Presented through a collaboration between

CME

Front Line in T2D

Advancing Care With Basal Insulin Excellence

Supported by an independent educational grant from Lilly.

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Faculty

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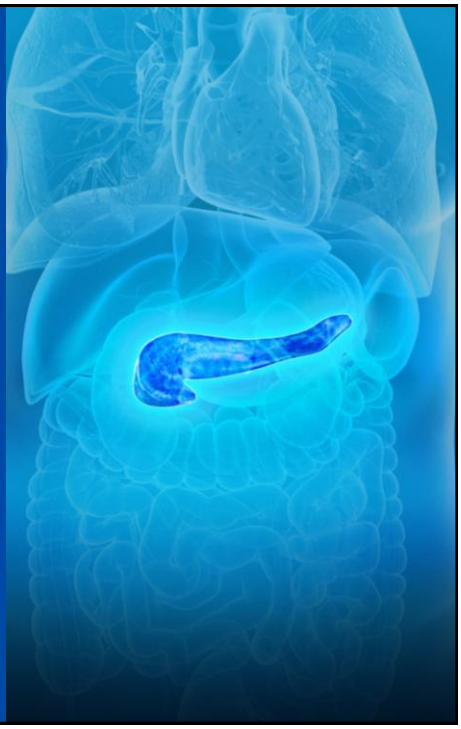

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Faculty Disclosures

Jennifer B. Green, MD

- Consultant or advisor for: Aqua; AstraZeneca; Bayer; BDI; Boehringer Ingelheim; Fractyl; Lilly; Novo Nordisk; Roche; Sparrow; Vertex; vTv; Zealand
- Contracted researcher for: Boehringer Ingelheim; Cour; GentiBio; Merck; Metsera
- Stock options: BDI

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- Consultant or advisor for: Abbott Diabetes Care; Boehringer Ingelheim; Novo Nordisk; Sanofi US
- Speaker or member of speaker's bureau for: Abbott Diabetes Care; Novo Nordisk; Sanofi US

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Participant Question 1

According to real-world data, at which baseline A1C level are patients with type 2 diabetes who initiate basal insulin most likely to achieve an A1C goal of less than 7% while experiencing the least amount of weight gain?

- 7.0–<8.0%
- 8.0–<9.0%
- 9.0–<10.0%
- 10.0–<11.0%

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Participant Question 2

How confident are you right now, in your ability to initiate and titrate basal insulin safely and effectively to improve outcomes in people with T2D?

1 - Not confident
2 - Slightly confident
3 - Moderately confident
4 - Mostly confident
5 - Very confident

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Guideline-Based Use of Basal Insulin

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Insulin Remains the Cornerstone of Diabetes Treatment

~537 million people had diabetes worldwide in 2021, and this is predicted to rise to 783 million by 2045[1]

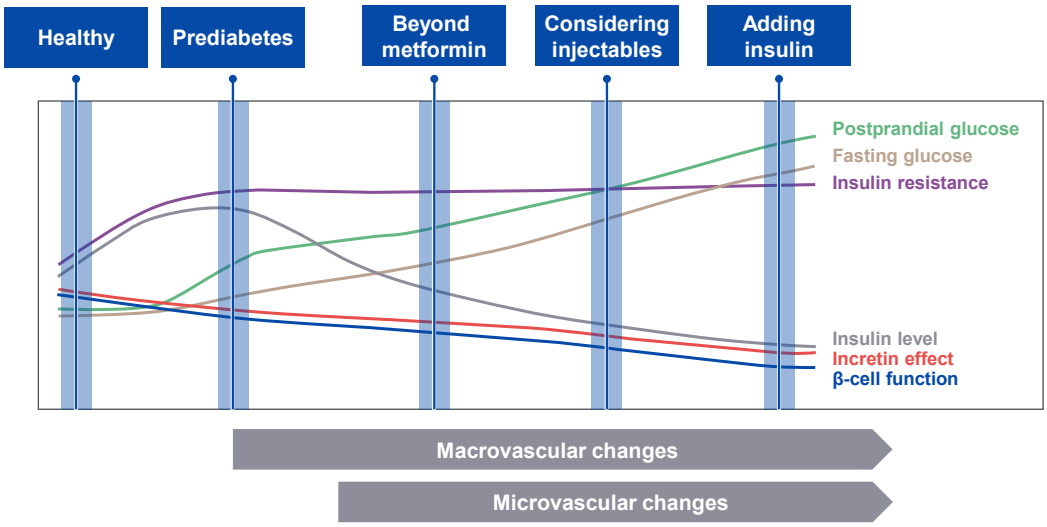
Up to 40% of people with diabetes (**150-200 million**) globally require insulin therapy[2-4]

Due to progressive nature of diabetes, many people with T2D eventually may require and benefit from insulin therapy[5]

T2D, type 2 diabetes.
1. IDF Diabetes Atlas (10th ed). International Diabetes Federation. 2022; 2. Garg S, et al. Diabetes Technol Ther. 2018;20:S21; 3. Buse J, et al. BMJ Open Diab Res Care. 2021;9:e002373;
4. Bolli G, et al. Acta Diabetol. 2022;59:1129; 5. ADA Professional Practice Committee. Diabetes Care. 2022;45:S125.

7

Natural History and Progression of T2D Defines Therapeutic Intervention



Kendall DM, et al. Am J Med. 2009;122(6 Suppl):S37-50.

8

Current Treatment Recommendations for Basal Insulin Use in Patients With T2DM[1-3]

Because of its high glycemic efficacy, insulin can be considered in virtually any patient who is not at goal despite use of noninsulin agents or if noninsulin agents are not tolerated

AACE[1]

- If A1C > 10% and/or BG ≥300 mg/dL with catabolic symptoms (eg, weight loss)
- Recommend GLP-1 RA or GIP/GLP-1 RA if not already in use
- If goals are unmet with a GLP-1 RA or GIP/GLP-1 RA, add basal insulin alone or as a basal insulin/GLP-1 combination injection

ADA[2]

- Symptoms of hyperglycemia (ie, polyuria or polydipsia) regardless of background therapy
- Evidence of ongoing catabolism (weight loss, hypertriglyceridemia, ketosis)
- A1C > 10% or blood glucose ≥ 300 mg/dL
- GLP-1 RA or GIP/GLP-1 RA preferred prior to insulin initiation, unless inappropriate or not preferred
- Longer duration of T2DM

ENDO[3]

- In patients aged ≥ 65 years who have not reached glycemic targets with metformin and lifestyle changes
  - Insulin should be used sparingly to reduce the risk of hypoglycemia in these patients
  - Glycemic treatment regimens should be kept as simple as possible

AACE, American Association of Clinical Endocrinology; ADA, American Diabetes Association; ENDO, Endocrine Society; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; RA, receptor agonist.

