Diabetes Treatment Guidelines

For more comprehensive information about current approaches to the diagnosis and treatment of diabetes, visit the American Diabetes Association Standards of Medical Care—2018 Website at *https://professional.diabetes.org/content-page/standards-medical-care-diabetes (Accessed 2018).*

Criteria for Diagnosis of Diabetes

Diagnostic Tool	Value Associated with Diagnosis of Diabetes
Fasting Plasma Glucose (FPG)#	≥ 126 mg/dL • In absence of unequivocal hyperglycemia, this number must be confirmed by repeat testing.
Random Plasma Glucose	≥ 200 mg/dL with symptoms (Polyuria; Polydipsia; Unexplained weight loss) • Value measured without regard to last meal • Only diagnostic with classic symptoms of hyperglycemia or hyperglycemic crisis
Oral Glucose Tolerance Test	≥ 200 mg/dL 2 hours post 75 g glucose challenge • In absence of unequivocal hyperglycemia, this number must be confirmed by repeat testing.
Hemoglobin A1c	≥ 6.5% • Performed in a laboratory using a method that is NGSP certified* and standardized to the DCCT assay**

 # = Fasting is defined as no caloric intake for at least 8 hours.

** National Glycohemoglobin Standardization Program; ** Diabetes Control and Complications Trial*

Practitioner may select one diagnostic tool above and in absence of unequivocal hyperglycemia should confirm results with repeat testing.

Criteria Associated with Increased Risk for Diabetes

Diagnostic Tool	Value Associated with Diagnosis of Diabetes
Impaired Fasting Glucose#	100 to 125 mg/dL
Impaired Glucose Tolerance	140 to 199 mg/dL • 2 hours post 75 g glucose challenge
Hemoglobin A1c	Range of 5.7% to 6.4%

 # = Fasting is defined as no caloric intake for at least 8 hours.

Asymptomatic patients with increased risk of diabetes who should be considered for further testing: adults of any age who are overweight or obese (BMI ≥ 25 kg/m^2 or BMI ≥ 23 kg/m^2 for Asian Americans) and who have one or more additional risk factors such as age ≥ 45. For all patients, testing should be initiated at age 45 and offered at 3-year intervals.

Updated by Jeanine P. Abrons, Elisha Andreas, and Molly Polzin

Associated Goals for Adults with Diabetes

Associated Goal	Value of Goal
Glycemic Control (A1c)	ADA*: < 7%[a] AACE**: < 6.5%[b]
Pre-Prandial Capillary Plasma Glucose	ADA: 80 to 130 mg/dL[a] AACE: < 110 mg/dL
Post-Prandial Capillary Plasma Glucose	ADA: < 180 mg/dL[a,c] AACE: < 140 mg/dL
Blood Pressure (Systolic)	ADA: < 140 mmHg[d] AACE: < 130 mmHg[e]
Blood Pressure (Diastolic)	ADA: < 90 mmHg AACE: < 80 mmHg

**American Diabetes Association (ADA) Standards of Medical Care 2018; **American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Type 2 Diabetes Management Algorithm 2018*

a: More or less stringent glycemic goals may be appropriate for individual patients. Goals should be based on duration of diagnosis, age/life expectancy, comorbid conditions (e.g., known cardiovascular disease or advanced microvascular complications), hypoglycemia unawareness, and other considerations.

b: For patients without concurrent serious illness and at low hypoglycemic risk; level ≥ 6.5% for patients with concurrent illness and at risk for hypoglycemia. A1c targets must be individualized.

c: Post-prandial glucose may be targeted if A1c goals are not met despite reaching pre-prandial glucose goals. Measurements should be made 1-2 hours after the beginning of a meal; generally represents peak levels.

d: Lower systolic goals (e.g., < 130 mmHg) may be considered for certain individuals such as younger patients, those with albuminuria, and/or those with hypertension and one or more atherosclerotic cardiovascular disease risk factors if safe and tolerable for the patient.

e: Less stringent goals may be considered for frail patients with complicated comorbidities or those who have adverse medication effects. More intensive goal (e.g., < 120/80 mmHg) should be considered for patients if this goal can be safely reached without adverse medication-related effects.

