



Diabetes Meds Update

2016

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Disclaimer and Important Info

- ▶ This content is for educational purposes only. Please see Package Insert for prescribing information.
- ▶ Beverly has no conflict of interest to disclose.
- ▶ For a lot more articles and information on this topic, go to DiabetesEd.net > Resources > Articles > Meds for Type 2 Diabetes

Articles on Diabetes Medications

Challenges with Insulin in the Inpatient Setting – 2016

U-800 Insulin Package Insert – 2016

Future of Insulin Analogs – 2016

Basal Insulin with GLP-1 Receptor Agonists – 2016

An overview of Concentrated Insulin Products – 2016

Insulin degludec/insulin (Daglong) for the treatment of type 2 Diabetes – 2016

iglatril – review of findings (technical paper)




Objectives

- ▶ Describe New Warnings on existing meds
- ▶ Discuss the meaning of a biosimilar insulin
- ▶ List the 4 available Concentrated Insulins
- ▶ Identify New Insulin /GLP-1 RA Combos




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Updates on Existing Meds

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Quick Question 1:

► Which of the following is a new warning for the DPP-IV Inhibitor?

- Contact Provider with sudden hearing loss
- Can increase risk of bladder cancer
- Increased risk of genital infections
- Report severe disabling joint pain immediately.

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DPP-4 Inhibitors – “Incretin Enhancers”

Januvia (sitagliptin) – Tradjenta (linagliptin)
 Onglyza (saxagliptin) Nesina (alogliptin)

▶ Action:

- ▶ Increase insulin release w/ meals
- ▶ Suppress glucagon

▶ Dosing:

Januvia – 100mg a day
 Onglyza – up to 5mg a day
 Tradjenta – 5mg a day
 Nesina – up to 25 mg a day

▶ Efficacy: Decreases A1c by 0.6 -0.8%

▶ Indication: For type 2s



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DPP-IV Inhibitor Updates

DPP – 4 Inhibitors “Incretin Enhancers”	Drug	Dose	Elimination	Notes
<ul style="list-style-type: none"> • Prolongs action of gut hormones • Increases insulin secretion • Delays gastric emptying 	sitagliptin (Januvia)	25 - 100 mg daily	eliminated via kidney*	* If creat elevated, see med insert for dosing. Side effects: headache and flu-like symptoms. Can cause severe, disabling joint pain. Contact MD, stop med. Report signs of pancreatitis. † Saxagliptin and alogliptin can increase risk of heart failure. Notify MD for shortness of breath, edema, weakness, etc. No wt gain or hypoglycemia. Lowers A1c 0.6%-0.8%.
	saxagliptin (Onglyza)†	2.5 - 5 mg daily	eliminated via kidney*, feces	
	linagliptin (Tradjenta)	5 mg daily	eliminated via feces	
	alogliptin (Nesina)*	6.25 - 25 mg daily	eliminated via kidney*	



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SGLT2 Inhibitors- “Glucoretics”

▶ **Action:** “Glucoretic” decreases renal reabsorption in the proximal tubule of the kidneys (reset renal threshold and increase glucosuria)

Class/Main Action	Name(s)	Daily Dose Range	Considerations
SGLT2 Inhibitors “Glucoretic” <ul style="list-style-type: none"> • Decreases glucose reabsorption in kidneys 	Canagliflozin (Invokana)	100 - 300 mg 1x daily	Side effects: hypotension, UTIs, increased urination, genital infections, ketoacidosis. Obtain GFR when starting and yearly: Invokana – stop med if GFR <45 Jardiance – do not start if GFR <45 Farxiga – stop med if GFR <60. Do not use Farxiga in pts with bladder cancer. Benefits: no hypo or weight gain. Jardiance lowers all-cause mortality by 32%. Lowers A1c 1.0%-2.0%. Lowers wt 1-3 lbs.
	Dapagliflozin (Farxiga)	5 - 10 mg 1x daily	
	Empagliflozin (Jardiance)	10 - 25 mg 1x daily	

▶ Efficacy:

