



Pharmacologic Management of Type 2 Diabetes in Persons Living with HIV-Insulin Therapies: It's a Slam Dunk!

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Objectives

- Identify injectable therapies used in the treatment of individuals with T2DM and HIV
- Design an insulin treatment plan for individuals with T2DM and HIV
- Monitor insulin therapy based on laboratory parameters and/or clinical presentation while accounting
- Identify counseling pearls for insulin therapies

ADA 2019 Treatment Algorithm

Initiation of Therapy

- Metformin monotherapy

Dual Therapy

- Consider if not at goal after 3 months of monotherapy or if HbA1c is $\geq 1.5\%$ from their goal
- **Consider ASCVD, CKD, and HF benefits**
- **Cost/hypoglycemia/weight gain should be considered in those without ASCVD, CKD, or HF**

Triple Therapy

- Consider if not at goal after 3 months of dual therapy
- **Consider ASCVD, CKD, HF cost, hypoglycemia, and weight gain**

Combination Injectable Therapy

- Consider if not at goal after 3 months of triple therapy
- Consider insulin if HbA1c is $\geq 10\%$ or BG is >300 mg/dl at diagnosis
- **Consider ASCVD, CKD, HF cost, hypoglycemia, and weight gain**



Insulin	Onset	Peak	Duration
Rapid Acting			
Lispro (Humalog®)	15-30 min	0.5-2.5 hr	3-6.5 hrs
Aspart (Novolog®)	10-20 min	40-50 min	3-5 hrs
Glulisine (Apidra®)	25 min	45-48 min	4-5 hrs
Afrezza®-inhaled insulin	15-30 min	53 min	160 min
Short Acting			
Humulin R ®, Novolin R ®	~30 min	1.5-3.5 hr	~8 hrs
Intermediate Acting			
Humulin N ®, Novolin N ®	1-2 hrs	4-12 hr	12+ hrs
Long Acting			
Glargine(Lantus®,Basaglar®, Toujeo®)	1/ 6 hr	Not sig	Up to 24/ >24hr
Detemir (Levemir®)	1-2 hrs	Not sig	7.6-24 hrs
Ultra Long-Acting			
Degludec (Tresiba®)	30-90 min	Not sig	42 hrs

Insulin Premix

Intermediate/Rapid	NPH/Regular	Ultra Long Acting/ Rapid
Novolog Mix 70/30® (aspart protamine/aspart)	Humulin 70/30® (NPH/Regular)	Ryzodeg 70/30® (degludec/aspart)
Humalog Mix 75/25® (lispro protamine/lispro)	Novolin 70/30® (NPH/Regular)	
Humalog Mix 50/50® (lispro protamine/lispro)		



New Basal Insulin-GLP 1 RA Combination Pens

- Insulin glargine and lixisenatide (Soliqua 100/33®)
- Insulin degludec and liraglutide (Xultophy 100/3.6®)



Insulin Injection Options

- Insulin vials:
 - Available as **100 units/ml** or **500 units/ml**
 - Majority of vials contain 10 ml of insulin
- Insulin Pens
 - Available as **U-100, U-200, U-300, U-500**
 - Majority of pens contain 3 ml of insulin

Injection Technique

Syringe and Vial

- Wash hands
- Inspect insulin
- Remove cap and alcohol the tip of the vial
- Draw the amount of air into the syringe that is equivalent to the number of units you wish to inject
- Inject the air into the vial and turn the vial upside down with the syringe
- Pull the plunger back on the syringe to the specified dose
- Inspect for air bubbles and tap to release
- Remove needle

Syringe and Vial

- Choose site of injection and alcohol the area
- Pinch a fold in the skin and inject at a 90 degree angle
- Hold syringe at site of injection for 10 seconds
- Discard

U-100 Insulin Syringes

Barrel Size	Insulin Quantities
3/10 ml (0.3 ml)	1-30 units
1/2 ml (0.5 ml)	1-50 units
1 ml	1-100 units