Updated by Jeanine P. Abrons, Molly Polzin and Elisha Andreas

Insulin and Insulin Analogues

Type	Generic Name (Trade Name)	Onset (hours)	Peak (hours)	Duration (hours)	Administration Route
Rapid Acting					
Analogue	**Aspart** (Novolog®)	0.2 to 0.3	1 to 3	3 to ≤ 5	Subcutaneous (SC) [Injection/CSII]
	Glulisine (Apidra®)	0.2 to 0.5	1.6 to 2.8		
	Lispro (Humalog®)	< 0.25	0.5 to 2.5		
Short Acting					
Human	**Regular** (Humulin R®; Novolin®)	0.5	2.5 to 5	4 to 12	Daily Maintenance Use: SC [Injection/CSII]; Continuous infusion may be used in other instances
	Regular U500 (Concentrated)			Up to 24	(SC) [Injection/CSII]
Intermediate Acting					
Human	**NPH** (Humulin-N®; Novolin-N®)	1 to 2	9 to 12	14 to 24	SC
Long Acting					
Analogue; Human	**Degludec** (Tresiba®)	~ 1	Not applicable	Not applicable	SC
	Detemir (Levemir®)	3 to 4	3 to 9	6 to 23	
	Glargine (Lantus®)		Not applicable	10.8 to > 24	
	Glargine (Basaglar®)			≥ 24	
	Glargine (Toujeo®)	6			
Insulin Combinations					
Combination	**Degludec + Aspart** (Ryzodeg® 70/30)	0.23	Not applicable	> 24	SC
	NPH + Regular (Humulin® 70/30; Novolin® 70/30)	0.5	2 to 12	18 to 24	
	Lispro protamine + Lispro (Humalog® Mix 50/50; Humalog® Mix 75/25)	0.25 to 0.5	50/50 Mix: 0.8 to 48 75/25 Mix: 1 to 6.5	14 to 24	
	Aspart protamine + Aspart (Novolog® Mix 70/30)	0.2 to 0.3	1 to 4	18 to 24	
	Glargine + GLP-1 Agonist (Soliqua® 100/33)	Not listed	2.5 to 3	T ½ = 3 h; Clearance = 35 L/h	
	Degludec + GLP-1 Agonist (Xultophy®)		Not applicable	> 24 (see individual drugs)	

CSII = continuous subcutaneous insulin infusion

Updated by Jasmine Mangrum and Jeanine P. Abrons

Oral Diabetes Medications

Drug Class	Generic Name / Brand Name	Usual Starting Dose	Maximum Daily Dose	Monotherapy Hypoglycemia Y/N	Notable Side Effects and Special Considerations
LONG-ACTING SECRETAGOGUES (Sulfonylureas; Second Generation)	**Glimepiride** (Amaryl®)	1 to 2 mg daily	8 mg	Y	· Weight gain · Possible sun sensitivity · Take with the first meal of the day.
	Glyburide (Micronase®)*/**	1.5 to 3 mg daily	12 mg Divide doses of ≥ 6 mg and take BID before meals		Not recommended in geriatric or those with renal insufficiencies. Active metabolites increase risk of prolonged hypoglycemia. *Glyburide and micronized glyburide are not bio-equivalent; re-titrate if patient transferred between products. **Dose adjustments should not be made more frequently than every 7 days.
	Glyburide (Diabeta®)**	2.5 to 5 mg daily	20 mg; Divide doses >10 mg		
	Glipizide (Glucotrol®)	5 mg	40 mg; Divide doses > 15 mg		Possible avoidance of sustained-release formulations in renal impairment.
	Extended release glipizide (Glucotrol® XL)**	5 mg	20 mg		**Dose adjustments should not be made more frequently than every 7 days.

Oral Diabetes Medications *(continued)*

Drug Class	Generic Name / Brand Name	Usual Starting Dose	Maximum Daily Dose	Monotherapy Hypoglycemia Y/N	Notable Side Effects	Special Considerations/ Notes
SHORT-ACTING SECRETAGOGUES	**Repaglinide** (Prandin®)*	New to blood glucose lowering agents or A1c < 8%: 0.5mg Prior treatment with blood glucose lowering agent or A1c ≥ 8%: 1 to 2 mg	16 mg (Maximum dose of 4 mg per meal)	Y	· Hypoglycemia	· Faster onset of action and shorter duration than sulfonylureas. · Take up to 30 minutes before each meal. · Skip dose with skipped meals. · Add a dose with added meals. *Use in patients with kidney disease at a reduced dose of 0.5 mg. Contraindicated with Gemfibrozil.
	Nateglinide (Starlix®)	120 mg 60 mg (in patients near A1c goal)	360 mg			
α-GLUCOSIDASE INHIBITORS	**Acarbose** (Precose®)	25 mg TID	100 mg TID < 60 kg: 50 mg TID	N	· Abdominal pain · Flatulence · Diarrhea	· Take with first bite of meals.
	Miglitol (Glyset®)	25 mg TID	100 mg TID			

