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

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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.

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.

Webinar Information

Visit www.onepenonepatient.org/webinar to find

- Webinar registration link
- Group viewing information and technical requirements
- CPE webinar processing information

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
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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

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- 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**
    - On-demand activity based on live webinar (1 hour CPE, available after November 1, 2016) – Note that individuals who claim CPE credit for live webinar are ineligible to claim credit for the on-demand activity.
    - 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, available after October 17, 2016)
        - 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)

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

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- Describe the benefits and limitations of the newer concentrated insulins
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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)

Lamos EM et al. *Ther Clin Risk Manag*. 2016; 12:389-400.

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

Owens DR. *Diabetes Technol Ther*. 2013; 15:776-85.

Traditional ("U-100") Basal Insulins

Duration Classification	Insulin	Onset	Peak	Duration
Intermediate-acting	NPH	2-4 hr	4-10 hr	Up to 20 hr
Long-acting	Insulin glargine	1-3 hr	None	24+ hr
	Insulin detemir	1-3 hr	Variable	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
	Insulin degludec	1-3 hr	None	24+ hr

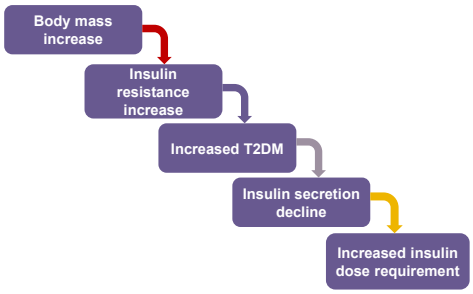
Crump T. Insulin chart. www.straighthealthcare.com/insulin-chart.html (accessed 2016 Aug 25).

Basal Insulin Dosing

- Typical starting dose for insulin naïve
  - 10 units daily
    or
  - 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

Lamos EM et al. *Ther Clin Risk Manag*. 2016; 12:389-400.
Crump T. Insulin chart. www.straighthealthcare.com/insulin-chart.html (accessed 2016 Aug 25).

The Need for Concentrated Insulins



Lamos EM et al. *Ther Clin Risk Manag*. 2016; 12:389-400.

Traditional vs. Concentrated Basal Insulins

	Insulin	Concentration
Traditional	NPH (Novolin N, Humulin N)	100 units/mL
	Insulin glargine (Lantus, Basaglar)	100 units/mL
	Insulin degludec (Tresiba)	100 units/mL
	Insulin detemir (Levemir)	100 units/mL
Concentrated	Regular (Humulin R U-500)	500 units/mL
	Insulin glargine (Toujeo)	300 units/mL
	Insulin degludec (Tresiba)	200 units/mL

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)
  - $T_{1/2}$: 4 hours
- Appropriate for patients requiring > 200 units of insulin/day

Lamos EM et al. *Ther Clin Risk Manag*. 2016; 12:389-400.

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/m^2 (mean 41.9 kg/m^2)
  - 18-75 years of age (mean 55.4 years)

Hood RC et al. *Endocr Pract*. 2015; 21:782-93.

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

Hood RC et al. *Endocr Pract*. 2015; 21:782-93.
Reutrakul S et al. *J Diabetes Sci Technol*. 2012; 6:412-20.
Dailey AM et al. *Diabetes Res Clin Pract*. 2012; 95:340-4.

U-500 Initiation Trial: Initiating U-500

- Step 1: Determining Total Daily Dose (TDD) of U-500

1 Month Prior: A1c >8% *And* Within 1 Week Prior: SMBG ≥183 mg/dL	1 Month Prior: A1c ≤8% *Or* Within 1 Week Prior: SMBG <183mg/dL
TDD: 100% of U-100 dose	TDD: 80% of U-100 dose

- Step 2: Determining Dose Proportions

	Before Breakfast	Before Lunch	Before Dinner
BID	60%	0%	40%
TID	40%	30%	30%

SMBG: Self-monitored blood glucose

Hood RC et al. *Endocr Pract*. 2015; 21:782-93.

