Diabetes Medications Reference
Non-Insulin Diabetes (Type 2) Agents - Oral and Injectable

Generic (Brand)	Mechanism of Action	Expected A1c Δ	Weight gain?	Dosing/ Administration	Half Life	Adverse Events* >5%	Contraindications+	Warnings	Notes	Monitoring**
Biguanides (Oral)										
Metformin (Glucophage®)	Decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity (increases peripheral glucose uptake and utilization)[1]	~1.5 [2]	Neutral to loss[2]	Initial dose: 500 mg twice daily or 850mg once daily[1] ER 500-2000 mg once daily, titrate slowly to mitigate GI s/s[1] Take with meals to avoid GI upset[1] ER tablet: take with evening meal	4-9 hrs[1]	B12 deficiency, neuropathy[39], diarrhea, nausea/vomiting, flatulence, asthenia, indigestion, abdominal discomfort, headache[3]	Renal disease or renal dysfunction (eGFR less than 30 mL/minute/1.73 m2) or abnormal creatinine clearance from any cause (shock, acute MI, or septicemia); acute/chronic metabolic acidosis with/without coma (including diabetic ketoacidosis).[1]	**BBW: Risk of lactic acidosis (correlated to renal function). Suspect lactic acidosis if acidotic but without evidence of ketoacidosis.** Do not initiate therapy if eGFR<45mL/min/1.73m[2][1]	Do not initiate in patients above 80 years old unless normal renal function is established[1]; titrate every 1-2 weeks to prevent diarrhea. Hold before and at least 48 hours after contrast media administration if eGFR<60mL/min/1.73m[2] or hepatic injury, alcoholism, heart failure.	B12, periodically; SCr; CrCl, eGFR yearly; hematologic parameters[1]
Sulfonylureas (Oral)										
Glimepiride (Amaryl®)	Stimulates insulin release, reduces glucose output from liver, increases insulin sensitivity[12-16]	~1.5[2]	Weight gain[2]	1-2 mg daily with first meal of the day[13]	5-9 hrs[13]	Hypoglycemia (especially in the elderly and with renal insufficiency), dizziness, asthenia, headache, nausea [2,18]	DKA[13]	Increased risk of cardiovascular mortality[12-17]; use with caution in patients with hepatic impairment (glipizide only)[14] glyburide not recommended CrCl<50 mL/min[15]	Patients with G6PD deficiency may be at increased risk of hemolytic anemia[12-17]; stress related states may necessitate discontinuation of therapy[12-17]	S/S of hypoglycemia (fatigue, sweating, numbness of extremities)[12-17]
Glipizide (Glucotrol®, Glipizide® XL)				5 mg daily with first meal of the day[14]	2-5 hrs[14]		DKA, DM1[14]			
Glyburide (DiaBeta®, Glynase Pres Tab®, Micronase®)				DiaBeta: 1.25- 2.5 mg daily with first meal of the day[15] Glynase: 0.75-1.5 mg daily with first meal of the day[15]	DiaBeta: 10 hrs; Glynase: 4 hrs[15]		concomitant use with bosentan, DKA,DM1[15]			
Tolazamide (Tolinase®)				100-250 mg daily with first meal of the day[16]	7 hrs[16]		DKA, DM1[16]			
Meglitinides (Oral)										