1. Samson SL, et al. Endocr Pract. 2026;32:473-518; 2. American Diabetes Association Professional Practice Committee for Diabetes. Diabetes Care. 2026;49(Suppl 1):S183-S215;
3. LeRoith D, et al. J Clin Endocrinol Metab. 2019;104:1520-1574.

9

Stop and Reflect

Think about the following question and how it relates to your practice:

"Think of your last 3 patients with T2D that you started on basal insulin — do you feel you initiated insulin at the right time in their disease course?"

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Basal Insulin Is Initiated too Late

A review of 22 studies conducted over a 10-year period in people with T2DM showed that initiation of basal insulin therapy is often delayed[1]

Median time to insulin initiation: **5.25 years[2]**

Mean A1C at insulin initiation: **8.7% to 9.8%**

71% of PCPs didn't initiate insulin until elevated A1C levels were confirmed twice[3]

PCP, primary care physician.
1. Gavin JR, Abaniel RM, Virdi NS. Diabetes Spectr. 2023;36(4):379-384. 2. Kostev K, et al. J Diabetes Sci Technol. 2019;13(6):1129-1134. Escalada J, et al. Diabetes Res Clin Pract. 2016;122:46-53.

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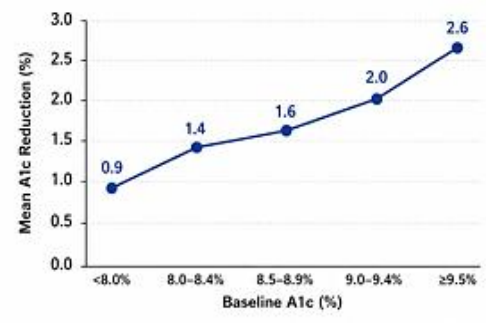
Higher Baseline A1C Predicts Larger A1C Reduction and Greater Weight Gain

Weight Gain After Insulin Initiation Is Often Proportional to the Degree of Hyperglycemia Correction Rather Than the Insulin Itself

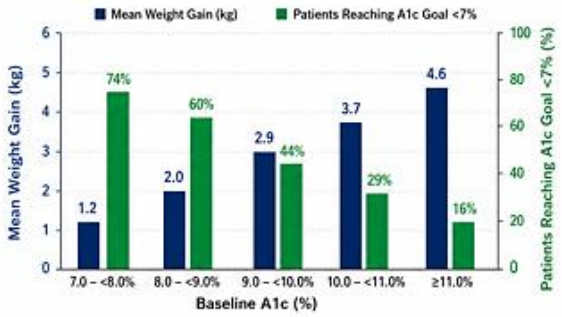
Mean A1c Reduction (%) by Baseline A1c

Greater baseline hyperglycemia is associated with larger reductions in A1c after insulin initiation.



Weight Gain (kg) and % Reaching A1c Goal < 7% by Baseline A1c

Individuals with higher starting A1c values tend to gain more weight and are less likely to reach A1c goal < 7%.



1. Riddle MC, et al. Diabetes. 2009;58(Suppl1):A125; 2. Fonseca V, et al. Diabetes Care. 2013.36:2162-2168.

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Summary

- Insulin is a core treatment strategy to achieve glycemic control in patients with T2D
  - It is not a “treatment of last resort”
  - It is important to help the patient “unpack” their concerns to address them proactively
- Starting basal insulin earlier is associated with lower rates of hypoglycemia and less weight gain
- Multiple basal insulin agents are available, including newer basal insulins with longer half-lives and less variability and risk for hypoglycemia

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CONTINUING EDUCATION | ENDOCRINE SOCIETY | Medscape EDUCATION

Initiation & Titration

Practical Approaches

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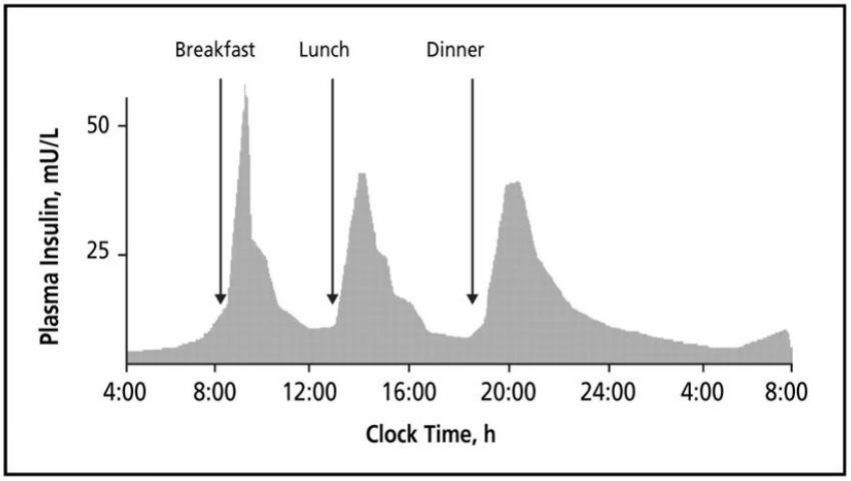
Physiologic Insulin Release



Thompson R, et al. Curr Paediatrics. 2006;16:117-122.

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Components of Insulin Action

Basal insulin

- Required for resting metabolic needs
- Suppresses glucose production at night and between meals
- Stays relatively constant
- Usually is half of total daily insulin needs

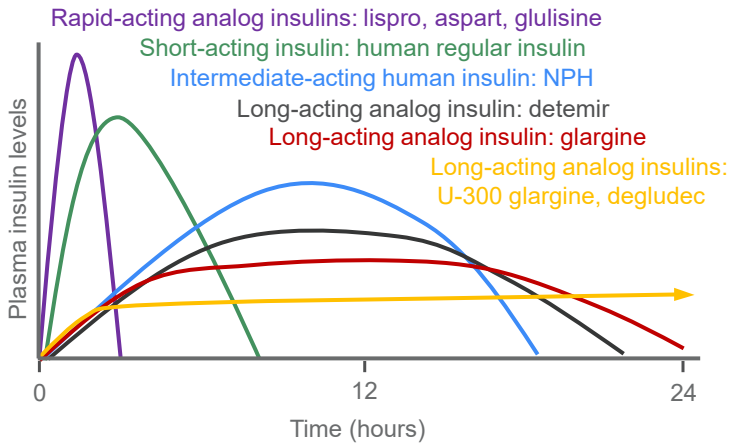
Prandial insulin

- Limits/prevent post-prandial hyperglycemia
- Physiologic 2-phase release
  - First phase immediate and lasts 1 to 2 hours
  - Delayed slower to peak second phase
- Each meal about 10% to 20% of daily insulin needs

Edelman S, et al. Osteopath Med Prim Care. 2007;1:9.

16

Pharmacokinetic Profiles of Rapid-, Short-, and Intermediate-, and Long-Acting Insulins



Hirsch IB. New Engl J Med. 2005;352:174-183.