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

TID

Dose to Adjust	SMBG Value to Base Adjustment From
Pre-breakfast	Pre-lunch
Pre-lunch	Pre-dinner
Pre-dinner	Fasting

BID

Dose to Adjust	SMBG Value to Base Adjustment From
Pre-breakfast	Pre-lunch
Pre-dinner	Fasting

SMBG (mg/dL)	Dose Titration (round to nearest 5 unit increment)
<70	-10%
70-130	No change
131-180	+5%
181-200	+10%
>200	+15%

Max Daily Increase: 30%

Max Daily Decrease: 20%

Adjustments based on 3-day mean except lows (only 1 required); 3 AM checks when increase in last 48 hr

Hood RC et al. *Endocr Pract*. 2015; 21:782-93.

Which of the following patients would be appropriate to consider for U-500 insulin initiation?

a. T1DM, A1c 9.2% on 80 units of insulin per day
b. T1DM, A1c 7.2% on 220 units of insulin per day
c. T2DM, A1c 9.8% on metformin 1000 mg BID + liraglutide 1.8 mg daily
d. T2DM, A1c 8.6% on metformin 1000 mg BID + insulin glargine U-100 100 units daily

RB is a 65-year-old woman with T2DM who currently injects U-500 50 units before breakfast and 35 units before dinner. Her A1c is 9.2%, and her SMBG log shows average pre-breakfast readings of 210 and average pre-dinner readings of 180. Which of the following describes the most appropriate adjustment plan for RB's U-500 at this time?

a. 55 units before breakfast, 47 units before dinner
b. 47 units before breakfast, 55 units before dinner
c. 55 units before breakfast, 45 units before dinner
d. 45 units before breakfast, 55 units before dinner

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)
  - $T_{1/2}$: 25 hours

Lamos EM et al. *Ther Clin Risk Manag*. 2016; 12:389-400.

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 naïve patients with T2DM
  - Mean body mass index: 32.4 kg/m^2
  - Concomitant treatment with metformin +/- dipeptidyl peptidase-4 inhibitor

Gough SC et al. *Diabetes Care*. 2013; 36:2536-42.

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

Gough SC et al. *Diabetes Care*. 2013; 36:2536-42.

Insulin Degludec: Dosing Points

- New start
  - TDD 10 units/day (T2DM)
  - 1/3 to 1/2 TDD with TDD = 0.2 to 0.4 units/kg (T1DM)
- Dose conversion from long- or intermediate-acting insulin: 1 to 1
- Titrate every 3-4 days
  - Based on fasting glucose goal of <90 mg/dL in BEGIN LOW VOLUME trial

Gough SC et al. *Diabetes Care*. 2013; 36:2536-42.

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)
  - $T_{1/2}$: 18-19 hours

Lamos EM et al. *Ther Clin Risk Manag*. 2016; 12:389-400.

Insulin Glargine (U-300): A1c Reduction

Comparator	Patient Population	A1c Baseline	A1c Reduction (Comparator)	A1c Reduction (Glargine U-300)
Glargine U-100[1]	T1DM; poor control	8.1%	-0.44%	-0.4%
Glargine U-100[2]	T2DM; poor control; basal/bolus insulin >42 units +/- metformin	8.2%	-0.8%	-0.8%
Glargine U-100[3]	T2DM; poor control; basal insulin plus metformin, DPP-4 inhibitor, TZD	8.2%	-0.56%	-0.57%
Glargine U-100[4]	T2DM; poor control; oral antidiabetic agents alone	8.5%	-1.5%	-1.5%

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

DPP-4 = dipeptidyl peptidase 4, TZD = thiazolidinedione

[1]Home P et al. *Diabetes*. 2014; 63(suppl 1A):LB19; [2]Riddle MC et al. *Diabetes Care*. 2014; 37:2755-62; [3]Yki-Jarvinen H et al. *Diabetes Care*. 2014; 37:3235-43; [4]Bolli GB et al. *Diabetes Obes Metab*. 2015; 17:386-94.

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

Lamos EM et al. *Ther Clin Risk Manag*. 2016; 12:389-400.
Ritzel R et al. *Diabetes Obes Metab*. 2015; 17:859-67.

