

INSULIN ALGORITHM FOR TYPE 2 DIABETES MELLITUS IN CHILDREN AND ADULTS



Glycemic Goals^{1,2}
Individualize goal based on patient risk factors

A1c ≤6% <7% <8%

FPG ≤110 120 140 mg/dL

2h PP ≤130 180 180 mg/dL

Once-daily Insulin Therapy

Morning - Basal insulin

Bedtime - Basal insulin or NPH

Before supper (Evening)
 NPH + R or F 2:1 ratio or
 Premix 70/30 or 75/25

Starting dose^{9,10}
 0.1-0.25 units/kg/day or
 6-10 units/day if patient is elderly or thin

Achieving Goals
 Adjust Basal insulin / Bedtime NPH based on FPG
 Adjust NPH + R or F / Premix based on bedtime glucose and FPG

Titration schedule⁹
 Add 1 unit of insulin each day to reach glycemic goals OR

If FPG:

>180 mg/dL	Add 6 units
If 141-180 mg/dL	Add 4 units
If 121-140 mg/dL	Add 2 units
If 100-120 mg/dL	Add 1 unit
If 80-99 mg/dL	No change
If <80 mg/dL	Subtract 2 units

Treatment Naïve³
A1c ≥10% or A1c <10% when considering early insulin initiation

If ketoacidosis or recent rapid weight loss, see Type 1 Diabetes algorithm

INITIAL OPTIONS^{3,4}

- Once-daily Insulin⁵ + oral(s)
- Multi-dose Insulin⁶ +/- oral(s)
- Intensive Insulin Management⁶ +/- oral(s)

Uncontrolled on non-insulin therapy:
 A1c <1% above goal

- Continue oral agent therapy +/- insulin secretagogue
- Stop GLP-1 agonist prior to insulin therapy

INITIAL OPTIONS⁴

- Once-daily Insulin⁵
- Multi-dose Insulin⁶
- Intensive Insulin Management⁶

Uncontrolled on non-insulin therapy:
 A1c ≥1% above goal

INITIAL OPTIONS⁴

- Multi-dose Insulin⁶
- Intensive Insulin Management⁶
- Once-daily Insulin⁵

Basal insulin = Glargine or Detemir
 Bolus insulin = Aspart or Glulisine or Lispro
 Fast-acting insulin = Aspart; Glulisine; Lispro
 F = Fast-acting insulin
 R = Regular insulin
 FPG = Fasting plasma glucose
 PP = Postprandial plasma glucose
 SMBG = Self-monitored blood glucose
 TDD = Total daily dose of insulin

Multi-dose Insulin Therapy (MDI)¹⁰

2 injections
 NPH with R or F (ratio 2:1) before AM and evening meal
or
 Premix 70/30 or 75/25 before AM and evening meal

3 injections (especially if nocturnal hypoglycemia)
 NPH with R or F morning; R or F⁷ evening; NPH bedtime or
 Premix (as above) morning, noon, evening

Starting dose^{8,9}: 0.3-0.5 units/kg/day, divided as follows:

	Before AM Meal	Before evening meal	At Bedtime
2 injections:	2/3 morning; 1/3 evening		
3 injections:		1/3 morning; 1/3 noon; 1/3 evening	
Premix:	1/3 morning; 1/3 noon; 1/3 evening		
NPH + R or F:			
	Before AM Meal	Before evening meal	At Bedtime
NPH	40% of TDD		25% of TDD
R or F	20% of TDD	15% of TDD	

Intensive Insulin Management¹⁰

Basal: Once-daily, either morning or bedtime (alternative: NPH morning and bedtime)

Bolus: Fast-acting insulin before each meal; (alternative: R may be used)

Premeal bolus insulin dose includes:

- Insulin to cover carbohydrate ingested¹¹ &
- Additional insulin to correct for high SMBG:
 ~1500/TDD for Regular;
 ~1800/TDD for Aspart/Glulisine/Lispro