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Recommended Times to Start Insulin

- New diabetes diagnosis, significant hyperglycemia of unknown type?
- When patient has catabolic symptoms or glucotoxicity
  - Polyuria, polydipsia, and weight loss
  - Fasting glucose > 300 mg/dl
- Pregnancy
- If you need controlled but relatively-quick control of glucose in the pre- and peri-operative period
- Serious systemic illness

ADA Standards of Care in Diabetes—2026. Diabetes Care. 2026;49(Suppl 1):S183–S236.

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Spectrum of Intermediate- and Long-Acting Basal Insulins

Insulin[1,2]	Available As	Conc.	Time of Action, h			Dosing Frequency
			Onset	Peak	Duration	
NPH (human)	Vials, pens	U100	1-2	6-14	10-16	Once or twice daily
Glargine (analog) U100	Vials, pens	U100	3-4	None	Up to 24	Once daily, any time, but at the same time every day
Glargine (biosimilar) U100	Pens	U100	3-4	None	24 (mean)	Once daily, any time, but at the same time every day
U300 Glargine (analog)	Pens	U300	6	None	24	Once daily, any time, but at the same time every day
Degludec (analog)	Pens	U100, U200	1	None	42	Once daily at any time of day
Icodec (analog)	Pens	U700	Not available	None	≈ 7 days; 168 hours	Once weekly

1. Vargas-Uricoechea H. J Clin Med Res. 2022;14:8-21. 2. Cleveland Clinic. Accessed June 5, 2026. https://my.clevelandclinic.org/health/drugs/13902-injectable-insulin-medications. 3. Singh AK et al. Diabetes Metab Synd. 2022;16:102615. 4. Goldman J et al. Ann Pharmacother. 2025;59:554-569.

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Issues That Affect Pharmacokinetics of Insulin

- Injection site
- Depth of injection
- Volume of injection
- Insulin type
- Exercise

Subcutaneous insulin

- Bypasses initial portal delivery
- Higher insulin exposure in muscle and adipose tissue
- Lower insulin exposure in the liver than endogenous insulin

Gradel AKJ, et al. J Diabetes Res. 2018:1205121. doi: https://doi.org/10.1155/2018/1205121. DeFronzo RA,et al. Nat Rev Dis Primers. 2015;1:15019.

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Stop and Reflect

Think about the following questions and how they relate to your practice

How am I titrating basal insulin in my patients? Are we getting our patients to goal?

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Guidelines Regarding Insulin Basal Insulin Dosing/Titration

Initiation Stage	ADA[1,2]
Initial dose	10 u/day **OR** 0.1 to 0.2 u/kg/day
Titration	• Set FPG goal • Choose evidence-based algorithm to reach goal without hypoglycemia (eg, increase dose 2 units every 3 days; increase 1 unit per day; increase 5 to 7 units weekly) • Hypoglycemia: reduce dose 10% to 20% if no clear cause is evident

BG, blood glucose; FPG, fasting plasma glucose; TDD, total daily dose.

1. ADA. Diabetes Care. 2022;45(supp 1): S1-S264; 2. Shubrook JH, et al. Prim Care Clin Office Pract. 2022;49:301-313; 3. Garber AJ et al. Endocr Pract. 2020;26:107-139.

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Guidelines Regarding Insulin Basal Insulin Dosing/Titration

Initiation Stage	ADA[1,2]	AACE[3]	
Initial dose	10 u/day **OR** 0.1 to 0.2 u/kg/day	HbA1c < 8% 0.1 to 0.2 u/kg/day	HbA1c > 8% 0.2 to 0.3 u/kg/day
Titration	• Set FPG goal • Choose evidence-based algorithm to reach goal without hypoglycemia (eg, increase dose 2 units every 3 days; increase 1 unit per day; increase 5 to 7 units weekly) • Hypoglycemia: reduce dose 10% to 20% if no clear cause is evident	• Goal: HbA1c < 7%, FPG < 110 mg/dL • Titration every 2 to 3 days • Fixed regimen: increase dose by 2 units • Adjustable regimen: FPG > 180 mg/dL: add 20% of TDD FPG 140 to 180 mg/dL: add 10% of TDD FPG 110 to 139 mg/dL: add 1 U • If hypoglycemia, reduce TDD by: 10% to 20% if BG < 70 mg/dL 20% to 40% if BG < 40 mg/dL	

BG, blood glucose; FPG, fasting plasma glucose; TDD, total daily dose.

1. ADA. Diabetes Care. 2022;45(supp 1): S1-S264; 2. Shubrook JH, et al. Prim Care Clin Office Pract. 2022;49:301-313; 3. Garber AJ et al. Endocr Pract. 2020;26:107-139.

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Best Practices in Daily Basal Insulin Initiation

"Fix the fasting first"

- Share with patient agreed A1c goal
- Corresponding fasting glucose goal

Use a weight-based dose

- 0.2 to 0.3 units/kg/day-starting dose (long-acting analog)
- 0.1 units/kg given before breakfast and dinner/bedtime if NPH

Set the titration schedule with patient (any schedule will do)

- 1 unit/day increase
- 3 units increase twice weekly (ADA 2 to 4 units)
- 5 to 7 units increase weekly

Set parameters when to stop titration

- Achieved AM glucose goal
- Had a hypoglycemic episode
- Reached 0.5 units/kg/day **(ceiling dose)**
- Always set the next appt to reassess

ADA. Diabetes Care. 2022;45(supp 1):S1-S264; Kuritzky L, et al. Clin Diabetes. 2019;37:368-376; Shubrook JH, et al. Prim Care Clin Office Pract. 2022;49:301-313.

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Best Practices In Daily Basal Insulin Initiation

Be careful to not "over-basalize"

- 0.5 units/kg/day: good time to stop and "look up"
- Look at stability of the fasting glucose
- Look at bedtime-to-AM change (BeAM)
- If stable move to mealtime glucose
- Basal insulin doses > 0.7 units/kg/day has diminishing returns and more hypoglycemia[1,2]

Once you achieve the fasting goal

- Move glucose readings to pre- and post-meal (instead of fasting)
- Allows you to see about mealtime excursions

Meneghini L, et al. Diabetes Care. 2013;36:858-864; Kuritzky L, et al. Clin Diabetes. 2019;37:368-376.

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Once-Weekly Basal Insulin Is an Emerging Option for Individualized Care

- Once-weekly insulins can potentially facilitate insulin replacement therapy
- Once-weekly dosing has the potential to reduce clinical inertia, and improve persistence, as has been seen with GLP-1 RAs and GIP/GLP-1 RAs
- New implementation strategies (eg, initiation, titration, switching, intensification) will be needed
- Understanding the risk and management of hypoglycemic events will be important to reassure clinicians and patients
- Clinician and patient education will be crucial

Candido R, et al. Acta Diabetol. 2026;63:313-323.