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
- Titrate every 3-4 days
  - Based on fasting glucose
  - Titrated over 12 weeks in EDITION trials

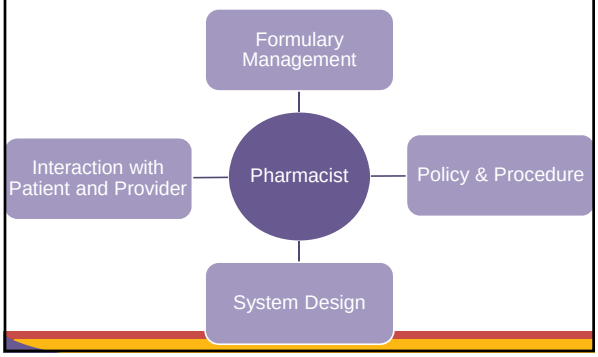
Home P et al. (EDITION 4). *Diabetes*. 2014; 63(suppl 1A):LB19.
Riddle MC et al. (EDITION 1). *Diabetes Care*. 2014; 37:2755-62.
Yki-Jarvinen H et al. (EDITION 2). *Diabetes Care*. 2014; 37:3235-43.
Bolli GB et al. (EDITION 3). *Diabetes Obes Metab*. 2015; 17:386-94.

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

Ensuring Safe Use of Concentrated Insulins in the Inpatient Setting

Pharmacist Role in Ensuring Inpatient Concentrated Insulin Safety



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

X ~~Pen or vial~~

Am J Health-Syst Pharm. 2008; 65:1272-83.
Gray et al. *Pharmacotherapy*. 2005; 25:1666-80.

Insulin Pen Use Safety Recap:

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

http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm133352.htm

www.cdc.gov/injectionsafety/clinical-reminders/insulin-pens.html (accessed 2016 Aug 25).

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

www.onepenonepatient.org (accessed 2016 Aug 25).

Best Practices for Insulin Pen Use in the Hospital

AJHP

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

- Ordering and documenting
- Labeling and dispensing
- Storing
- Administering
- Policies and procedures
- Monitoring, planning and evaluating

Haines ST et al. *AJHP.* 2016; 73(suppl 5): in press.

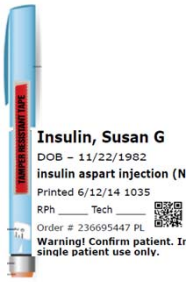
Insulin Pen Policy & Procedure: Defining Expectations

- 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

www.onepenonepatient.org/toolkit (accessed 2016 Aug 25).

Strategies to Prevent Insulin Pen Sharing

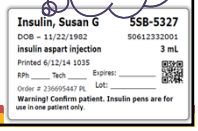
- Tamper-evident tape over cap/barrel
- Label securely affixed to barrel, with patient identifiers
- Patient-specific storage location
- Incorporate barcode scanning technology
  - Right insulin
  - Pen for right patient



www.onepenonepatient.org/toolkit (accessed 2016 Aug 25).

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*



Insulin Pen Administration Technique

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

Step	Step Performed
1	**Retrieves** insulin pen device from hospital-approved patient-specific storage area
2	**Expiration** is documented on label
3	**Obtains** replacement pen if expiration date is not documented or if expired*
4	**Displays** use of proper hand hygiene prior to patient contact
5	**Performs** patient identification (according to hospital policy)
6	**Checks** medication label
7	**Scans** the patient's ID band and the insulin pen bar code (prospectively, prior to administration) [when applicable]*
8	**Mixes** insulin by gently tilting pen device back and forth 8-10 times or rolling in palm of hands (**NPH insulin only**)*
9	**Swabs** rubber stopper with alcohol swab
10	**Attaches** new disposable needle onto the pen
11	**Primes** pen before injection (e.g. dials 2 units on the dose selector, points needle up so that bubbles are forced to top, and firmly presses plunger until drop of insulin appears; repeat if needed until drop of insulin appears; if no drop appears after 6 attempts, changes pen device)
12	**Dials** correct dose (e.g. based on patient-specific order)
13	**Selects** appropriate injection site (e.g. abdomen, back of arm, thigh)
14	**Pinches** fold of skin* at the injection site, **holds** pen at 90 degree angle* to skin, and **inserts** pen needle all the way into the skin
15	**Lets go** of skin fold and **injects** the entire dose of insulin
16	**Keeps** plunger pressed and **holds** against the skin for at least 5 seconds after injection is given
17	**Removes** and **discards** needle in appropriate sharps container
18	**Returns** pen device to hospital-approved patient-specific storage area in a timely manner (e.g. within 15 minutes of injection or prior to giving medications to another patient)

www.onepenonepatient.org/toolkit (accessed 2016 Aug 25).
Lutz MF et al. *AJHP*. 2016; 73(suppl 5): in press.