Starting dose^{8,9}:
 1. 0.3-0.5 units/kg/day (1:1 basal:bolus ratio SQ)
Or
 2. If current dose >0.5 units/kg/day
 Basal dose = 80% Total daily NPH or
 80% Total long-acting component of premix
 Bolus dose = 80% of basal dose divided between 3 meals

Pramlintide
 Consider as adjunct therapy to insulin in patients unable to stabilize post-prandial glucose

Follow A1c every 3-6 months and Adjust Regimen to Maintain Glycemic Goals

Footnotes:

- 1. Intensify management if:** Absent/stable cardiovascular disease, mild-moderate microvascular complications, intact hypoglycemia awareness, infrequent hypoglycemic episodes, recently diagnosed diabetes. **Less intensive management if:** Evidence of advanced or poorly controlled cardiovascular and/or microvascular complications, hypoglycemia unawareness, vulnerable patient (ie, impaired cognition, dementia, fall history). SEE "A1c Goal" treatment strategy for further explanation. A1c is referenced to a non-diabetic range of 4-6% using a DCCT-based assay. ADA Clinical Practice Recommendations. *Diabetes Care* 2009;32(suppl 1):S19-20.
2. Current glucose meters give values corrected to plasma glucose.
3. May also begin combination oral agent therapy. See [Glycemic Control Algorithm for Type 2 Diabetes Mellitus in Children and Adults](#).
4. Combining metformin with insulin therapy has been shown to result in less weight gain and better glycemic control with lower insulin requirements.
5. Continue combination oral agent therapy ± sulfonylurea.
6. Continue metformin (± 3rd oral agent); probably discontinue sulfonylurea.
7. Fast-acting insulin is given with the start of each meal. Regular insulin to be given 30-60 minutes before meals.
8. Dosage may differ in children and adolescents; consider referral to pediatric endocrinologist/comprehensive diabetes specialty team.
9. Start lower and increase slower for thin/elderly/complicated patients.
10. Consider referral to pediatric/adult endocrinologist/diabetes specialty team (option – insulin pump, Pramlintide).
11. Typical "carb" bolus = 1 unit bolus insulin covers 500/TDI x g carbohydrate from meal (~10-15 gm); **strongly recommend referral to Registered/Licensed Dietitian or Certified Diabetes Educator with experience in diabetes nutrition counseling (see Worksheet D).**

INITIATION OF ONCE DAILY INSULIN THERAPY FOR TYPE 2 DIABETES MELLITUS IN CHILDREN AND ADULTS¹

Glycemic Goals^{2,3}

Individualize goal based on patient risk factors

A1C ≤6% <7% <8%

FPG ≤110 120 140 mg/dL
2h PP ≤130 180 180 mg/dL

Treatment Naïve³
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If ketoacidosis or recent rapid weight loss, see Type 1 Diabetes algorithm

Oral Agent Failure;
A1c above target

Abbreviations:

FPG: Fasting plasma glucose
SMBG: Self-monitored blood glucose
PP: Postprandial plasma glucose

Initiate Insulin Therapy with daily Glargine or Detemir or bedtime NPH^{5,6}

Beginning Dosage: 10 units or 0.1-0.25 units/Kg

Titration Schedule (Adjust Every 2-3 Days)

If FPG:

>180 mg/dL	Add 6 units
If 141-180 mg/dL	Add 4 units
If 121-140 mg/dL	Add 2 units
If 100-120 mg/dL	Add 1 unit
If 80-99 mg/dL	No change
If <80 mg/dL	Subtract 2 units

OR

Add 1 unit insulin each day until fasting SMBG is at goal

If A1c remains >A1c goal over 3 months, discontinue oral secretagogue, continue oral insulin sensitizer(s) and initiate multi-dose insulin or intensive insulin therapy¹ or consult an endocrinologist

Footnotes:

