

Treating Type 2 Diabetes Mellitus: Basal Insulin Initiation and Titration

Key Message 4: Basal insulin may be initiated as a second agent if HbA1C goal is not achieved after 3 months of maximally tolerated monotherapy. Insulin may also be initiated in newly diagnosed patients who are symptomatic and have a baseline HbA1C >9%

Insulin Initiation^[1, 2]

The American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) have different strategies for initiating basal insulin therapy, as shown in Table 1.

ADA	AACE	
10 U/day or 0.1 – 0.2 U/kg/day (usually in combination with metformin +/- non-insulin agent)	HbA1C < 8%	HbA1C >8%
	Total Daily Doss (TDD) = 0.1 – 0.2 U/kg	Total Daily Doss (TDD) = 0.2 – 0.3 U/kg

Insulin Titration^[1, 2]

Dose titration may be needed based on patients' average fasting blood glucose (FBG) goals. Table 2 shows the titration strategies from the AACE and the ADA.

ADA	AACE
Adjust 10 - 15% or 2 – 4 units once or twice weekly to reach FBG target.	Titrate every 2 – 3 days: <ul style="list-style-type: none"> • Fixed regimen: increase TDD by 2 U • Adjustable regimen: <ul style="list-style-type: none"> • FBG >180 mg/dL: add 20% of TDD • FBG 140 – 180 mg/dL: add 10% of TDD • FBG 110 -139 mg/dL: add 1 unit

Hypoglycemia^[1, 2]

Insulin possess a high risk of hypoglycemia, defined as a FBG <70 mg/dL. Symptoms of hypoglycemia include shakiness, irritability, confusion, tachycardia, sweating, hunger, cognitive dysfunction, seizures, and coma. If hypoglycemia occurs due to insulin, the TDD of the basal insulin should be reduced (Table 3).

ADA	AACE
Decrease dose by 4 units or by 10 -20%	Reduce TDD by: <ul style="list-style-type: none"> • BG < 70 mg/dL: 10 – 20% • BG < 40 mg/dL: 20 – 40%

Pharmacodynamics of Basal Insulin

	Insulin glargine (Basaglar, Lantus, Toujeo) ^[3-5]	Insulin detemir (Levemir) ^[6]	Insulin degludec (Tresiba) ^[7]
Onset (hours)	3 to 6	3 to 4	1
Peak (hours)	No pronounced peak	3 to 9	12
Duration (hours)	~11 to > 24	6 to 24 hours (dose dependent)	>24

Insulins			
Mechanism of Action: Regulates glucose metabolism by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production			
Basal Insulin (Long-acting)			
Drug	Dosing	% of HbA1C Lowering potential	Side effects /Notes
Insulin degludec ^[7] (Tresiba) Insulin Detemir (Levemir) ^[6] Insulin Glargine (Basaglar, Lantus, Toujeo) ^[3-5]	Administer subcutaneously once daily at any time <i>Levemir permits once or divided doses twice daily</i>	>1.5 %	SIDE EFFECTS hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema and weight gain ADVANTAGES once daily dosing
Bolus Insulin (Rapid-acting)			
Insulin Lispro (Humalog) ^[8] Insulin Aspart (Novolog) ^[9]	Administer subcutaneously 15 minutes before meals or immediately after meals	>1.5 %	SIDE EFFECTS hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema and weight gain
Oral insulin inhalation powder (Afrezza) ^[10]	Inhale by mouth at the beginning of meals		BLACK BOX WARNING Risk of acute bronchospasm in patients with chronic lung disease. Use if contraindicated in patient with chronic lung disease such as asthma or COPD SIDE EFFECTS Hypoglycemia, acute bronchospasm, cough, sore throat or irritation ADVANTAGE oral administer insulin
Short-acting Insulins			
Regular Insulin (Humulin R, Novolin R) ^[11, 12]	Administer subcutaneously 30 minutes before meals	>1.5 %	SIDE EFFECTS hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema and weight gain
Concentrated regular Insulin (Humulin R U-500, Humulin R U-500 Kwikpen) ^[13]	Administer subcutaneously 30 minutes before meals		NOTES Regular Insulins are available as combination with intermediate – acting insulins <i>Concentrated regular insulin</i> – 5 times as concentrated as regular insulin U-100. Recommended when patient requires > 200units/day of insulin
Intermediate-Acting Insulins			
NPH Insulin (Humulin N, Novolin N) ^[14, 15]	Administer subcutaneously once or twice daily	>1.5 %	SIDE EFFECTS hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema and weight gain NOTES NPH insulin are cloudy, can be mix with rapid or short-acting insulins

References

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