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Repaglinide (Prandin®)	Blocks ATP dependent K^+ channels, depolarizes membrane causing Ca^{2+} entry, causing insulin release from beta cells; glucose dependent[8,9]	~1-1.5[2]	Weight gain[8,9]	0.5 mg **(2, 3 or 4 times)** daily 15 minutes prior to meal[8]	1 hr[8]	Hypoglycemia, URI, sinusitis, nausea, diarrhea, arthralgia, back pain, headache[10]	DKA, DM1, concurrent gemfibrozil[8]	Care should be taken in those susceptible to glucose lowering effects[8,9]	Concurrent use with NPH insulin not indicated[8];	
Nateglinide (Starlix®)				120 mg three times daily 15 minutes prior to meal[9]	1.5 hrs[9]	Upper Respiratory Infection (URI)[11]	DKA, DM1[9]		Indicated for adjunctive therapy with metformin[9]; combination with sulfonylureas not recommended[9]	Weight; lipid profile[9]
Thiazolidinediones (Oral)										
Pioglitazone (Actos®)	PPAR ɣ agonist - increases the number of gene products involved in glucose and lipid metabolism; causes sodium reabsorption[4,5]	~0.5-1.4[2]	Weight gain, possibly from fluid retention[4,5]	15-30 mg daily without regard for meals[4]	3-7 hrs parent drug, 17-24 hrs total[4]	URI, headache, sinusitis, myalgia, pharyngitis, edema, hypoglycemia[4,6]	**Class III/IV heart failure[4,5]**	**BBW - Not recommended for use in any patient with symptomatic heart failure, contraindicated in Class III/IV HF.[4,5]** Increased risk of bladder cancer [4,5]	Dose related edema, increased fracture risk in women. Use with caution in those with hepatic dysfunction; hematologic effects, may decrease Hgb/Hct.	S/S of heart failure, LFTs prior to therapy and periodically, routine ophthalmic exam, s/s bladder cancer[4]
Rosiglitazone (Avandia®)				4 mg daily without regard for meals[5]	3-4 hrs[5]	URI, injury, headache, edema[5,7]	**Class III/IV heart failure[4,5]**		Hematologic effects - may reduce Hgb/Hct[5]; do not initiate in active liver disease or hepatic dysfunction (ALT>2.5x ULN), possible increased risk of MI[5]	S/S heart failure, LFTs[5]
Dipeptidyl peptidase IV inhibitors (Oral)										
Sitagliptin (Januvia®)	Inhibits DPP-IV (dipeptidyl peptidase 4) which results in prolonged incretin levels. Incretin increases insulin synthesis, decreases glucagon secretion (which results in decreased hepatic glucose production). Incretin is inactivated by DPP IV[23,24,25]	~0.5-1[2]	neutral[2]	100 mg daily without regard for meals; see renal dose adjustment[23]	12 hrs[23]	Nasopharyngitis[26]		Pancreatitis - reports of hemorrhagic and necrotizing[23,24]	Not for DKA; no info on HF; no info on hepatic impairment; use caution in renal impairment; not for DM1; concomitant use of insulin secretagogue may increase risk of hypoglycemia[23,24]	Renal function[23,24] **Sitagliptin** dose renal impaiment: CrCl ≥ 30 and < 50 mL/min, 50 mg daily; CrCl <30 mL/min 25 mg daily.
Saxagliptin (Onglyza®)				5 mg daily without regard for meals; see renal dose adjustment[24]	2.5 hrs[24]	URI, UTI, Headache[27]			Use with caution in renally impaired patients (sitagliptin and saxagliptin only)[23,24];concomitant use of insulin secretagogue may increase risk of hypoglycemia[24,25]	**Saxagliptin** dose for renal impairment: CrCl ≤ 50 mL/min, 2.5 mg daily
Linagliptin (Tradjenta®)				5 mg daily without regard for meals[25]	12 hrs[25]	Nasopharyngitis[28]		Linagliptin Bullous pemphigoid, pancreatitis (monitor lipase, uric acid)		**Llinagliptin**: No dosage adjustment for renal/hepatic