- ▶ Weight loss of 1-3 lbs Reduce A1C ~0.7-1.5%



Decreases Glucose Reabsorption



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EMPA-REG OUTCOME[®]: Summary

- ▶ Empagliflozin used in trial for 3 years in 1,000 patients with type 2 diabetes at high CV risk:
- ▶ Empagliflozin reduced hospitalisation for CHF 35%
- ▶ Empagliflozin reduced CV death by 38%
- ▶ Empagliflozin improved survival by reducing all-cause mortality by 32%
- ▶ Need more research to determine this is a class effect



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Metformin – New GFR Guidelines

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Biguanides • Decreases hepatic glucose output • First line med at diagnosis of type 2	metformin (Glucophage)	500 - 2500 mg (usually BID w/ meal)	Side effects: nausea, bloating, diarrhea, B12 deficiency. To minimize GI Side effects, use XR and take w/ meals. Obtain GFR before starting. <ul style="list-style-type: none"> • If GFR <30, do not use. • If GFR <45, don't start Metformin • If pt on Metformin and GFR falls to 30-45, eval risk vs. benefit; consider decreasing dose. For dye study, if GFR <60, liver disease, alcoholism or heart failure, restart metformin after 48 hours if renal function stable. Benefits: lowers cholesterol, no hypo or weight gain, cheap. Approved for pediatrics, 10 yrs + Lowers A1c 1.0%-2.0%.
	Riomet (liquid metformin)	500 - 2500mg 500mg/5mL	
	Extended Release-XR (Glucophage XR) (Glumetza) (Fortamet)	(1x daily w/dinner) 500 – 2000 mg 500 – 2500 mg	



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Action	Insulin Name	Onset	Peak	Effective Duration	Considerations	
Bolus	Aspart (Novolog)	5 - 15 min	30 - 90 min	< 5 hrs	Bolus insulin lowers after-meal glucose. Post meal BG reflects efficacy.	
	Lispro (Humalog)*					
	Glulisine (Apidra)					
Short Acting	Regular*	30 - 60 min	2 - 3 hrs	5 - 8 hrs	Basal insulin controls BG between meals and nighttime. Fasting BG reflects efficacy.	
Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs		
Basal	Detemir (Levemir)	3 - 8 hrs		6 - 24 hrs	Side effects: hypoglycemia, weight gain. Typical dosing range: 0.5-1.0 units/kg body wt/day.	
	Long Acting	Glargine (Lantus)*	2 - 4 hrs	No peak		20 - 24 hrs
		Glargine (Basaglar)	2 - 4 hrs	No peak		< 42 hrs
Basal + Bolus	Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	Discard open vials after 28 days. For pen storage guidelines, see package insert.	
	50/50 = 50% NPH + 50% Reg					
	Novolog® Mix - 70/30 Humalog® Mix - 75/25 or 50/50 Ryzodeg Mix 70/30 (degludec/aspart)					5 - 15 min



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Cost Per Vial in Northern CA

Per vial cost	Walmart		
Regular Insulin	\$25*		
NPH	\$25*		
70/30	\$25*		
Humalog	\$200		
Novolog	\$197		
Apidra	\$180	\$246	\$178
Levemir	\$300	\$300	\$300
Lantus	\$226	\$221	\$206



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Glargine (Basaglar) “Copy Cat” or “Biosimilar Insulin”

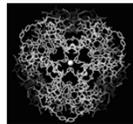
- ▶ Insulin considered a “biological drug product”
- ▶ Patent on “biologicals” last 12 yrs
 - ▶ Insulin patent sold in 1923 for \$1
 - ▶ Patent can be extended by making small improvements
- ▶ Insulin manufacturer’s have maintained exclusivity for 93 years.. Until now
- ▶ Patent on glargine expired in 2015



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Glargine (Basaglar) – Eli Lilly

- ▶ Can’t use the term generics for *large* molecule biologicals because they are manufactured in living organisms (bacteria and yeast)
- ▶ Each batch may be slightly different
- ▶ Correct term is “biosimilar”
- ▶ Currently - Pharmacist to contact Provider before switching to biosimilar
 - ▶ Future – may be same as generics
- ▶ FDA working on standardized insulin naming system



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Are Insulin Biosimilars identicals?