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Case Study: Maria

Maria is a 58-year-old female T2DM 10 years
Current weight 100 kg, with baseline HbA1c = 8.4%

Medications

- Metformin 1000 mg BID
- Glipizide 10 mg BID
- Linagliptin 5 mg QD
- Glargine 22 units HS

Reports Today

- She is very frustrated
- She checks her glucose each morning as recommended: ranges from 80 mg/dl to 140 mg/dl
- Her blood glucose is often above 200 mg/dL

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Faculty Discussion: What Are Your Next Steps to Help Maria?

- Add meal-time insulin
- Stop one of the agents
- Stop her insulin and DPP-4 inhibitor, and add a GLP-1RA or GLP-1RA/GIP
- Change or stop glargine
- Check if she's titrating

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Case Study Continued: Maria Returns for Follow-Up

❑ **Maria comes back for a recheck**

- You stopped glipizide
- You increased the insulin glargine to 26 units, and then titrated to 34 units over the next 3 weeks

❑ **She is not having any hypoglycemia**

❑ **Her AM readings 110 to 150 mg/dl**

- After dinner 120 to 180 mg/dl
- Current HbA1C = 7.3% (baseline, 8.4%)

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Summary

- Pharmacologic insulin replacement should try to mimic normal insulin physiology
- There is a wide spectrum of basal and prandial insulins that allow for individualization of treatment; avoid overbasalization
- Strong knowledge of time action curves improve insulin selection and safety of insulin use
- Newer ultra-long-lasting insulins appear to be safe and effective options
- Insulin calculations improve specificity of treatment

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Addressing Barriers

Adherence, Hypoglycemia, and Injection Burden

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Stop and Reflect

Think about the following question and how it relates to your practice:

What is the biggest barrier to insulin use in my practice and ***how am I*** going to address it?

(Is it patient driven, provider driven, or both?)

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Patient- and Provider-Level Barriers to Insulin Initiation

Patients		HCPs
Perceived lack of benefits	Hypoglycemia	Perceived patient resistance
Fear of needles	Weight gain	Lack of experience
Lack of confidence in titrating doses	Need for injections and blood tests	Time constraints
Long-term adverse events	Complexity of delivering insulin (eg, titrations)	Lack of support/ resources
Impact on social life	Adherence	Therapeutic inertia

Potential solutions

- Diabetes education
- Address misconceptions
- Nurse or pharmacist-led management
- Written instructions
- Titration apps

Karter AJ, et al. Diabetes Care. 2010;33:733; Minze MG, et al. J Fam Pract. 2011;60:577; Brod M, et al. Patient. 2014;7:437-450; Ng CJ, et al. Int J Clin Pract. 2015;69:1050-1070; Berard L, et al. Diabetes Obes Metab. 2018;20:301–308; Perreault L, et al. J Am Board Fam Med. 2019;32:431-447.

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Insulin Use Inertia

- **You have 3 months to achieve your goal when starting insulin[1]**
  - ADA recommends treatment intensification every 3 to 6 months if not at A1c goal
    - Timely intensification and use of insulin if A1c is above 10%
    - Most people would be on insulin at 1 to 2 years if not at goal
    - The mean time to insulin is 4.3 years[2]
- **Only 31% of eligible T2D patients had their insulin treatments intensified[2]**
- **Another study found a lower risk of insulin initiation in Black (aHR 0.77, *P* = .008) and Hispanic participants (aHR 0.66, *P* < .001) relative to White participants[3]**
  - Socioeconomic factors were not associated with insulin initiation
- Those who do not achieve target glucose at **3 months are** less likely to achieve at **24 months[1]**

ADA, American Diabetes Association; T2D, type 2 diabetes.
1. Khunti K, et al. Diabetes Obes Metab. 2020;22:722–733. 2. Khunti K, et al. Diabetes Obes Metab 2016;18:401–409; 3. Pilla SJ, et al. J Gen Intern Med. 2018;33:839-846.

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Key Steps to Overcome Insulin Inertia

- ✓Do not use insulin as a weapon
- ✓Insulin does not have to be forever
- ✓First injection in the office
- ✓Start a weight-based dose/patient titration plan with a ceiling dose
- ✓Maximize the value of glucose readings
- ✓Always look at injection sites

Khunti K et al. Diabetes Obes Metab. 2020;22:722–733; Khunti K, et al. Diabetes Obes Metab. 2016;18:401–409; Meneghini L, et al. Diabetes Care. 2013;36:858-864; Kuritzky L, et al. Clin Diabetes. 2019;37:368-376.

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Concerns Among Patients About Hypoglycemia and Weight Gain

- Concerns about hypoglycemia and weight gain are real
  - Weight gain on insulin: mean = 4 lbs, though in one study, 24% gained > 10 lbs
  - Discuss ways to mitigate those adverse effects
  - Slow titration
- Explain the risks to patients:
  - Not using insulin when it is needed leads to an increased risk of both microvascular disease (kidney failure, blindness) and macrovascular disease (heart attack, stroke)

GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; RA, receptor agonist.
Balkau B, et al. Diabetes Care. 2014;37:2108-2113; Obesity Medicine Association. Accessed June 3, 2026. https://obesitymedicine.org/blog/insulin-and-weight-gain-understanding-the-connection; Zakir M, et al. Cureus. 2023;15:e45835.

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Tools and Tech: Supporting Adherence

- ✓ **CGM**: Real-time feedback reduces fear and improves engagement
  - Libre and Dexcom for Type 1 or 2 diabetes; tracks glucose 24/7
- ✓ **Nurse-led or pharmacist-led support programs**: Structured follow-up improves titration and A1C outcomes
- ✓ **Smartphone apps**

Pharmacy Times website. Accessed June 3, 2026. https://www.pharmacytimes.com/view/pharmacist-led-cgm-programs-improve-glycemic-outcomes-in-outpatient-setting.
Alhaiti A. BMC Nursing. 2025;24:846.

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Summary

- Many provider and patient barriers exist to insulin use
- Clarify what an insulin injection looks like today
- Educate patients about hypoglycemia and weight gain
- Clinical inertia and patient fears can contribute to preventable microvascular ad macrovascular complications
- Motivational interviewing and shared decision-making are 2 useful communication tools
- Utilize nurse- or pharmacist-led support programs: structured follow-up improves titration and A1C outcomes
- There are numerous tech tools to support adherence such as CGM and smartphone apps

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New and Emerging Therapies

Once Weekly Basal Insulin

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Reported Nonadherence to Daily Basal Insulin Therapy

69% to 87% of patients reported missing basal insulin dose injections

33% of patients reported missing basal insulin dose injections at least once/month

3.6 to 4.3 missed doses in a month significantly impacts glucose control

Reason	Patients, % (Rank)
Too busy	18.9 (1)
Traveling	16.2 (2)
Skipped meal	15.0 (3)
Stress or emotional problems	11.7 (4)
Embarrassing to inject in public	9.7 (5)
Challenging to take it at the same time everyday	9.4 (6)
Forgot	7.4 (7)
Too many injections	6.0 (8)
Avoid weight gain	4.0 (9)
Regimen is too complicated	3.8 (10)
Injections are painful	2.6 (11)

Rosenstock J, et al. Endocr Rev. 2024;45:379-413; ADA Professional Practice Committee. Diabetes Care. 2024;47; Robinson S, et al. Diabetes Technol Ther. 2021;23:844-856; Peyrot M, et al. Diabet Med. 2012;29:682-689.