See page 15 for enlarged view

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?
    - Scan correct pen?
    - Manual documentation without scanning correct pen?

www.onepenonepatient.org/toolkit (accessed 2016 Aug 25).
Lutz MF et al. *AJHP*. 2016; 73(suppl 5): in press.

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)

Designing the System for Safety: Transitions of Care

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

Insulin Lispro, Human, 100 UNIT/ML SQ Solution Pen-injector
inject 8 Units into the skin 3 times daily with meals
Insulin Degludec 200 UNIT/ML SQ Solution Pen-injector
inject 26 Units into the skin once daily.
Insulin Glargine 300 UNIT/ML SQ Solution Pen-injector
inject 22 Units into the skin once daily.
INSULIN REGULAR HUMAN 500 UNIT/ML SQ Solution
inject 110 Units into the skin twice daily before breakfast and dinner.

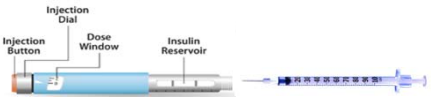
- ISMP Recommendations
  - First line: drug name, patient-specific dose, directions
  - Second line: concentration

ISMP Newsletter Acute Care Edition. January 28, 2016.
ISMP Newsletter Acute Care Edition. March 10, 2016.

See page 16 for enlarged view

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

Cohen MR. *Am J Health-Syst Pharm*. 2010; 67(suppl 8):S17-21.
Grissinger M. *P & T*. 2010; 35:245, 266.
Grissinger M. *P & T*. 2011; 36:615-6.

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

ISMP Newsletter Acute Care Edition. June 16, 2016.

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

Insulin Regular (U-500): Now

- Pen
  - 3 mL (1,500 units)
  - 5-unit increments
    - 5 – 300 units per injection

- Vial and U-500 syringe
  - 20 mL (10,000 units)
  - 5-unit increments
    - 5 – 250 units per injection

No safety needle?

KEY CONCEPT

Actual doses displayed: Conversions eliminated!

ISMP Newsletter Acute Care Edition. July 14, 2016 (permission to use image).
Humulin R U-500 prescribing information. Indianapolis, IN: Eli Lilly and Company. July 2016.

Considering Concentrated Pens on Formulary: A Tale of Two Hospitals

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

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

Humulin R U-500 prescribing information. Indianapolis, IN: Eli Lilly and Company. July 2016.

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

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

See page 16 for enlarged view

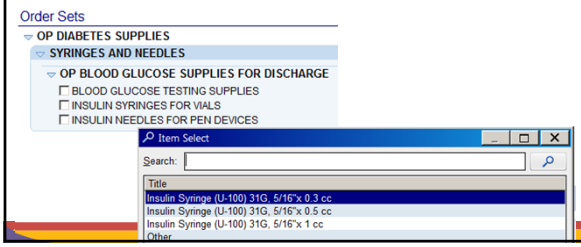
Designing the System for U-500 Insulin Safety

- Policy and procedure
  - Store vial in pharmacy, segregated
  - Restrict U-500 syringe purchases to pharmacy
  - Require pharmacy and endocrinology consults
  - Formulation-specific dispensing
    - If vial: Dose-specific syringe directly to nurse
    - If pen: Approved patient-specific storage
  - Double checks
- System
  - Order sets or panels
    - Insulin, consults, labs
  - Route, dose, frequency constraints
  - Clinician reminders
  - Transition information
    - Best-practice reminders
    - Discharge patient education

www.onepenonepatient.org/resources (accessed 2016 Aug 25).
ISMP Newsletter Acute Care Edition. May 5, 2016.