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										impairment
Alogliptin (Nesina®)		0.56 - 0.59 [40]	neutral [40]	25 mg daily with or without food[40]	21 hrs[40]	Headache, pruritis [40]		Pancreatitis, serious hypersensitivity reactions (anaphylaxis, angioedema, Stevens-Johnson syndrome), hepatic failure[44]	Dosing adjustment is needed for renal impairment [40]	Hepatic function test prior to initial therapy; Renal function: CrCl ≥30 and < 60 mL/min dose 12.5 mg daily; CrCl ≥15 and < 30 mL/min or with end stage renal disease (CrCl <15 mL/min) dose 6.25 mg daily[44]
Glucosidase inhibitors (Oral)										
Acarbose (Precose®)	Competitive inhibitor of α-amylase and intestinal brush border of α-glucosidases, resulting in delayed hydrolysis of carbs and therefore less absorption of glucose[19,20]	~0.5-0.8[2]	Neutral, may counteract weight gain of sulfonylureas[21,22]	Initial: 25 mg daily with the first bite of each main meal; increase by 25 mg every 1-2 months[19]	2 hrs[19]	GI (flatulence, bloating, abdominal discomfort, and diarrhea) - symptoms tend to be at the start of medication[19,20]	DKA or cirrhosis; inflammatory bowel disease, colonic ulceration, history or symptoms of partial intestinal obstruction, or a patient who has issues with disorders of digestion or absorption, or if gas would deteriorate condition of patient[19,20]	Use with caution in hepatic/renal impairment; not recommended if (Scr>2g/dL, CrCl<25mL/ min)[19,20]	Rarely elevated serum aminotransferase levels (acarbose only, at highest dose)[19;] not recommended in patients with renal impairment[19,20]	Serum transaminases every 3 months for first year and periodically afterward; renal function; BP[19]
Miglitol (Glyset®)				Initial: 25 mg daily with the first bite of each main meal; increase by 25 mg every 1-2 months[20]	2 hrs[20]			Abdominal pain, diarrhea-usually self-limiting. Avoid if Scr>2g/dL, CrCl<25mL/ min[19,20]		
Sodium glucose co-transporter 2 (SGLT2) inhibitor (Oral)										
Canagliflozin (Invokana®)	Lowers blood glucose levels in the blood stream by inhibiting SGLT2 receptors in the kidney. This allows glucose to pass in the kidney and be eliminated in the urine.	0.91 - 1.16 [37]	Loss [37]	100 mg daily in the morning with or without food, may increase to 300 mg daily if eGFR is ≥60 mL/min/1.73 m2[38,41]	100 mg: 10.6 hrs; 300 mg: 13 hrs[38]	UTI, genital mycotic infection, hyperkalemia, increase LDL[38]	Severe renal impairment (eGFR <30 mL/minute/1.73 m2); end-stage renal disease or patients on dialysis.[42,43,45] **Do not initiate dapagliflozin if eGFR <60 mL/minute/1.73 m2[43]** **Do not initiate**	**Acute kidney injury** especially if predisposed (low blood volume, on diuretics, ACE inhibitors, ARBS or NSAIDs, CHF). Increased leg and foot amputations. **Diabetic ketoacidosis (sometimes euglycemic)**. Increased bone fractures,	The severity of UTI and genital mycotic infection is mild to moderate. However BUN is elevated up to 49.5 - 57 compare to placebo [37] Can cause initial hypotension especially in elderly patients, patients on loop diuretics and renal impairment patients. Can cause mild hypoglycemia with insulin and other	Renal function and volume status (baseline and periodically during treatment); potassium; LDL-C; genital mycotic infections and UTI/urosepsis/pyelonephritis; blood pressure; ketoacidosis
Dapaglifozin (Farxiga®)		0.8-1.2[42]	Loss[42]	5 mg daily in the morning with or without food, may increase to 10 mg daily[40,41]	13 hrs[41]	UTI, female genital mycotic infections, nasopharngitis, hypovolemia, increase LDL[42]				