Are they exactly the same? "With any insulin, I always want patients to understand that these drugs are grown in batches – not manufactured by combining chemicals," says Alissa R. Segal, Pharm.D., RPh, CDE, CDTC, a Clinical Pharmacist at the Joslin Diabetes Center and associate professor of pharmacy practice at MCPHS University, both in Boston. "Insulin is grown using yeast or bacteria cells. There are very rigorous quality assurance protocols in place, but there can be changes in the cells over time. And that can translate into very small changes from batch to batch. With follow-on biologics like insulin, the manufacturing process is similar to the original – but not an exact copy. So there may be slight differences in the way it affects you."

<http://www.diabeticlifestyle.com/type-1-diabetes/cheaper-insulin-way>



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Degludec and Ryzodeg

▶ Degludec (Tresiba)

- ▶ An ultra long acting insulin - lasts up to 42 hours
- ▶ Takes 3-4 days to reach steady state
- ▶ Available in u-100 and u200 pens*
 - ▶ *200 units per mL vs 100 units per mL)
- ▶ Seems to cause less hypo
- ▶ Adjust dose every 3-4 days
- ▶ Wait at least 8 hours between doses
- ▶ Good at room temp for 8 wks



▶ Ryzodeg 70/30

- ▶ mixture of insulin degludec and aspart



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Why Degludec (Tresiba)?

Once-daily Tresiba®: When schedules change, dose timing can too
Continued efficacy for your patients even if a dose is delayed or schedules change¹



Juggles a busy family life

Unpredictable work hours

Relies on caregiver for injection

Travels



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Concentrated & Inhaled Insulins DiabetesEd.net

Name/Concentration	Insulin/Action	Considerations
Humulin Regular U-500 • 500 units insulin/mL • KwikPen or Vial	Regular Bolus / Basal	5 xs concentration of u-100 insulin. Indicated for pts taking 200+ units insulin daily. 3 mL Pen – Once opened, good for 28 days. 20 mL Vial – Once opened, good for 40 days. Use designated U-500 insulin syringe.
Humalog KwikPen U-200 200 units insulin/mL	Lispro (Humalog) Bolus	2 xs concentration of u-100 insulin. 3 mL Pen. Once opened, good for 28 days
Toujeo Solostar U-300 Pen 300 units insulin/mL	Glargine (Lantus) Basal	3 xs concentration of u-100 insulin 1.5 mL Pen. Once opened, good for 42 days
Tresiba FlexTouch U-200 Pen 200 units insulin/mL	Degludec (Tresiba) Ultra basal	2 xs concentration of u-100 insulin 3 mL Pen. Once opened, good for 8 weeks

All concentrated insulin pens and the U-500 syringe automatically deliver correct dose (in less volume). No, conversion, calculation or adjustments required. For example, if order reads 30 units, dial the concentrated pen to 30 units or draw up 30 units on the U-500 syringe. Important – never withdraw concentrated insulin from the pen using a syringe.

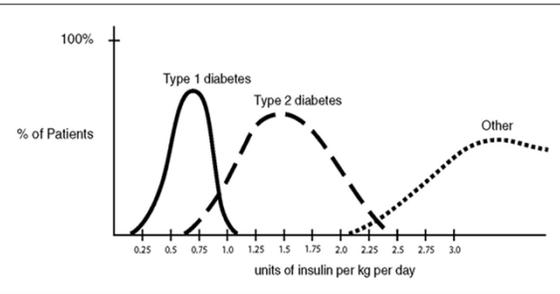
Inhaled Insulin

Action	Insulin Name	Dose Range	Onset	Peak	Duration	Considerations
Bolus – Rapid-acting	Afrezza Inhaled regular human insulin	4, 8, and 12 unit cartridges before meals	15 min	1 hr	3 hrs	Assess lung function. Avoid in lung disease – bronchospasm risk. Side effects: hypo, cough, throat irritation.