- For the complete approach to insulin initiation in Type 2 Diabetes Mellitus, see Insulin Algorithm for Type 2 Diabetes Mellitus in Children and Adults.
- Intensify management if:** Absent/stable cardiovascular disease, mild-moderate microvascular complications, intact hypoglycemia awareness, infrequent hypoglycemic episodes, recently diagnosed diabetes. **Less intensive management if:** Evidence of advanced or poorly controlled cardiovascular and/or microvascular complications, hypoglycemia unawareness, vulnerable patient (ie, impaired cognition, dementia, fall history). SEE "A1c Goal" treatment strategy for further explanation. A1c is referenced to a non-diabetic range of 4-6% using a DCCT-based assay. ADA Clinical Practice Recommendations. *Diabetes Care* 2009;32(suppl 1):S19-20.
- Current glucose meters give values corrected to plasma glucose.
- Usually with an insulin secretagogue (sulfonylurea, repaglinide or nateglinide) and sensitizer (metformin or thiazolidinedione). See Glycemic Control Algorithm.
- The pharmacokinetic profile of NPH compared to that of glargine or detemir is less predictable, therefore can result in blood sugar variations and increased nocturnal hypoglycemia. Cost of glargine or detemir is 1.5-2 times that of NPH. Lispro 75/25 or Aspart 70/30 can be considered at pre-supper adjusting dosage according to bedtime and fasting SMBG.
- IMPORTANT: See package insert for dosing.**
- If daytime hypoglycemia develops, contact healthcare professional.

WORKSHEET

Advancing to Intensive/Physiologic Basal: Bolus Insulin Therapy



TEXAS DIABETES
COUNCIL
Revised 1/27/10

Note: “Analog” = Rapid Acting (Bolus) Analog insulin throughout this document.

A. Conversion from once-daily insulin to intensive/physiologic insulin replacement:

Oral therapy failure: Once-daily glargine was added to the oral regimen and titrated to 30 units per day. How do you add analog insulin if the patient reports the following SMBG values?

	FPG	2-hr pp Brkfst	2-hr pp Lunch	2-hr pp Dinner
Case 1	105	140	140	240
Case 2	105	140	190	240
Case 3	105	190	240	240

Case 1

- Continue the oral agents (\pm sulfonylurea) and 30 units glargine or detemir (or NPH)
- There are 2 approaches for adding analog (RAI) 10-15 minutes before a meal:

#1	Arbitrary start: 5 units Titrate: Add 2 units every 2 days to reach 2-hr pp goal
#2	Carb-counting 1 unit/50 mg/dL over 2-hr pp goal <i>PLUS</i> 1 unit/15 grams carbohydrate Titrate: Add 1 unit/50 mg/dL >2-hr pp goal every 2 days

Cases 2 and 3

As above, but add and titrate analog before each meal where the postprandial glucose is above goal. Also, see part D, below for more information on how to optimize the use of analog insulin. Re-evaluate each week to be certain that about half of the total daily dose is basal and half is bolus insulin.

B. Conversion from once-daily premix to intensive/physiologic insulin replacement:

Oral therapy failure: Once-daily 70/30 premixed insulin was added and titrated to 30 units per day. The fasting glucose is at goal, but daytime control is poor. How do you convert to physiologic insulin therapy?

- Basal insulin dose:** The first step in the conversion is based on the total dose of intermediate-acting insulin. In this case, the person is taking 21 units of NPH or aspart-protamine insulin ($70\% \times 30 \text{ units} = 21 \text{ units}$). So, give 21 units basal glargine (use “unit-for-unit” conversion for once-daily intermediate regimens.) *Remember, do not stop oral agents (+ sulfonylurea) at this time.*
- Bolus insulin dose:** There are several ways to start the analog.
 - See Case 1, page 2 (Arbitrary start or Carb-counting)
 - Begin with the previous dose of fast-acting insulin, divide it before meals and titrate every 2 days. In this case, the person was using 30 units of 70/30 or about 9 units of fast-acting insulin ($30\% \times 30 \text{ units} = 9 \text{ units}$). So give 3 units of analog before each meal and titrate every 2 days as per Case 1.