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Empagliflozin (Jardiance®)		-0.7-0.8[45]	Loss[45]	10mg daily in the morning with or without food. May increase to 25mg daily.[45]	12.4hrs [45]	UTI, female genital mycotic infections. [45]	**empagliflozin if eGFR <45 mL/minute/1.73 m2[45]**	hypotension, increased hematocrit, lipid abnormalities, hyperkalemia. eGFR 30 - <60mL/min/ 1.73m^2 initiation of therapy not recommended. Do not use in bladder cancer.[42,43,45]	antidiabetic medications.[42]	[42,43,45]
GLP1 Agonist (Injectable)										
Exenatide (Byetta® IR, Bydureon® (ER))	Incretin analog (glucagon like peptide 1 =GLP-1 agonist) which increases glucose dependent insulin, decreases inappropriate glucagon secretion, increases β-cell growth/replication, slows gastric emptying, and decreases food intake[29,30]	~0.5-1% (IR); ~1.5-1.9% (ER)[29]	loss due to reduced intake[29,30]	Bydureon (ER): 2 mg subQ once every 7 days[29] Byetta: 5 mcg subQ twice daily within 60 minutes before morning and evening meal for 1 month, then 10 mcg subQ once daily[29]	IR: 2.4 hrs; ER: 2 weeks[29]	nausea, vomiting, dyspepsia[31]	Byetta® only: Diabetes ketoacidosis, diabetic coma or precoma, CrCl,30mL/min, dialysis.[2] All except Byetta®: Medullary thyroid carcinoma (personal or family history, multiple endocrine neoplasia syndrome type 2, pregnancy. [29,30]	**BBW - dose/duration dependent thyroid tumors have developed in animal studies (Bydureon and liraglutide only)[29,30]**	Reports of acute pancreatitis (both hemorrhagic and necrotizing); not for DM1; not for patients with gastroparesis or severe gastrointestinal disease; not recommended in severe renal impairment (CrCl <30mL/min)[29]; immunogenicity-patients may develop antibodies to drug, greater likelihood with once weekly formulation than with twice daily. Exenatide has highest antibody titers of approved GLP-1 agonists. If worsening glucose control or increased injection site reactions, consider alternative agent [50] Instruct patient on Bydureon® reconstitution, inject immediately after dose prepared.[29]	Renal function, s/s pancreatitis [29]
Liraglutide (Victoza® – diabetes indication; Saxenda®- weight loss indication)		~1%[30]		Initial: 0.6 mg subQ daily for 1 week then 1.2 mg subQ daily for one week; may increase to 1.8 mg/day subQ without regard to meals; don't mix with other meds[29,30] Saxenda only: may increase to maximum dose of 3mg daily.[30]	13 hrs[30]	Nausea, diarrhea, vomiting, constipation, headache[32,] hypoglycemia, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase, amylase[30].			Acute pancreatitis reported; little experience in hepatic impairment; use with caution in renally impaired patients; not for DM1; insulin secretagogues may cause hypoglycemia; may reduce the rate and extent of absorption of orally administered drugs[30]	Renal function, s/s pancreatitis, depression, suicidal thoughts/ behavior[30]

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Albiglutide (Tanzeum®)		0.7-0.9%[33]	Average weight loss of 1.4 kg due to reduced intake[33]	Initial: 30 mg subQ once weekly, may increase to 50 mg[33] administer with or without meals on the same day every week[33]	5 days[33]	Upper respiratory tract infection (URTI), diarrhea, nausea, and injection site reaction[33]	Medullary thyroid carcinoma (personal or family history, multiple endocrine neoplasia syndrome, history of pancreatitis[33]	**BBW - risk of thyroid C-cell tumors[33]**	REMS- serious risks include potential risk of medullary thyroid carcinoma and acute pancreatitis. Due to these risks, albiglutide is not recommended as first-line therapy for patients inadequately controlled on diet and exercise[34] www.TANZEUMREMS.com. Requires drug reconstitution prior to use, instruct patient on mixing and injection within 8 hours of reconstitution and technique (inject and hold for 5 seconds to ensure dose)[33]	Renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions[34].
Dulaglutide (Trulicity®)		0.7-0.8%[46]	Loss[46]	I0.75 mg subQ once weekly, increase to 1.5 mg weekly for better glycemic control if needed. If a dose is missed administer within 3 days of missed dose.[46]	5 days[46]	Nausea, vomiting, diarrhea, abdominal pain, decreased appetite[46]	Personal or family history of medullary thyroid carcinoma (MTC); patients with multiple endocrine neoplasia syndrome type 2 (MEN2)[46]	**BBW - risk of thyroid C-cell tumors[46]** Pancreatitis, hypoglycemia, renal impairment, adverse GI effects[46].	Not for treatment of Type 1 diabetes mellitus or diabetic ketoacidosis, slows gastric emptying and may impact absorption of concomitantly administered oral meds.[47]	Renal function, report severe adverse GI symptoms, s/s pancreatitis, plasma glucose.[47]
Lixisenatide (Adlyxin®)		-0.18-0.83[49]	Loss[49]	Initiate 10mcg once daily for 14 days, on day 15 increase dose to 20 mcg once daily. Administer subcutaneously within 1 hour before first meal of day.[49]	3 hours[49]	N/V/D, headache, dizziness, hypoglycemia.[49]	Hypersensitivity to Lixisenatide or any product components.[49]	About 2.4% of patients develop anti-lixisenatide antibodies, monitor for allergic reactions/ injection site reactions. Pancreatitis reported.[48]	Patients with eGFR 15-29mL/min/1.73m^2-use with caution, monitor renal function and GI side effects closely. Not recommended if eGFR<15mL/min/1.73m^2. May delay GI absorption of drugs. Administer 1 hour before/11 hours after oral contraceptives, antibiotics/APAP 1 hour before[49]. immunogenicity-patients may develop antibodies to drug. If worsening glucose control or increased injection site reactions, consider alternative agent [49,50]	Renal function, report severe adverse GI symptoms, s/s pancreatitis, HbA1c, plasma glucose[48].
Amylin analogues (Injectable)										

