    - Insulin U-100 (U-100 units) vs. tuberculin (mL)
- 2016
  - Pen delivery device
  - Syringe designed to measure U-500 insulin

Considering Concentrated Pens on Formulary: A Tale of Two Hospitals

<table>
<thead>
<tr>
<th></th>
<th>Hospital A (With Pens)</th>
<th>Hospital B (No Pens)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff education</td>
<td>- Staff familiarity</td>
<td>- Staff unfamiliar</td>
</tr>
<tr>
<td></td>
<td>- Policy and procedure in place</td>
<td>- Policy and procedure and staff education must be developed</td>
</tr>
<tr>
<td></td>
<td>- Staff education in place</td>
<td>(Low usage frequency = questionable competency?)</td>
</tr>
<tr>
<td>System safety measures</td>
<td>- In place..... (hopefully!)</td>
<td>- Must be prospectively developed</td>
</tr>
<tr>
<td>Pen needle supply</td>
<td>- Hospital provides to all patient care units</td>
<td>- Hospital-provided – feasible?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Must pharmacy dispense?)</td>
</tr>
</tbody>
</table>

Which of the following is true regarding the addition of concentrated insulin pens to formulary?

a. Staff training on appropriate use is unnecessary
b. May be less practical in hospitals without pens
c. Newer pens lack infection transmission risk
d. Replaces need for U-100 insulin on formulary

U-100 Insulin and Tuberculin Syringes: Extinct?

- Vial approved only with U-500 insulin syringe
  - “Patients using the vial must be prescribed the U-500 insulin syringe to avoid medication errors.”
  - “Use only a U-500 insulin syringe with U-500 vial.”
- Dose and measurement conversions removed for U-100 and tuberculin syringes

U-100 Insulin and Tuberculin Syringes: Extinct? Not Quite!

- Role of the pharmacist: U-500 patient interview
  - New start or continuation?
  - If continuation, confirm:
    - Pen or vial/syringe at home?
    - Dose and measurement method?
      - Patient explanation and demonstration
    - Inpatient order consistent with home regimen?
      - If “no”... Notify prescriber

© 2016 American Society of Health-System Pharmacists
Designing the System for U-500 Insulin Safety

• Policy and procedure
  – Store vial in pharmacy, segregated
  – Restrict U-500 syringe purchases to pharmacy
  – Require pharmacy and endocrinology consultations
  – Formulation-specific dispensing
    • If vial: Dose-specific syringe directly to nurse
    • If pen: Approved patient-specific storage
  – Double checks

System
  – Order sets or panes
  – Insulin, consults, labs
  – Route, dose, frequency constraints
  – Clinician reminders
  – Transition information
    • Best-practice reminders
    • Discharge patient education

See page 16 for enlarged view

See page 17 for enlarged view

Key Takeaways

• Key Takeaway #1
  – Early insulin therapy may be required by some patients to achieve glycemic control. Concentrated insulins offer a mechanism for meeting the large insulin dosing requirements of some patients using a smaller injection volume.

• Key Takeaway #2
  – Some other key benefits of concentrated basal insulins include pen injector availability, reduced hypoglycemia, less weight gain (glargine U-300), daily dosing (degludec U-200 and glargine U-300).

• Key Takeaway #3
  – Pharmacists have a role in ensuring safe transitions of care and administration of concentrated insulins by establishing policies and procedures, good communication among patients and the interprofessional healthcare team, and supportive system design.