Oral Diabetes Medications *(continued)*

Drug Class	Generic Name / Brand Names	Usual Starting Dose	Maximum Daily Dose	Monotherapy Hypoglycemia Y/N	Notable Side Effects	Special Considerations/Notes
DPP-4 INHIBITORS	**Alogliptin** (Nesina®)*	25 mg Daily	Generally not dosed over 25 mg Daily	N	· Usually well tolerated · Headache · GI upset · Naso-pharyngitis · Potential pancreatitis	*Renal impairment dose reduction required · CrCl 30 to 60 mL/min: 12.5 mg Daily · CrCl <30 mL/min: 6.25 mg Daily
	Sitagliptin phosphate (Januvia®)**	100 mg Daily	100 mg Daily			**Renal impairment dose reduction required · CrCl 30 to 50 mL/min: 50 mg Daily · CrCl < 30 mL/min: 25 mg Daily
	Saxagliptin (Onglyza®)***	2.5 mg or 5 mg Daily	5 mg Daily			***Renal impairment dose reduction required · CrCl ≤ 50 mL/min: 2.5 mg Daily ***Limit dose to 2.5 mg when co-administered with a strong CYP450 3A4/5 inhibitor
	Linagliptin (Tradjenta®)	5 mg Daily	5 mg Daily			none
SODIUM GLUCOSE TRANSPORTER 2 INHIBITORS (SGLT2)	**Canagliflozin** (Invokana®)*	100 mg Daily	300 mg Daily	N	·Genitourinary infection · Dehydration · Renal failure · Hypotension · Increased serum K+ · Increased LDLs	*Renal impairment dose reduction required · eGFR (estimated glomerular filtration rate): 45 to 60 mL/min: 100 mg Daily · eGFR < 45 mL/min: Use not recommended
	Dapagliflozin (Farxiga®)**	5 mg Daily	10 mg Daily			**Renal impairment dose reduction required · eGFR < 60 mL/min: Use not recommended · eGFR < 30 mL/min: Contraindication
	Empaglifozin (Jardiance®)***	10 mg Daily	25 mg Daily			***Renal impairment dose reduction required · eGFR < 45 mL/min: Use not recommended · eGFR < 30 mL/min: Contraindicated
DOPAMINE AGONIST	**Bromocriptine** (Cycloset®)	0.8 mg Daily	4.8 mg Daily	N	· Dizziness · GI upset	· Increase by 0.8 mg weekly interval · Take within 2 hours of waking in morning · Take with food to lessen GI upset
BILE ACID SEQUESTRANTS	**Colesevelam** (Welchol®)	3.75 g Daily or in divided doses of 1.875 g BID	3.75 g Daily or in divided doses of 1.875 g BID	N	· Constipation · Elevated triglycerides	· Not recommended with GI motility disorders · May cause decreased absorption of certain medications · Take with meals

Oral Diabetes Medications *(continued)*

Drug Class	Generic Name/ Brand Name	Usual Starting Dose	Maximum Daily Dose	Monotherapy Hypoglycemia Y/N	Notable Side Effects	Special Considerations/Notes
BIGUANIDES	**Metformin (Glucophage®)/ Metformin Oral Solution** (Riomet®)	500 mg BID to 850 mg Daily	2,550 mg daily in 2 to 3 divided doses	N	• **Black Box Warning:** Lactic Acidosis • **Other Side Effects:** GI effects	• Contraindicated in renal dysfunction • Females: Serum creatinine >1.4 mg/dL • Males: Serum creatinine >1.5 mg/dL • Use food to lessen GI side effects
	Metformin Extended Release (Fortamet®*, Glumetza®, Glucophage XR®)	500 mg to 750 mg Daily	2,000 mg daily (*2500 mg daily)			
THIAZOLIDINEDIONES	**Pioglitazone HCl** (Actos®)**	15 mg Daily	45 mg Daily	N	• **Black Box Warning:** Heart Failure • **Other Side Effects:** Peripheral edema Fracture May result in bladder cancer increased risk with longer use	• Contraindicated in New York Heart Association (NYHA) Class III/IV heart failure • Monitor liver function tests before and periodically with use • Safety program exists for Avandia
	Rosiglitazone Maleate (Avandia®)***	4 mg Daily or Divided	8 mg Daily, If Not On Insulin		• ***Black Box Warning:** Higher MI risk	