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"



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 TOC when patient receiving concentrated insulin
e. Review hospital's P&P for ensuring insulin pen safety

Insulin Glargine (U-300): A1c Reduction

Comparator	Patient Population	A1c Baseline	A1c Reduction (Comparator)	A1c Reduction (Glargine U-300)
Glargine U-100[1]	T1DM; poor control	8.1%	-0.44%	-0.4%
Glargine U-100[2]	T2DM; poor control; basal/bolus insulin >42 units +/- metformin	8.2%	-0.8%	-0.8%
Glargine U-100[3]	T2DM; poor control; basal insulin plus metformin, DPP-4 inhibitor, TZD	8.2%	-0.56%	-0.57%
Glargine U-100[4]	T2DM; poor control; oral antidiabetic agents alone	8.5%	-1.5%	-1.5%

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

DPP-4 = dipeptidyl peptidase 4, TZD = thiazolidinedione

[1]Home P et al. *Diabetes*. 2014; 63(suppl 1A):LB19; [2]Riddle MC et al. *Diabetes Care*. 2014; 37:2755-62; [3]Yki-Jarvinen H et al. *Diabetes Care*. 2014; 37:3235-43; [4]Bolli GB et al. *Diabetes Obes Metab*. 2015; 17:386-94.

Insulin Pen Administration Technique

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

Step	Step Performed
1	**Retrieves** insulin pen device from hospital-approved patient-specific storage area
2	**Expiration** is documented on label
3	**Obtains** replacement pen if expiration date is not documented or if expired*
4	**Displays** use of proper hand hygiene prior to patient contact
5	**Performs** patient identification (according to hospital policy)
6	**Checks** medication label
7	**Scans** the patient's ID band and the insulin pen bar code (prospectively, prior to administration) [when applicable]*
8	**Mixes** insulin by gently tilting pen device back and forth 8-10 times or rolling in palm of hands (**NPH insulin only**)*
9	**Swabs** rubber stopper with alcohol swab
10	**Attaches** new disposable needle onto the pen
11	**Primes** pen before injection (e.g. dials 2 units on the dose selector, points needle up so that bubbles are forced to top, and firmly presses plunger until drop of insulin appears; repeat if needed until drop of insulin appears; if no drop appears after 6 attempts, changes pen device)
12	**Dials** correct dose (e.g. based on patient-specific order)
13	**Selects** appropriate injection site (e.g. abdomen, back of arm, thigh)
14	**Pinches** fold of skin# at the injection site, **holds** pen at 90 degree angle# to skin, and **inserts** pen needle all the way into the skin
15	**Lets** go of skin fold and **injects** the entire dose of insulin
16	**Keeps** plunger pressed and **holds** against the skin for at least 5 seconds after injection is given
17	**Removes** and **discards** needle in appropriate sharps container
18	**Returns** pen device to hospital-approved patient-specific storage area in a timely manner (e.g. within 15 minutes of injection or prior to giving medications to another patient)

www.onepenonepatient.org/toolkit (accessed 2016 Aug 25).
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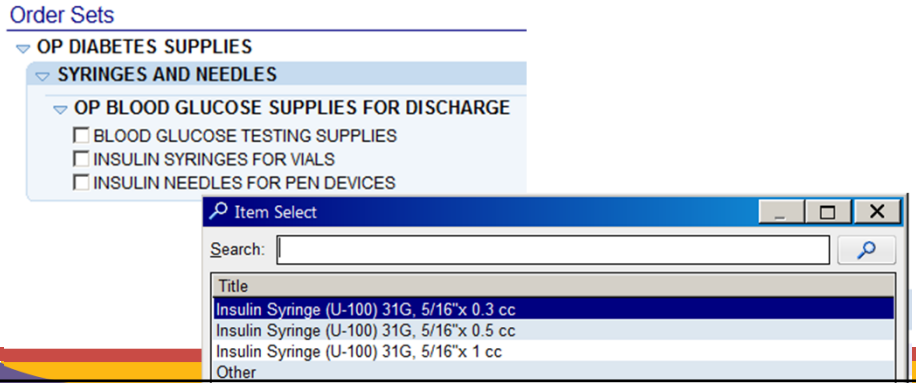

Self-assessment Questions

1. Basal plus rapid-acting insulin create imperfect substitute for endogenous insulin production in patients with type 1 diabetes mellitus.
    a. True.
    b. False

2. Which of the following accurately describes how insulin glargine U-300 compares with insulin glargine U-100?
    a. Higher rates of A1c goal achievement.
    b. Higher total daily dose requirement.
    c. Less weight gain in patients with T2DM.
    d. More nocturnal hypoglycemia.

3. 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.

4. 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.

Answers

1. a
2. b
3. c
4. a