C. Conversion from twice-daily premix to intensive/physiologic insulin replacement:

Oral therapy failure in an 80 kg person: 70/30 premixed insulin was started and advanced to 60 units per day: 40 units before breakfast and 20 units before dinner. The fasting glucose was at goal, but wide glycemic excursions occurred at other times during the day and night. How do you convert this person to physiologic insulin therapy? There are several approaches. Use which ever method you want.

- a. Start over and begin insulin at 0.5 units/kg. Give half as basal insulin and half as analog, divided before meals. In this case, the starting dose would be 40 units per day. Start giving 20 units glargine each morning and about 7 units analog before each meal. Titrate the basal and bolus insulins every 2 days to fasting and 2-hr postprandial goals.
- b. Conversion based on current insulin usage:

Basal dose: The first step in the conversion is based on the **80% of the total dose of intermediate-acting insulin**. In this case, the person is taking 42 units of NPH or aspart-protamine insulin ($70\% \times 60 \text{ units} = 42 \text{ units}$). When a person is taking multiple doses of intermediate-acting insulin, we give only 80% as glargine. So, give 34 units basal glargine ($80\% \times 42 = \sim 34$). Remember, *do not stop oral agents (+ sulfonylurea) at this time*.

Bolus insulin dose: There are several ways to start the analog.

- i. See Case 1, page 3 (*Arbitrary start or Carb-counting*)
 - ii. Begin with the previous dose of fast-acting insulin, divide it before meals and titrate every 2 days. In this case, the person was using 60 units of 70/30 or 18 units of fast-acting insulin ($30\% \times 60 \text{ units} = 18 \text{ units}$). So, give 6 units of analog before each meal and titrate every 2 days as per Case 1.
- c. The **“80%-80%” rule**: Similar to the above method, but yields an ideal ratio of basal:bolus insulin in one step. The dose of basal glargine will be 80% of the total intermediate insulin, and the analog will be 80% of the glargine dose, divided before meals.

Basal dose: = 80% of total intermediate insulin
= $80\% \times 42 \text{ units}$ ($70\% \times 60 = 42$)
= 34 units glargine

Analog dose: = 80% of the glargine dose, divided TID
= $80\% \times 34 \text{ units} = 27 \text{ units}$
= 27 units, divided tid = 9 units
= 9 units aspart, glulisine or lispro before meals

Note: Total dose of insulin is conserved and an ideal ratio between basal and bolus will always result with the “80%-80%” method.

D. Optimizing analog insulin use

Tight control of blood glucose requires that the patient participates in the management of their diabetes. This includes monitoring their blood glucose and learning to count carbohydrates or “carb count.” The following material explains how to calculate the dose of analog required to cover a meal and how to add extra analog to correct a hyperglycemic event.

a. Determining the dose of analog insulin to use before a meal

The “Rule of 500” is used to determine how many grams of carbohydrate 1 unit of analog insulin will cover. When this number is known, then the person can easily give the correct dose of analog by simply counting the grams of carbohydrate they intend to eat at the meal.

Specifically, 500 divided by the total daily insulin dose (500/TDI) yields the number of grams of carbohydrate that 1 unit of analog will cover. For example, if a person has established that they require about 50 units of insulin per day, then it follows that 1 unit of analog will cover 10 grams of carbohydrate ($500/50 = 10$). If the person carb counts 140 grams in the dinner meal, then the dose of analog will be 14 units given 10 minutes before eating.

b. Correcting for hyperglycemia

The “Rule of 1800” is used to determine how much insulin to use to bring a high glucose reading back to goal. Even with tight control, hyperglycemia occurs and people need to be able to correct this situation.