Updated by Jasmine Mangrum and Jeanine P. Abrons

Combination Oral Diabetes Medications

Drug Class	Generic Name/ Brand Name	Dosage Range	Common Side Effects	Special Considerations/Notes ▸
COMBINATION OF CLASSES	**Alogliptin + Metformin** (Kazano®)*	Current dose of individual drugs to Alogliptin 25 mg/Metformin 2000 mg Daily	• Upper respiratory infection (URI) • Nasopharyngitis • Headache • Hypoglycemia • Gastrointestinal (GI) symptoms	• Dose divided twice daily with meals.
	Dapagliflozin + Metformin (Xigduo XR®)	Based upon current dose of individualized drugs: 5 mg/500 mg to 10 mg/2000 mg Daily		• Dosed once daily • Fungal infection
	Glipizide + Metformin (Metaglip®)	Glipizide 2.5 mg/Metfromin 250 mg or 500 mg** to 10 mg/200 mg in divided doses		• Dosing based on if patient not controlled by diet/exercise alone, with a sulfonyurea &/or metformin, & fasting plasma glucose (FPG) • Start dose: no > than current daily dose of components; ↑ every 2 weeks
	Glyburide + Metformin (Glucovance®)	1.25 mg/250 mg Daily or Twice Daily** to 20 mg/2000 mg Daily With Meals		• Hypoglycemia & GI are ↑ with higher initial doses • Risk of anemia in G6PD deficiency
	Linagliptin + Metformin (Jentadueto®)	See Notes to 5 mg/2000 mg Daily		• Given in divided doses or once daily • Initial dose based on whether on metformin or not
	Pioglitazone + Metformin (Actoplus Met®, Actoplus Met XR®)	**Immediate Release (IR):** Pioglitazone 15 mg/Metformin 500 to 850 mg** Daily or Twice Daily **Extended Release (ER):** Pioglitazone 15 to 30 mg/Metformin 1000 mg Daily or Twice Daily Max: Pioglitazone 45 mg/ Metformin 2000 mg Daily		• Dosing based on New York Heart Association (NYHA) heart failure (HF) class, control on metformin or pioglitazone monotherapy adequacy • Slowly ↑ based on weight gain, edema, signs/symptoms of HF • Metformin doses > 3,000 mg tolerated better if divided 3 times daily • Dose adjustment with strong CYP2C8 inhibitors • Lower extremity edema
	Repaglinide + Metformin (PrandiMet®)	See Notes to Repaglinide 10 mg/Metformin 2500 mg Daily		• Dose 2 to 3 times daily with meals • Dose based on dosing of individual drugs at start & adequacy of control • High incidence of notable side effects
	Rosiglitazone + Metformin (Avandamet®)	See Notes to Rosiglitazone 8 mg/Metformin 2000 mg		• Dose based on if patient taking individual drugs at start & adequacy of control **& should not be used with Insulin**