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Pramlintide (Symlin®)	Synthetic analog of human amylin co-secreted with insulin by pancreatic beta cells; reduces postprandial glucose increases via the following mechanisms: 1) prolongation of gastric emptying time, 2) reduction of postprandial glucagon secretion, and 3) reduction of caloric intake through centrally-mediated appetite suppression[33]	~0.5[35]	loss[36]	Initial: Type 1: 15 mcg subQ immediately prior to meals (≥250 kcal or ≥30 g of carbs); may titrate (every 3 days in 15mcg increments) to 30-60 mcg subQ daily[35,36] **Initial:** Type 2 60 mcg subQ immediately prior to major meals (≥250 kcal or ≥30 g of carbs); may titrate to 120 mcg subQ daily[35,36] **Do not mix** with other injectable medications; administer oral medications either 1hour before or 2hours after pramlintide [35]	1 hr[35]	Nausea, headache, anorexia, vomiting, abdominal pain, fatigue, dizziness, coughing, pharyngitis (placebo+insulin vs Symlin+insulin)[36]	Confirmed diagnosis of gastroparesis, hypoglycemia unawareness[35]	**BBW - concomitant use with insulin has been associated with an increased risk of insulin-induced severe hypoglycemia[35]**	Use with caution in patients with history of nausea[35]	Prior to therapy: hypoglycemic history and body weight; during therapy: urine sugar and acetone, pre+post prandial glucose, bedtime glucose, electrolytes, lipid profile[33]

*greater than placebo and occurring in greater than 5% of patients - as monotherapy **in addition to HbA1c and blood glucose +in addition to hypersensitivity to product/product components
ACE- ACE inihibitor; ARB-angiotensin receptor blocker; BBW=black box warning; BP=blood pressure; BUN=blood urea nitrogen; CHF-congestive heart failure; CrCl=creatinine clearance; DKA=diabetic ketoacidosis; DM1=diabetes mellitus type 1; eGFR=estimated glomerular filtration rate; ER=extended release; GI=gastrointestinal; Hct-hematocrit; HF=heart failure; Hgb-hemoglobin; IR=immediate release; LFT=liver function test; LDL=low density lipoprotein; MI-myocardial infarction NPH= neutral protamine Hagedorn; NSAID-non-steroidal anti-inflammatory drug; N/V/D=nausea, vomiting, diarrhea; REMS=Risk Evaluation & Mitigations Strategies; SCr-serum creatinine; SubQ=subcutaneous; S/S=signs/symptoms, ULN-upper limit of normal; URI=upper respiratory tract infection; UTI=urinary tract infection; Δ=change

General Resources

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