Specifically, 1800 divided by the total daily insulin dose yields a value indicating how much 1 unit of analog insulin will lower the blood glucose. Thus, if a person uses 90 units of insulin per day, then 1 unit of analog will reduce the blood glucose by 20 mg/dL ($1800/90 = 20$). *This augment dose of insulin can be used by itself to correct hyperglycemia, or added to the bolus dose if glucose is high before a meal.*

References:

1. Riddle MC, Rosenstock J, Gerich, J. *Diabetes Care*, 2003; 26:3080-3086.
2. Spellman CW, Renda SM, Davis SN. *Realizing the Potential of Insulin Therapy in Type 2 Diabetes: A Case Presentation-Based Monograph*, presented at the American College of Osteopathic Internists 64th Annual Convention; Chicago, IL (September 30, 2004).
3. www.texasdiabetescouncil.org



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Reviews/Important Articles:

- Abraira C, Colwell J, Nuttall F, et al. Cardiovascular events and correlates in the Veterans Affairs Diabetes Feasibility Trial. Veterans Affairs Cooperative Study on Glycemic Control and Complications in Type II Diabetes. *Arch Intern Med.* 1997;157(2):181-8.
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- DeWitt DE, Dugdale DC. Using new insulin strategies in the outpatient treatment of diabetes: clinical applications. *JAMA.* 2003;289(17):2265-9.
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- Hirsch IB. Insulin analogues. *N Engl J Med.* 2005;352(2):174-83.

Once Daily Insulin

Morning vs. Bedtime NPH

- Groop LC, Widen E, Ekstrand A, et al. Morning or bedtime NPH insulin combined with sulfonylurea in treatment of NIDDM. *Diabetes Care.* 1992;15(7):831-4.

Morning vs. Bedtime Glargine

- Fritsche A, Schweitzer MA, Haring HU. Glimepiride combined with morning insulin glargine, bedtime neutral protamine hagedorn insulin, or bedtime insulin glargine in patients with type 2 diabetes. A randomized, controlled trial. *Ann Intern Med.* 2003;138(12):952-9.

NPH vs. Glargine

- Riddle MC, Rosenstock J, Gerich J. The treat-to-target trial: randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. *Diabetes Care.* 2003;26(11):3080-6.

Once Daily Vs. Twice Daily Regimen

- Raskin P, Allen E, Hollander P, et al. Initiating insulin therapy in type 2 Diabetes: a comparison of biphasic and basal insulin analogs. *Diabetes Care.* 2005;28(2):260-5.

Multiple Dose Insulin Regimens (2-Shot Regimens)

NPH/Regular vs. NPH/ short acting analogue therapy

- Vignati L, Anderson JH Jr, Iversen PW. Efficacy of insulin lispro in combination with NPH human insulin twice per day in patients with insulin-dependent or noninsulin-dependent diabetes mellitus. Multicenter Insulin LisproStudy Group. *Clin Ther.* 1997;19(6):1408-21.

70% NPH/ 30% Regular vs. Humalog Mix 75/25 TM or Novolog Mix 70/30TM

- Roach P, Yue L, Arora V. Improved postprandial glycemic control during treatment with Humalog Mix25, a novel protamine-based insulin lispro formulation. Humalog Mix25 Study Group. *Diabetes Care.* 1999;22(8):1258-61.
- Boehm BO, Home PD, Behrend C, et al. Premixed insulin aspart 30 vs. premixed human insulin 30/70 twice daily: a randomized trial in Type 1 and Type 2 diabetic patients. *Diabet Med.* 2002;19(5):393-9.

Multiple Dose Insulin Regimens (3-Shot Regimens)

- Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract.* 1995;28(2):103-17.

Intensive Insulin Therapy

- Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract.* 1995;28(2):103-17.
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- Bretzel RG, Arnolds S, Medding J, et al. A direct efficacy and safety comparison of insulin aspart, human soluble insulin, and human premix insulin (70/30) in patients with type 2 diabetes. *Diabetes Care.* 2004;27(5):1023-7.