Needle Length	mm length
15/64"	6 mm
5/16"	8 mm
1/2"	12.7 mm



Insulin Pen Teaching General Rules

- Wash hands with soap and water/hand sanitizer
- Remove cap and inspect insulin to ensure it is either clear or cloudy
- Alcohol the tip of the pen (this may vary between pens as some pens do not require this step)
- Remove the protective seal on the pen needle, attaching it straight onto the pen
 - Do not attach needle at an angle
 - Rotate it clockwise
- Prime pen to 2 units.
- Remove larger (outer) cap and smaller (inner) cap of pen needle



Insulin Pen Teaching General Rules

- While holding the pen upright, tap the insulin reservoir a few times to remove any air bubbles that may have formed and then press down on the injection button.
- Dial pen to the prescribed number of units.
- Alcohol the site of injection
- Pinch skin slightly and inject at a 90 degree angle into site of injection

Insulin Pen Teaching General Rules

- Hold injection in site for 6 or 10 seconds (depending on insulin)
- Remove from stomach.
 - *The number of units remaining should read zero to ensure the patient has received the entire dose*
- Place larger cap on pen needle and remove
 - Rotate counter clockwise
 - No need to recap with smaller cap
- Discard needle appropriately
- Place cover over insulin pen

GLP-1 Pen Counseling Pearls

- Injection technique similar to insulin pen
- Priming and prepping pen will differ from insulin pen instructions

Injection Sites

- Abdomen (2 inches away from belly button)
- Back of arms
- Outer thighs
- Buttock

Injectable Therapies: Where Do We Start?

- GLP 1 RA vs. Insulin
- Consider insulin as first injectable option if:
 - HbA1c is very high (>10% or 11%)
 - Evidence of catabolism, polyuria, or polydipsia
 - T1DM is possible
- If patient is on both GLP-1RA and basal insulin consider combination products
 - Limitations in insulin dosing and cost may be a barrier to use

ADA: Initiation of Basal Insulin

Basal Insulin
(usually with metformin +/- non insulin agent)

Start: 10 units/day or 0.1-0.2 units/kg/day
Adjust: 10-15% or 2-4 units once-twice weekly
to reach FBG target (*can consider self-titration*)
For hypoglycemia: Identify cause; consider
dose reduction by 4 units or 10-20%

ADA: Insulin Intensification

Start: 10 units/day or 0.1-0.2 units/kg/day
Adjust: 10-15% or 2-4 units once-twice weekly to reach FBG target
For hypoglycemia: Identify cause; consider dose reduction by 4 units or 10-20%



If not controlled after reaching FBG target or if basal dose is $>0.7-1$ units/kg/day, consider PPG treatment with mealtime insulin

ADA: Insulin Intensification

If not controlled after reaching FBG target or if basal dose is >0.7-1 units/kg/day, consider PPG treatment with mealtime insulin

Add 1 rapid insulin injection before largest meal

Start: 4 units, 0.1 units/kg, or 10% of basal dose. If HbA1c is <8%, may decrease basal by same amount
Adjust: Increase dose by 1-2 units or 10-15% once-twice weekly until SMBG target is reached
For hypoglycemia: Identify cause; consider dose reduction by 2-4 units or 10-20%

Not at goal

Change to premixed insulin twice daily

Start: Unit to unit conversion or (10-12 units or 0.3 units/kg in insulin-naïve patients)
Adjust: Increase dose by 1-2 units or 10-15% once-twice weekly until SMBG target is reached
For hypoglycemia: Identify cause; consider dose reduction by 2-4 units or 10-20%

Not at goal

Add ≥ 2 rapid insulin injections before meals (basal-bolus)

Start: 4 units, 0.1 units/kg, or 10% of basal dose/meal
If HbA1c is <8%, may decrease basal by same amount
Adjust: Increase dose by 1-2 units or 10-15% once-twice weekly until SMBG target is reached
For hypoglycemia: Identify cause; consider dose reduction by 2-4 units or 10-20%

