Table 17
Recommended Steps for the Addition of Insulin to Antihyperglycemic Therapy

Glucose value	Total daily dose	Notes/caveats
Step 1. Start basal (long-acting insulin)		
A1C <8%	0.1 to 0.2 units/kg	Consider discontinuing SU therapy; basal analogs preferred over NPH; bedtime dose preferred
A1C >8%	0.2 to 0.3 units/kg	
Step 2. Titrate basal insulin every 2-3 d to reach glycemic goals[a]		
Fixed regimen	Increase by 2 units/d	
Adjustable regimen		
FBG >180 mg/dL	Add 4 units	
FBG 140 to 180 mg/dL	Add 2 units	
FBG 110 to 139 mg/dL	Add 1 unit	
Step 3. Monitor for hypoglycemia		
BG <70 mg/dL	Reduce by 10% to 20%	
BG <40 mg/dL	Reduce by 20% to 40%	

Abbreviations: A1C = hemoglobin A1c; BG = blood glucose; d = day; FBG = fasting blood glucose; NPH = Neutral Protamine Hagedorn; SU = sulfonylurea.
[a] For most persons with T2D taking insulin, glucose goals are A1C <7% and fasting and premeal blood glucose <110 mg/dL in the absence of hypoglycemia. A1C and FBG targets may be adjusted based on a person's age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk.

who require intensification of therapy, one should consider adding a GLP-1 RA and/or an SGLT2i, which would provide good glycemic lowering (especially with GLP-1 RA), reduction in weight and BP, and a low risk for hypoglycemia. Other medications that have a low risk for hypoglycemia are DPP-4 inhibitors and TZDs. Medications that tend to be less expensive than others are SUs and TZDs.

Insulin Use in T2D

Insulin is usually initiated in those with T2D when combination therapy with other agents fails to attain or maintain glycemic goals, or when an individual, whether drug naïve or on a treatment regimen, presents with an A1C level >9.0% and symptomatic hyperglycemia.[73,1062] Once insulin is initiated, its beneficial A1C effect is stable for 2 to 4 years in the majority of persons.[1063] Most persons with T2D who require intensification of antihyperglycemic therapy with a GLP-1 RA or insulin should initially be prescribed a GLP-1 RA. Insulin could then be added if further intensification is required. Several RCTs show that GLP-1 RAs vs basal insulin have equal or better glucose lowering, low risk for hypoglycemia, and weight reduction vs weight gain.[1021,1064]

Insulin therapy may be initiated as a basal, basal-bolus, prandial, or premixed regimen, although for most persons with T2D, starting with a basal insulin analog added to the existing antihyperglycemic regimen is preferred[1065] (Tables 17 and 18). The combination of insulin with any antihyperglycemic agent raises the potential for hypoglycemia. Persons should be closely monitored, and those on SUs or glinides may require dosage reductions or discontinuation of the oral agent. TZDs can be associated with weight gain, edema, and increased risk of CHF in combination with insulin. Basal insulin analogs are preferred over NPH insulin because of a reduced risk of hypoglycemia.[1066-1071] Newer "ultra-long-acting" basal insulin analogues, insulin glargine U300, and insulin degludec have been shown to be associated with less hypoglycemia than insulin glargine U100.[1072,1073] The insulin regimen to be prescribed and the exact treatment goals should be discussed with the person with DM.

Insulin-treated persons should be instructed in performance of BGM. Most insulin-treated persons with T2D should conduct BGM ≥2 times daily and ideally at least before each injection of insulin. The frequency and timing should be dictated by the particular needs and goals of the individual, as well as hypoglycemia risk. Emerging evidence suggests benefits of CGM use in insulin-treated persons with T2D[170,1074] (see **Q3. When and how should glucose monitoring be used?**).

Premixed insulins are popular with some persons, but they provide less dosing flexibility and have been associated with a higher frequency of hypoglycemia compared to basal and basal-bolus regimens in many, but not all studies.[1075-1079] Nevertheless, there are some persons for whom a simpler regimen is a reasonable compromise, and for this population, analog premixed insulins will provide better glycemic control with less hypoglycemia than the traditional, more affordable premixed NPH regimens.[1080] The analog premixed insulin insulin degludec/insulin aspart may provide reductions in nocturnal hypoglycemia compared to glargine U100,[1081] but a basal bolus regimen with an ultra-long-acting basal insulin analog and a rapid-acting prandial insulin analog may achieve more effective control with less hypoglycemia.[1082] Different concentrations of the rapid-acting analogue may be beneficial in some populations.[1083] With the BIAsp 30 preparation (premixed insulin analogue containing 30% soluble, rapid-acting insulin aspart and 70% intermediate-acting protamine-bound aspart in each injection), for higher A1C levels, a third injection prior to lunch may be preferable.[1084]

When mealtime glucose control is needed or when glycemic goals are not met on a basal insulin regimen plus oral agents or a GLP-1 RA, insulin therapy intensification to a basal-bolus regimen (using a rapid-acting insulin analog or inhaled insulin) should be considered (Table 19). Ultra-rapid acting insulins can reduce postprandial glycemic peak, but this effect on long-term complications is unknown.[1085,1086] In addition, insulin human inhalation powder, a rapid-acting inhaled insulin, is effective at reducing postprandial peak, and studies in persons with T1D demonstrated that hypoglycemia was reduced with use of this inhaled insulin relative to insulin aspart,[1087] but overall glycemic efficacy measured by A1C may not be as great as subcutaneous insulin.[1088,1089]

CSII or insulin pumps are options for persons with T2D taking basal and prandial injections (MDI) of insulin.[153,1090] Persons with T2D may also benefit from the use of a wearable device that delivers for basal insulin a continuous subcutaneous infusion of rapid-acting insulin and also allows 2-unit boluses of insulin when the wearer depresses a button.[1091]

Many people with T2D treated with MDI and CSII should also be using CGM, and a significant number of those treated using the wearable, patch-like device described above or receiving injections of basal insulin only would benefit greatly by use of CGM. More information about insulin pumps, CGM (including differences between rtCGM, isCGM), and open-loop and hybrid closed-loop (HCL) use of both insulin pumps and CGM can be found elsewhere in this guideline and in the 2021 AACE Advanced Diabetes Technology guideline.[153]

Use of the amylin analog pramlintide in conjunction with bolus insulin improves both glycemia and weight in persons with T2D.[1092,1093] GLP-1 RAs and DPP-4 inhibitors have properties similar to those of pramlintide and also increase endogenous insulin secretion. The combination of basal insulin and incretin therapy decreases basal glucose and PPG and may minimize weight