What will you do as a follow up to today's program? (Select all that apply.)

a. Identify patients who can potentially benefit from switching
b. Recommend dose when transitioning from U-100 to concentrated
c. Discuss concentrated insulins with interprofessional team
d. Ensure safe transition of care when patient receiving concentrated insulin
e. Review hospital’s P&P for ensuring insulin pen safety
Insulin Glargine (U-300): A1c Reduction

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Patient Population</th>
<th>A1c Baseline</th>
<th>A1c Reduction (Comparator)</th>
<th>A1c Reduction (Glargine U-300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glargine U-100¹</td>
<td>T1DM; poor control</td>
<td>8.1%</td>
<td>-0.44%</td>
<td>-0.4%</td>
</tr>
<tr>
<td>Glargine U-100²</td>
<td>T2DM; poor control; basal/bolus insulin &gt;42 units +/- metformin</td>
<td>8.2%</td>
<td>-0.8%</td>
<td>-0.8%</td>
</tr>
<tr>
<td>Glargine U-100³</td>
<td>T2DM; poor control; basal insulin plus metformin, DPP-4 inhibitor, TZD</td>
<td>8.2%</td>
<td>-0.56%</td>
<td>-0.57%</td>
</tr>
<tr>
<td>Glargine U-100⁴</td>
<td>T2DM; poor control; oral antidiabetic agents alone</td>
<td>8.5%</td>
<td>-1.5%</td>
<td>-1.5%</td>
</tr>
</tbody>
</table>

Trend: Higher TDD with U-300 than U-100 insulin glargine
11-15% T2DM and 17.5% T1DM


Insulin Pen Administration Technique

- How many steps?
- Define expectations
  - Policy and procedure
  - Staff education
- Monitor practice
  - Knowledge surveys
  - Direct observations

Designing the System for Safety: Transitions of Care

- 100, 200, 300, 500 = Dose or concentration?
  - Home medication list
  - eMAR
  - Discharge prescription

- **ISMP Recommendations**
  - First line: drug name, patient-specific dose, directions
  - Second line: concentration

<table>
<thead>
<tr>
<th>U-500 Dose (Actual Units)</th>
<th>U-500 Pen (Actual Units)</th>
<th>U-500 Syringe (Actual Units)</th>
<th>U-100 Syringe (U-100 Unit Markings)</th>
<th>Tuberculin Syringe (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>25</td>
<td>25</td>
<td>5</td>
<td>0.05</td>
</tr>
<tr>
<td>50</td>
<td>50</td>
<td>50</td>
<td>10</td>
<td>0.10</td>
</tr>
<tr>
<td>75</td>
<td>75</td>
<td>75</td>
<td>15</td>
<td>0.15</td>
</tr>
<tr>
<td>100</td>
<td>100</td>
<td>100</td>
<td>20</td>
<td>0.20</td>
</tr>
<tr>
<td>125</td>
<td>125</td>
<td>125</td>
<td>25</td>
<td>0.25</td>
</tr>
<tr>
<td>150</td>
<td>150</td>
<td>150</td>
<td>30</td>
<td>0.30</td>
</tr>
<tr>
<td>175</td>
<td>175</td>
<td>175</td>
<td>35</td>
<td>0.35</td>
</tr>
<tr>
<td>200</td>
<td>200</td>
<td>200</td>
<td>40</td>
<td>0.40</td>
</tr>
<tr>
<td>225</td>
<td>225</td>
<td>225</td>
<td>45</td>
<td>0.45</td>
</tr>
<tr>
<td>250</td>
<td>250</td>
<td>250</td>
<td>50</td>
<td>0.50</td>
</tr>
<tr>
<td>275</td>
<td>275</td>
<td>--</td>
<td>55</td>
<td>0.55</td>
</tr>
<tr>
<td>300</td>
<td>300</td>
<td>--</td>
<td>60</td>
<td>0.60</td>
</tr>
<tr>
<td>325</td>
<td>--</td>
<td>--</td>
<td>65</td>
<td>0.65</td>
</tr>
<tr>
<td>350</td>
<td>--</td>
<td>--</td>
<td>70</td>
<td>0.70</td>
</tr>
<tr>
<td>375</td>
<td>--</td>
<td>--</td>
<td>75</td>
<td>0.75</td>
</tr>
<tr>
<td>400</td>
<td>--</td>
<td>--</td>
<td>80</td>
<td>0.80</td>
</tr>
<tr>
<td>425</td>
<td>--</td>
<td>--</td>
<td>85</td>
<td>0.85</td>
</tr>
<tr>
<td>450</td>
<td>--</td>
<td>--</td>
<td>90</td>
<td>0.90</td>
</tr>
<tr>
<td>475</td>
<td>--</td>
<td>--</td>
<td>95</td>
<td>0.95</td>
</tr>
<tr>
<td>500</td>
<td>--</td>
<td>--</td>
<td>100</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Designing the System for Safety: Discharge