Case 1

- MG is a 43 YOF who presents to clinic with a PMH significant for HIV and T2DM
- Her current medications include: Symtuza once daily, metformin 1000 mg BID, and Canagliflozin 300 mg once daily
- Pertinent labs include:
- HbA1c: 8.4%
- What would you recommend?
 - Medication
 - Follow up
 - Labs

140	101	19	180
3.8	20	0.8	

Case 1

- MG follows your recommendations and initiates Bydureon 2 mg once weekly along with the below medications
- Her current medications include: Symtuza once daily, metformin 1000 mg BID, and Canagliflozin 300 mg once daily
- Pertinent labs include:
- HbA1c: 7.4%
- What would you recommend?
 - Medication
 - Follow up
 - Labs

140	101	19	160
3.8	20	0.8	

Case 1

- You decide to initiate a basal insulin for MG. She currently weighs 90 kg.
- Her current medications include: Symtuza once daily, metformin 1000 mg BID, Bydureon 2 mg once weekly, and Canagliflozin 300 mg once daily
- Pertinent labs include:
 - HbA1c: 7.4%
 - What would you recommend?
 - Insulin detemir, degludec, glargine (10 units or weight based dosing)
 - NPH?

140	101	19	160
3.8	20	0.8	

Hypoglycemia Classification

Level	Glycemic Criteria (mg/dl)	Description
Hypoglycemia Alert Value (Level 1)	<70	Sufficiently low
Clinically Significant Hypoglycemia (Level 2)	<54	Clinically significant hypoglycemia
Severe Hypoglycemia (Level 3)	No Specific Value	Hypoglycemia associated with severe cognitive impairment requiring external assistance

Hypoglycemia

- Symptoms:
 - Shakiness
 - Rapid heartbeat
 - Sweating
 - Dizziness
 - Anxious
 - Hunger
 - Blurry vision
 - Weakness/fatigue
 - Headache
 - Irritable
- Hypoglycemia can occur after sudden increase in exercise




Hypoglycemia

- 7-15% of patients on insulin will experience hypoglycemia annually with 1-2 % experiencing severe hypoglycemia
- Treat with **ONE** of the following (**15-20** grams of carbohydrates-simple sugars):
 - 3 to 4 glucose (dextrose) tablets
 - ½ cup or 4 ounces of fruit juice or soft drink (not diet)
 - 5 to 6 pieces of hard candy
 - 2 tablespoons of raisins
 - 1 tablespoon of honey or syrup
- Recheck blood glucose in **15** minutes, if still less than goal, retreat with **ONE** of the above
- Be sure to have a small meal once blood sugar is above goal
- **If a patient feels as though they are hypoglycemic and cannot check their blood glucose, they should still treat**

Case 2

- Patient is currently injecting 50 units BID of Novolog 70/30® and presents with the below values:

	AC Breakfast	2 hr post breakfast	2 hr post lunch	2 hr post dinner
Average BG (mg/dl)	82 	120	170	220

Case 3

- JR is a 50 YOM who presents to DM clinic. He is taking the following medications.
- Lantus 40 units qHS for the past 3 months, metformin 1000 mg BID x5 years, glipizide 10 mg BID x2 years and Symtuza
- Fasting BG averages between 80-100 mg/dl
- HbA1c is 9% today
- What do you do?

Case 3 Continued

- JR returns to clinic with the following averages

Meal	Before Breakfast	2 hour post breakfast	Before Dinner	2 hour post dinner
BG (mg/dl)	90	150	200	220

When would you initiate 4-5 units of rapid acting insulin?

- A. Before breakfast
- B. Before lunch ←
- C. Before dinner
- D. Both B and C are correct
- E. A, B, and C are correct

Summary

- Consider patient related factors in decision making
- Utilize drug information resources to identify drug interactions

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