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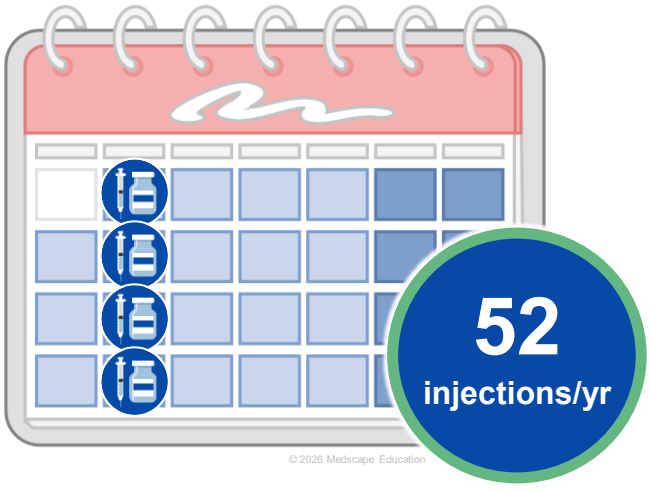
FEWER INJECTIONS = IMPROVED ADHERENCE



Once-weekly formulations of GIP/GLP-1RAs and GLP-1 RAs are associated with significantly better adherence than once-daily formulations[1]

Similar benefits may be observed with once-weekly basal insulins

Qiao Q, et al. Diabetes Metab Syndr Obes. 2016;9:201-205.

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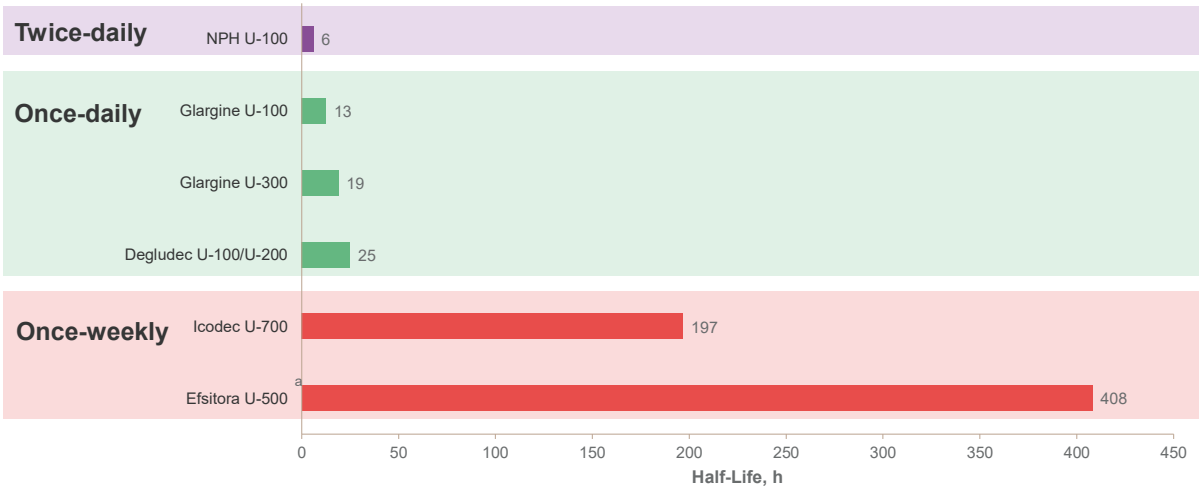
Weekly Insulins Have a Much Longer Half-Life Compared With Daily Insulins[1-2]



1. Rosenstock J, et al. Endocr Rev. 2024;45:379-413; 2. Almoud EN, et al. Front Endocrinol (Lausanne). 2024;14:1285147.

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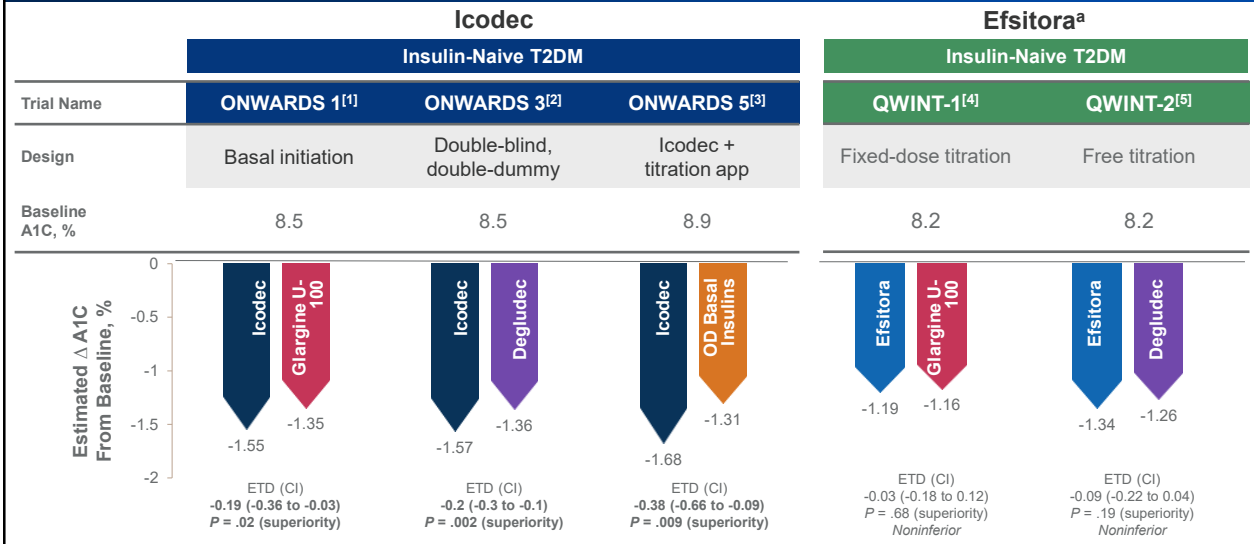
Once-Weekly Basal Insulin Has Similar or Superior Efficacy As Once-Daily Basal Insulin in Insulin-Naive PwT2DM



BBT, basal bolus therapy; MDI, multiple daily injections.
1.Rosenstock J, et al. N Engl J Med. 2023;389:297-308; 2. Mathieu C, et al. Lancet. 2023;401:1929-1940; 3. Philis-Tsimikas A, et al. Lancet. 2025;405:2279-2289; 4. Rosenstock J, et al. New Engl J Med. 2025;393:325-335.