Combination Oral Diabetes Medications *(continued)*

Drug Class	Generic Name/ Brand Name	Usual Dosage Range	Notable Side Effects	Special Considerations/Notes
COMBINATION OF CLASSES	**Saxagliptin + Metformin** (Kombiglyze XR®)	Use individual dose of agents to Max: 2.5 to 5 mg Saxagliptin/ Metformin 1000 to 2000 mg Daily	• Headache • Diarrhea • Upper respiratory infection (URI) • Hypoglycemia • Nasopharyngitis	• Dose based on use of individual drugs, adequacy of control, or use with insulin • Dose adjustment based on use with strong CYP 3A4/5 medication
	Sitagliptin + Metformin (Janumet®; Janumet XR®))	Starting doses based on prior use of individual drugs to Sitagliptin 100 mg/Metformin 2000 mg Daily		• Dose based on use of individual drugs, adequacy of control, or use • Convert from immediate release (IR) to extended release (XR) using same total daily dose (up to max) but adjust frequency
	Rosiglitazone + Glimepiride (Avandaryl®)	Rosiglitazone 4 mg/Glimepiride 1 or 2 mg Daily to Rosiglitazone 8 mg/ Glimepiride 4 mg Daily		• Carefully titrate dose if debilitated, malnourished or in adrenal insufficiency • May take 2 weeks/2 to 3 months to see full effects
	Pioglitazone + Glimepiride (Duetact®)	Pioglitazone 30 mg/ Glimepiride 2 or 4 mg to Pioglitazone 45 mg/Glimepiride 8 mg Daily		• Dosing based on New York Heart Association (NYHA) heart failure (HF) class, control on individual drugs & adequacy of control (Causes edema/weight gain)
	Alogliptin + Pioglitazone (Oseni®)	See Notes to Alogliptin 25 mg/ Pioglitazone 45 mg Daily		• Dosing based on New York Heart Association (NYHA) heart failure (HF) class, control on individual drugs, adequacy of control on diet & exercise & insulin • Dose adjustment with strong CYP 2C8 inhibitors • Should not use if at end stage renal disease (ESRD)
	Sitagliptin + Simvastatin (Juvisync®)	Sitagliptin 100 mg/Simvastatin 40 mg**; Max: Dose of simvastatin maximum based on concurrent drug use		• Dose based on use of individual drugs, adequacy of control, or use with niacin • Maximum dose alterations: with amlodipidine, amiodarone, ranolazine, diltiazem, dronedarone, verapamil, & lomitapide
	Empagliflozin + Metformin (Synjardy®)	Individualized based on patients current regimen to Empagliflozin 25 mg/ Metformin 2000 mg Daily		• Dose based on if patient taking individual drugs at start & adequacy of control or use with insulin
	Empagliflozin + Linagliptin (Glyxambi®)	Empagliflozin 10 mg/Linagliptin 5 mg to Empagliforzin 25 mg/Linagliptin 5 mg		• If present, correct volume depletion prior to initiation • Urinary tract infection (UTI)

*Note: ▸= used for uncontrolled type 2 diabetes; * = Use alone or in combination; ** = Dose selection based upon additional criteria*

Injectable Type 2 Diabetes Medications

Drug Class	Generic Name/Brand Name	Usual Starting Dose	Maximum Daily Dose	Notable Side Effects	Special Considerations/Notes
GLP-1 AGONISTS	**Exenatide** (Byetta®)	5 mcg twice daily	10 mcg twice daily	• Headache • Hypoglycemia • Nausea • Diarrhea • Injection site reaction	• Administer 60 minutes prior to a meal • Subcutaneous administration • Box warning: risk of developing thyroid C-cell tumors
	Exenatide Extended Release (Bydureon®)	2 mg once weekly	Not applicable	• Headache • Hypoglycemia • Nausea • Diarrhea • Injection site nodule	• Subcutaneous administration • Box warning: risk of developing thyroid C-cell tumors • Use right away after mixing • Take with or without food
	Albiglutide (Tanzeum®)	30 mg once weekly	50 mg once weekly	• Hypoglycemia • Diarrhea • Injection site reactions	• Subcutaneous administration • Box warning: risk of developing thyroid C-cell tumors • Take with or without food
	Dulaglutide (Trulicity®)	0.75 mg once weekly	1.5 mg once weekly	• Nausea • Diarrhea • Vomiting	• Subcutaneous administration • Box warning: risk of developing thyroid C-cell tumors • Take with or without food
	Liraglutide (Victoza®)	See notes	1.8 mg once daily	• Tachycardia • Headache • Hypoglycemia • Nausea • Constipation • Vomiting	• 0.6 mg once daily for 1 week, then increase to 1.2 mg once daily; may increase up to 1.8 mg once daily if optimal glycemic response not achieved with 1.2 mg once daily • Initial starting dose is intended to reduce GI symptoms and does not provide effective glycemic control • Subcutaneous administration • Box warning: risk of developing thyroid C-cell tumors • Take with or without food • Drink non-caffeine liquids

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