- Prompt insulin regular U-500 syringe prescribing
  - Discharge order set
    - “Insulin Syringe (Concentrated U-500) 31G, 6mm x 0.5mL”
Assessment Test

This assessment test has been provided as a study aid only. Follow the prompts at the end of the presentation to claim credit. Credit must be claimed within 60 days of completing the activity.

1. Early insulin initiation in patients with type 2 diabetes mellitus has which of the following possible effects?
   a. Increases rate of β-cell destruction.
   b. Decreases insulin sensitivity.
   c. Potentiates endothelial dysfunction.
   d. Protects against end-organ damage.

2. Which of the following patients would be appropriate to consider for U-500 insulin initiation?
   a. T1DM with A1c of 9.2% on 80 units of insulin per day.
   b. T1DM with A1c of 7.2% on 220 units of insulin per day.
   c. T2DM with A1c of 9.8% on metformin 1000 mg twice daily and liraglutide 1.8 mg daily.
   d. T2DM with A1c of 8.6% on metformin 1000 mg twice daily and insulin glargine U-100 100 units daily.

3. RB is a 65-year-old woman with T2DM who uses a U-500 insulin pen to inject U-500. She is currently receiving 250 units before breakfast and 175 units before dinner. Her A1c is 9.2%, and her self-monitored blood glucose (SMBG) log shows average pre-breakfast readings of 210 and average pre-lunch readings of 180. Which of the following describes the most appropriate adjustment plan for RB's U-500 at this time?
   a. Increase morning dose by 10%, increase evening dose by 15%.
   b. Increase morning dose by 15%, increase evening dose by 10%.
   c. Increase morning dose by 5%, increase evening dose by 15%.
   d. Increase morning dose by 15%, increase evening dose by 5%.

4. Which of the following accurately describes how insulin degludec U-200 compares with insulin glargine U-100?
   a. Improved A1c control.
   b. Higher daily dose requirement.
   c. More weight gain.
   d. Higher rate of hypoglycemia.

5. Which of the following accurately describes how insulin glargine U-300 compares with insulin glargine U-100?
   a. Less hypoglycemia.
   b. Lower total daily dose requirement.
   c. Higher rates of A1c goal achievement.
   d. Comparable weight loss in patients with T2DM.
6. Pharmacists can help ensure the safe use of concentrated insulins in the hospital by establishing a policy and procedure that establishes expectations for standardized care using these products.
   a. True.
   b. False.

7. Scanning the insulin pen manufacturer barcode when dispensing, followed by scanning the order-specific barcode before administration can
   a. Help track the location of a dispensed insulin pen.
   b. Verify correct insulin dispensed and correct patient’s pen used to administer.
   c. Ensure insulin pens are reordered before empty.
   d. Result in duplicate scans on barcode administration reports.

8. If a U-100 insulin syringe is used to withdraw a dose from a concentrated insulin pen cartridge, which patient safety risk may occur that is unique to concentrated insulins?
   a. Inaccurate dose delivery caused by introduction of air.
   b. A significant insulin underdose.
   c. A significant insulin overdose.
   d. Increased risk of needlestick injury.

9. Which of the following safety risks with insulin regular U-500 is mitigated by introduction of a pen and a U-500 syringe?
   a. Dosing confusion between units and volume measures.
   b. Infection transmission risk.
   c. Needlestick injury.
   d. Dispensing of wrong insulin product.