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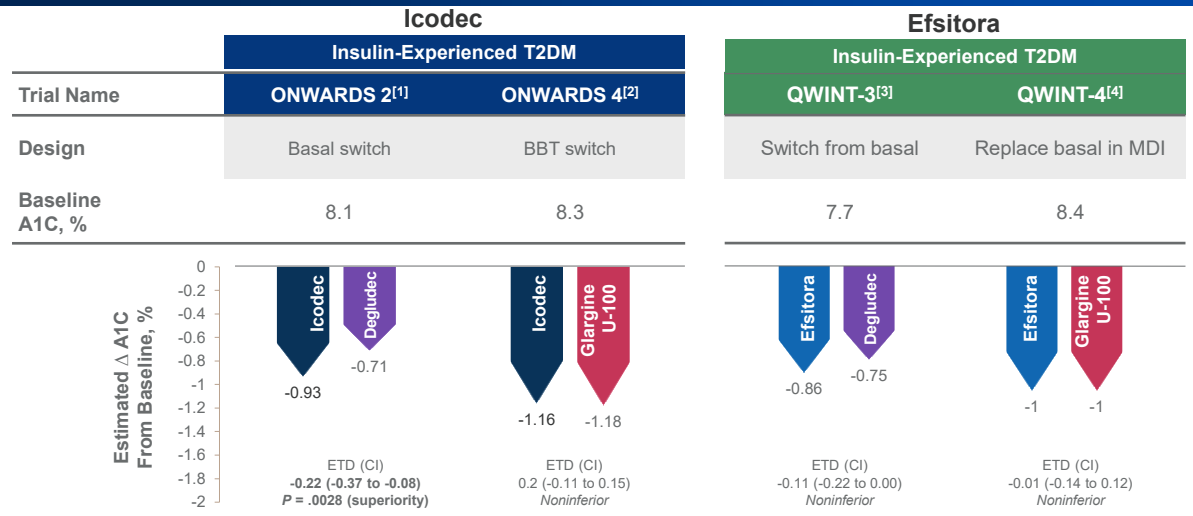
Once-Weekly and Once-Daily Basal Insulin Have Similar Efficacy in Insulin-Experienced PwT2DM



BBT, basal bolus therapy; MDI, multiple daily injections.
1. Philis-Tsimikas A et al. Lancet Diabetes Endocrinol. 2023;11:414-425; 2. Mathieu C, et al. Lancet. 2023;401:1929-1940;
3. Philis-Tsimikas A, et al. Lancet. 2025;405:2279-2289; 4. Blevins T et al. Lancet. 2025;405:2290-2301.

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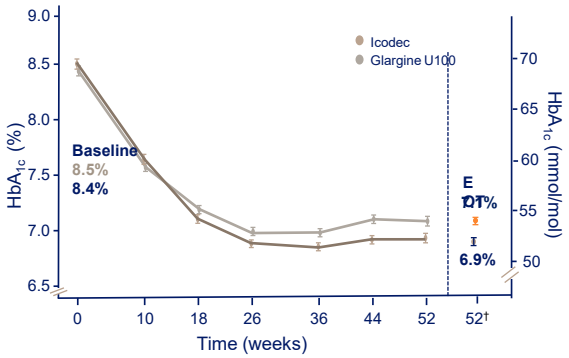
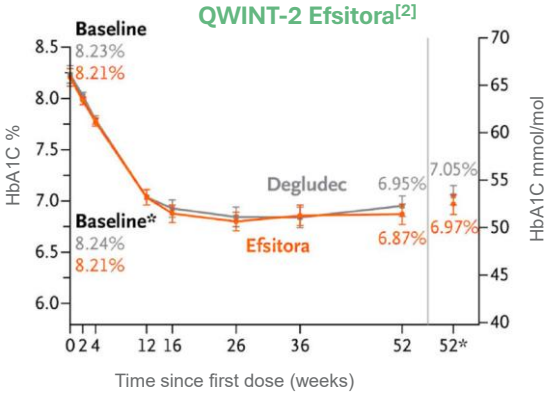
Once-weekly Insulins: Hemoglobin A1c Level Over Time

Time for attainment of glycemic control is similar for QW and QD insulin dosing in insulin-naive patients

ONWARDS-1 Icodec[1]



QWINT-2 Efsitora[2]



At week 52 the estimated **mean HbA_{1c} change from baseline was greater with icodec (−1.55%) vs glargine U100 (−1.35%);** non-inferiority and superiority were confirmed[1]

1. Rosenstock J, et al. N Engl J Med 2023;10.1056/NEJMoa2303208; 2. Wysham C, et al. N Engl J Med. 2024;391:2201-2211.

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Meta-Analysis: Insulin Icodec Safety Outcomes

	Hypersensitivity Events			Injection Site Reactions		
	Icodec	Daily Insulin	Odds Ratio	Icodec	Daily Insulin	Odds Ratio
ONWARDS 1	33	39	0.84	7	12	0.58
ONWARDS 2	9	5	1.84	3	1	3.03
ONWARDS 3	7	13	0.53	25	13	2.02
ONWARDS 4	6	7	0.85	2	2	1.00
ONWARDS 5	14	14	0.99	5	7	0.71
	Clinically-significant Hypoglycemia			**Severe Hypoglycemia**		
	Icodec	Daily Insulin	Odds Ratio	Icodec	Daily Insulin	Odds Ratio
ONWARDS 1	48	49	0.98	1	3	0.33
ONWARDS 2	37	19	2.11	0	1	0.33
ONWARDS 3	24	13	1.93	0	0	NR
ONWARDS 4	148	160	0.85	4	2	2.01
ONWARDS 5	64	42	1.58	0	4	0.11

There was a higher incidence of level 1 hyperglycemia with icodec vs comparators, but no significant difference in clinically significant level 2, 3 or combined level 2/3 hyperglycemia with icodec vs daily basal insulin analogues

Clinically significant hypoglycemia was defined as a blood glucose level of < 54 ng/dL (< 3.0 mmol/L) confirmed with a blood glucose meter. Severe hypoglycemia was defined as hypoglycemia with severe cognitive impairment requiring external assistance for recovery.
Shetty S, et al. Diabetes Obes Metab. 2024;26:1069-1081.

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Meta-Analysis: Insulin Efsitora Safety Outcomes

	Hypersensitivity Reactions			Injection Site Reactions		
	Efsitora	Daily Insulin	Risk Ratio	Efsitora	Daily Insulin	Risk Ratio
QWINT-1	6	10	0.60	7	6	1.17
QWINT-2	42	31	1.34	11	8	1.36
QWINT-3	34	16	1.07	14	6	1.18
QWINT-4	11	4	2.75	1	0	3.0

	Clinically-Significant Hypoglycemia			Severe Hypoglycemia		
	Efsitora	Daily Insulin	Risk Ratio	Efsitora	Daily Insulin	Risk Ratio
QWINT-1	103	118	0.88	1	1	1.0
QWINT-2	130	97	1.33	0	6	0.08
QWINT-3	268	123	1.1	6	2	1.52
QWINT-4	198	198	1.0	5	5	1.0

Serious adverse events, hypersensitivity reactions, injection-site reactions and hypoglycemia events were comparable between efsitora and comparators

Clinically significant hypoglycemia was defined as a blood glucose level of < 54 ng/dL (< 3.0 mmol/L) confirmed with a blood glucose meter. Severe hypoglycemia was defined as hypoglycemia with severe cognitive impairment requiring external assistance for recovery.
Mehmood H, et al. Endocrinol Diabetes Metab. 2025;8:e70126.