The information listed here are not guidelines. Please consult prescribing information for details. REV 10/2016 © 2016



Insulin Dosing Type 1 & 2



The graph plots the percentage of patients against the units of insulin per kg per day. The x-axis ranges from 0.25 to 3.0 units/kg/day. The y-axis represents the percentage of patients from 0% to 100%. Three curves are shown: a solid line for Type 1 diabetes peaking at approximately 0.75 units/kg/day, a dashed line for Type 2 diabetes peaking at approximately 1.5 units/kg/day, and a dotted line for Other patients peaking at approximately 3.0 units/kg/day.



More than 200 units a day?

Your patients injecting more than 200 units of insulin per day may be ready for a change

LEARN MORE >

UNITS OF INSULIN **210** 260 336

- Maria* has type 2 diabetes with severe insulin resistance
- Her A1C is not at goal
- She is taking multiple insulin injections per day
- Approximately half of her current 100 units of insulin is mealtime insulin and half is long-acting insulin

Indication for Humulin® R U-500
Humulin R U-500 (Concentrated) is indicated as an adjunct to diet and exercise to improve glycemic control in adults and children with type 1 and type 2 diabetes mellitus.



Humulin Regular U-500

Concentrated & Inhaled Insulins

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Name/Concentration	Insulin/Action	Considerations
Humulin Regular U-500 • 500 units insulin/mL • KwikPen or Vial	Regular Bolus / Basal	5 x concentration of u-100 insulin. Indicated for pts taking 200+ units insulin daily. 3 mL Pen – Once opened, good for 28 days. 20 mL Vial – Once opened, good for 40 days. Use designated U-500 insulin syringe.



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Consider U-500 High Potency Insulin

5 x's the concentration of u100

- ▶ 500 units per mL vs 100 units per mL
- ▶ 20 mL a vial. 500 units per mL= 10,000 unit
- ▶ Costs ~ \$400-\$1,200 per vial
- ▶ Less volume



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Dedicated U-500 Insulin Syringe

- ▶ Manufactured by BD
- ▶ Available in November 2016
- ▶ No photos available yet
- ▶ U-500 Insulin FDA Post reads

The BD U-500 Insulin Syringe is the first and only insulin syringe developed for patients taking Humulin R U-500 insulin. The BD U-500 Insulin Syringe features a 6mm x 31G syringe needle, the shortest insulin syringe needle available today, which is designed to deliver insulin injections into the subcutaneous tissue while minimizing the risk of intramuscular injection. The BD U-500 Insulin Syringe also has clearly marked dosage labeling designed to distinguish between other syringes, to help prevent confusion and incorrect dosing. The new insulin syringe is a 0.5mL syringe with clear, bold U-500 scale markings in 5-unit increments and allows for dosing up to 250 units. The syringe package and components are color coded to align with the Humulin-R U-500 insulin green and aqua color scheme.



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U-500 Updated Package Insert

DOSAGE AND ADMINISTRATION

- Adhere to administration instructions to reduce the risk of dosing errors. (2.1, 2.3, 2.4, 5.1)
- HUMULIN R U-500 is available as a KwikPen or multiple dose vial. Patients using the vial must be prescribed the U-500 insulin syringe to avoid medication errors. (2.1)
- Individualize dose of HUMULIN R U-500 based on metabolic needs, blood glucose monitoring results and glycemic control goal. (2.2)
- Administer HUMULIN R U-500 subcutaneously two or three times daily 30 minutes before a meal. Rotate injection sites to reduce the risk of lipodystrophy. (2.1, 2.2)
- Do NOT mix HUMULIN R U-500 with other insulins. (2.1)
- Do NOT administer HUMULIN R U-500 intravenously or intramuscularly. (2.1)
- Do NOT perform dose conversion when using the HUMULIN R U-500 KwikPen. The dose window of the HUMULIN R U-500 KwikPen shows the number of units of HUMULIN R U-500 to be injected. (2.3)
- Do NOT transfer HUMULIN R U-500 from the HUMULIN R U-500 KwikPen into any syringe. (2.3)
- Do NOT perform dose conversion when using a U-500 insulin syringe. Use only a U-500 insulin syringe with the HUMULIN R U-500 vial. (2.4)

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All Concentrated Insulins No calculation required

- ▶ All concentrated insulin pens and the U-500 syringe automatically deliver the correct dose in less volume.
- ▶ No conversion, calculations or adjustments required.
- ▶ For example, if order reads:
"30 units Toujeo U-300 Solostar Pen"
Dial the pen to 30 units.