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Once Weekly Insulin
Examining Hypoglycemia Risk in Patients With T2D

Study 1: Icodec
Two-period crossover study of icodec in patients on insulin ± oral glucose-lowering therapy vs responses to 2x and 3x doses of icodec with insulin glargine[1]

Study 2: Efsitora
Two-period crossover study of efsitora vs insulin glargine in situations associated with greater risk for hypoglycemia (ie, prolonged fasting and/or exercise, double dose of insulin)[2]

Study Results
No increased risk for hypoglycemia under any conditions
Mean nadir glucose was similar
CGM derived duration of hypoglycemia similar between QW and QD insulin
Level 1 hypoglycemia resolved spontaneously or after 15 gm carbohydrates in all groups

1. Pieber TR, et al. Diabetologia. 2023;66:1413-1430; 2. Heise T, et al. Diabetes Ther. 2024;15:1785-1797.

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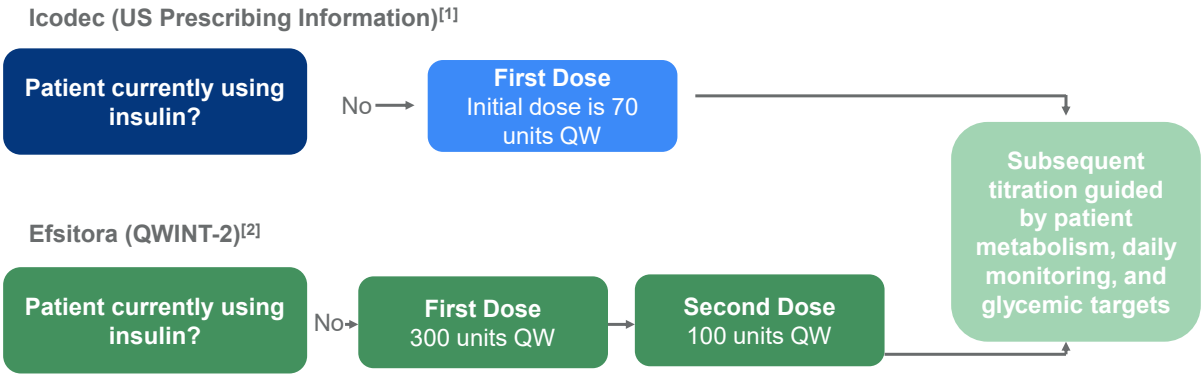
Once-Weekly Insulin: Dosing for Insulin Naive Patients



1. Icodec [PI]. Approved 2023; 2. Rosenstock J, et al. Diabetes Care. 2023;46:e121-e123.

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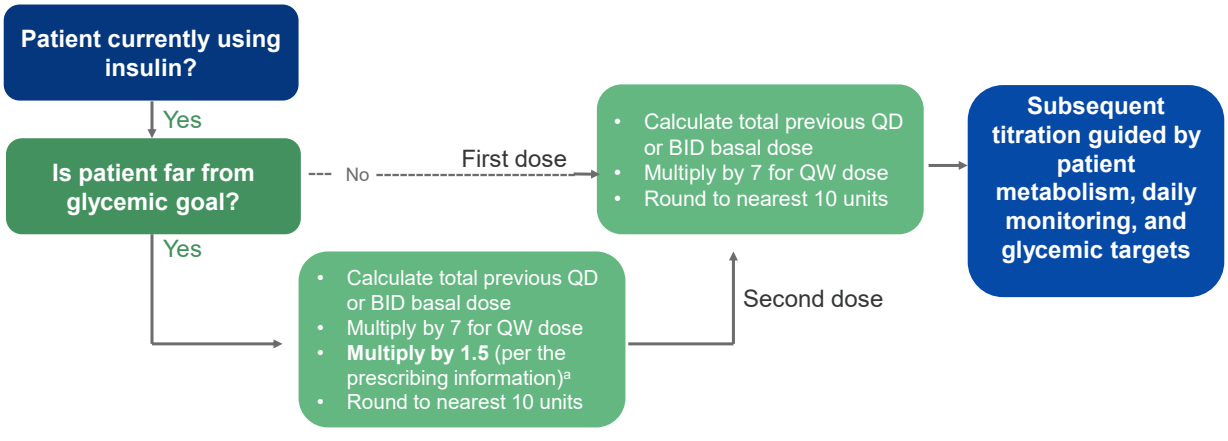
Icodec Initiation and Titration[1]



A lower multiple may be necessary in patients with a history of severe hypoglycemia on insulin therapy

[a]For an insulin with a very long half-life, such as weekly insulins, a loading dose may be useful to reach effective insulin concentrations to safely enable patient-tailored insulin titrations to reach glucose targets
US FDA. June 5, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761326Orig2s000lbl.pdf.

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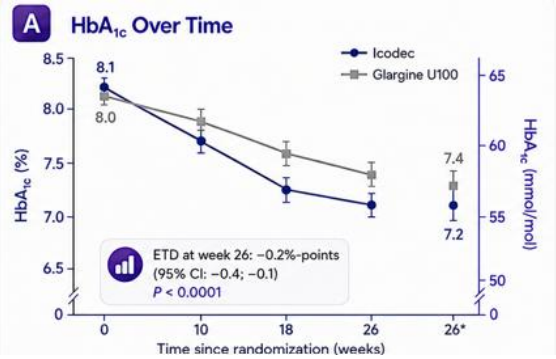
ONWARDS 10: Icodec (vs Glargine) Without a Loading Dose in PwT2D on Basal Insulin

Glycemic Control and Fasting Glucose Over Time



Icodec showed significantly greater reduction in A1c at week 26 vs glargine U100 ($P < .0001$)

Rosenstock J, et al. Diabetes Obes Metab. 2026. doi: 10.1111/dom.70813. [Epub ahead of print].

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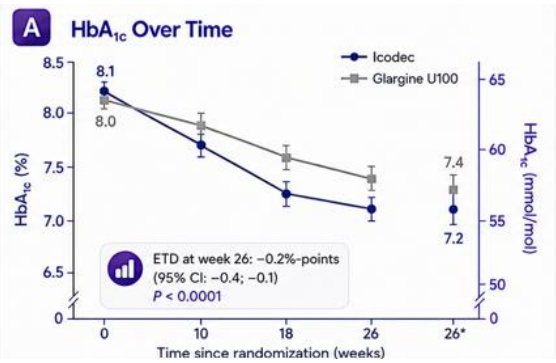
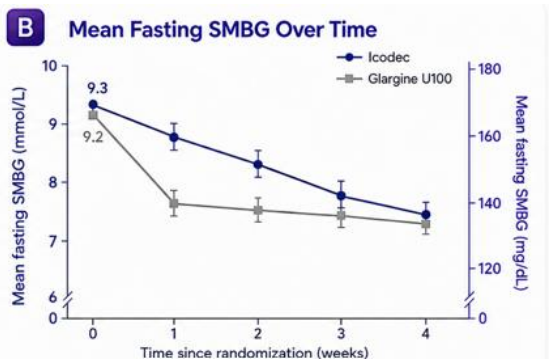
ONWARDS 10: Icodec (vs Glargine) Without a Loading Dose in PwT2D on Basal Insulin

Glycemic Control and Fasting Glucose Over Time





Icodec showed significantly greater reduction in A1c at week 26 vs glargine U100 ($P < .0001$)

Insulin glargine U100 demonstrated consistently lower SMBG during the first 4 weeks

Rosenstock J, et al. Diabetes Obes Metab. 2026. doi: 10.1111/dom.70813. [Epub ahead of print].

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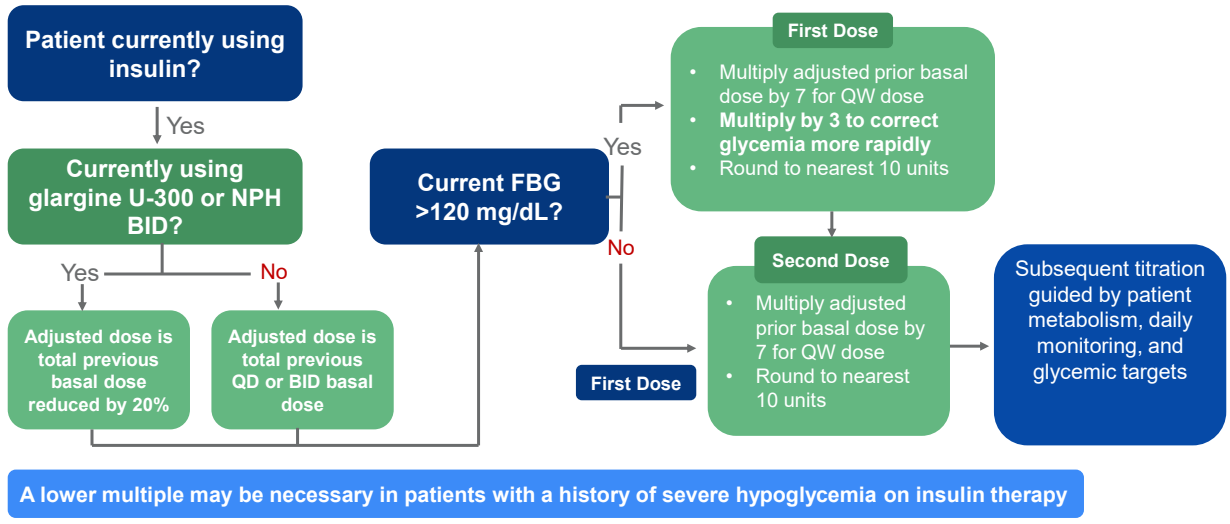
Efsitora Initiation and Titration in Clinical Trials



1. Wysham C, et al. N Engl J Med. 2024;391:2201-2211; 2. Philis-Tsimkas A, et al. Lancet. 2025;405:2279-2289.

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Stop and Reflect

Think about the following question and how it relates to your practice

What strategies am I going to employ when back in clinic to assist patients who want to change from daily to weekly basal insulin?

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Once-Weekly Insulin: Patient Selection

- Patient with difficulty adhering to daily insulin use
- Older adult with cognitive or physical limitations
- Patient with T2D plus comorbidities and polypharmacy
- GLP-1 RA or GIP/GLP-1 RA user with suboptimal A1C
- A patient struggling with orals but unsure about injections
- Patient with hectic work/personal schedule or travels often
- Patient preference

Shubrook JH. Fed Pract. 2024;41:S47-S52.

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Case Study: Joe, A 58-yr-old Man With 10 yr History T2D

- **Joe is a 58-year-old man with 10-year history of T2D.**
  - He has been in good control since diagnosis and has no known complications of diabetes.
  - He travels extensively for work and reports that taking his insulin is challenging.
  - He doesn't like to take it with him and struggles with timing related to changes in time zones.
- **Current medications: metformin XR 1500 mg QD, tirzepatide 10 mg QW, insulin degludec 30 units QAM, rosuvastatin 20 mg QD and losartan 100 mg QD**
- **Examination: BMI – 29 kg/m^2, BP – 118/72, otherwise is normal.**
- **Labs: A1c – 7.8%, eGFR – 68 ml/min/1.73 m^2, LDL – 63 mg/dl, uACR – 12 mg/gCr.**

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Case Study: Joe Switches to Once-Weekly Insulin Icodec

- **After discussing the options, he is interested in changing to once-weekly insulin**
- **To calculate dose:**
  - Take baseline daily dose times 7 [30 x 7 = 210 units] for his weekly dose
  - For the first dose, multiply by 1.5 = 315 units
- **He should be instructed to take 315 units for first dose, then 1 wk later take 210 units for second dose; at wk 3 consider titration**
- **If needed, titration should occur weekly and should follow guidelines, based upon median of past three days:**
  - BG < 80 – decrease by 20 units
  - 80 – 130 – keep same dose
  - > 130 – increase by 20 units

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Case Study: Joe's Follow Up Visit

- He follows up 3 months later
- He has increased his dose to 280 units weekly and reports that he is taking his insulin on the same day as he takes his tirzepatide
- He reports no hypoglycemia and no increase in body weight
- A1c = 6.8%

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Summary

- Once-weekly basal insulins are promising options that address many of the barriers associated with once-daily formulations among patients and providers
- Compared to once-daily basal insulin, both efsitora and icodec offer comparable glycemic control, similar safety profile, reduced injection burden, greater patient satisfaction and the potential to improve adherence, based on clinical trials
- Instances of hypoglycemia were infrequent across studies and deemed not clinically significant

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PARTICIPANT QUESTION 1

According to real-world data, at which baseline A1C level are patients with type 2 diabetes who initiate basal insulin most likely to achieve an A1C goal of less than 7% while experiencing the least amount of weight gain?

- 7.0–<8.0%
- 8.0–<9.0%
- 9.0–<10.0%
- 10.0–<11.0%

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PARTICIPANT QUESTION 2

How confident are you right now, in your ability to initiate and titrate basal insulin safely and effectively to improve outcomes in people with T2D?

1 - Not confident
2 - Slightly confident
3 - Moderately confident
4 - Mostly confident
5 - Very confident

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