All concentrated insulin pens and the U-500 syringe automatically deliver correct dose (in less volume). No conversion, calculation or adjustments required. For example, if order reads 30 units, dial the concentrated pen to 30 units or draw up 30 units on the U-500 syringe. Important – never withdraw concentrated insulin from the pen using a syringe.

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Dosing Strategies u-500

- ▶ U-500 (5 x's more potent) – Less volume required
 - ▶ Dosing – take total daily needs and split into 2-3 doses
 - ▶ 2 doses: 60% am / 40% pm or
 - ▶ 3 doses: 40/30/30 or 40/40/20
- ▶ No basal insulin needed, because U-500 has bolus and basal action
- ▶ Needs careful monitoring/ education



U-500 insulin: When More With Less Yields Success: *Diabetes Spectrum* March 20, 2009 vol. 22 no. 2 116-122

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Glargine (Toujeo) Solostar Pen U-300

- ▶ Glargine U-300 (Toujeo) vs Glargine U-100
 - ▶ Need 10-14% higher dose than previous U-100 dose
 - ▶ Start with 1:1 conversion and adjust based on FBG
 - ▶ Less nocturnal and hypoglycemia.
 - ▶ Similar weight gain to U-100
 - ▶ Extend release of U-300 results in smoother, stable more prolonged profile
 - ▶ More injection site reactions with U-300
 - ▶ Max 80 units injection
 - ▶ Comes in 1.5mL pen/450 units (3 or 5 pack)
 - ▶ Once opened, keep at room temp. Toss after 42 days.



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Glargine (Toujeo) Solostar Pen U-300

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 - ▶ Max 80 units injection
 - ▶ Comes in 1.5mL pen/450 units (3 or 5 pack)
 - ▶ Once opened, keep at room temp. Toss after 42 days.



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Toujeo U-300 Solostar Pen

Getting to know the Toujeo® SoloStar® pen

Toujeo® is available in the redesigned SoloStar® pen

Based on an award-winning design, the Toujeo® SoloStar® pen features:



Plus, the Toujeo® SoloStar® pen can be used for up to 42 days once opened.



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Degludec (Tresiba) FlexTouch U-200 Pen

- ▶ Concentration – 200 Units/mL
- ▶ Max 160 units injection
- ▶ Comes in 3mL pen/600 units (3 pack)
- ▶ Dose increments – 2 units
- ▶ Once opened, keep at room temp. Good for 8 weeks



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Concentrated Insulin

Pros

- ▶ As pts are getting heavier, more insulin is needed
- ▶ More insulin in less volume
- ▶ Patients need less insulin -

Cons

- ▶ Risk of incorrect administration
- ▶ Cost
- ▶ Making sure orders are written correctly



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Key Teaching Points

- ▶ Never withdraw concentrated insulin from a pen into a syringe
- ▶ All concentrated insulin pens and the U-500 insulin syringe automatically deliver the correct dose in less volume.
- ▶ No conversion, calculation or adjustment required.
- ▶ When writing Rx include type of insulin, concentration, delivery device and dose.



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Basal Insulin + GLP-1 RA

▶ Benefits

- ▶ Improved glycemic control
- ▶ Low risk of hypoglycemia
- ▶ Less weight gain
- ▶ Less treatment burden (one shot a day)
- ▶ Safe and effective alternative to basal/bolus

▶ Side Effects

- ▶ Hypoglycemia, weight gain (insulin)
- ▶ Nausea, vomiting, pancreatitis (GLP-1 RA)



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- Meds Management – Level 2 (recorded and ready)
- Pattern Management Gone Crazy – Level 2 (recorded and ready)
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- Diabetes Medication Update (Join us for live webinar on Oct 13th) [Click here](#) to join the FREE webinar

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