DIABETES MELLITUS MEDICATIONS 2012

ORAL GLUCOSE-LOWERING AGENTS

RX	Avail. Dosage	Initial Dose	Initial Dose (elderly)	Dose Adjustment Schedule	Usual Maint. Dosage	Max. Effecttive Dose	A1C Lowering	Wt	Renal Dosing	Hepatic Dosing	Lab Monitoring	Common Side Effects	Contraindications/ Precautions
Drug Class: Sulfonyureas Actions: Stimulates insulin secretion; lowers fasting plasma glucose Indications: Type 2 diabetes as monotherapy or in combination with insulin, metformin, DPP-IV inhibitors, incretin mimetics, or TZDs													
Glipizide	5 mg 10 mg	5 mg	2.5 mg/day	Increase by 2.5 to 5 mg (> 15 mg/day = BID) after 1-2 wks	5-15 mg/ day	20 mg/day	1.0-2%	+	N/A	Start at 2.5 mg/ day	N/A	• hypoglycemia • weight gain	• Use caution in people with sulfa allergies • Use glyburide with caution due to greater risk of hypoglycemia • Use caution with renal or hepatic insufficiency (glipizide or glimepiride preferred choices) • Immediate release and extended release glipizide doses are not equivivalent
Glipizide ER	2.5 mg 5 mg 10 mg		5 mg/day	Increase by 5 mg after 1-2 wks	5-10 mg/ day	20 mg/day							
Glimepiride	1 mg 2 mg 4 mg	1-2 mg	1 mg	Increase by 1-2 mg after 1-2 wks	1-4 mg/ day	8 mg/day			Start at 1 mg/ day and monitor	Mild--start at 1 mg (monitor) Severe--avoid			
Glyburide	1.25 mg 2.5 mg 5 mg	2.5-5 mg	1.25 mg/ day	Increase by 2.5-5 mg after 1-2 wks	1.25-10 mg/day	10 mg/day			Do NOT use if CrCl < 50 ml/min	Conser-vative 1.25 mg/ day			
Drug Class: Biguanides Actions: Targets hepatic cells; decreases hepatic glucose production; does not stimulate insulin secretion; lowers fasting plasma glucose Indications: Type 2 diabetes as monotherapy or in combination with any other agent or insulin; overweight; dyslipidemic; children (approved for ≥ age 10)													
Metformin	500 mg 850 mg 1000 mg	500 mg BID	Use with caution, especially if > 80 years	Increase by 500 mg after 1-2 wks	1000-2000 mg/day	2550 mg/day (10-16 yo = 2000 mg/day)	1.0-2%	0/-	Contrain-dicated if SCr ≥ 1.5 males, ≥ 1.4 females or eGFR < 50	Avoid due to risk of lactic acidosis	BUN, Cr & CBC: prior to initiation then yearly. LFTs: prior to initiation. Vitamin B12 levels: every year for those at high risk of Vitamin. B12 deficiency	• diarrhea • nausea • abdominal bloating • anorexia	• Do not use with hepatic insuf-ficiency • Consult with diabetes specialist is recommended for SCr > 1.5 or eGFR < 50 • Uncompensated CHF • Excessive alcohol intake • Over age 80 (caution) • Acetazolamide • Withhold therapy for 48 hours after iodinated contrast media is used • May cause ovulation to resume in anovulatory, premenopausal women
Metformin ER	500 mg 750 mg	500 mg			500-2000 mg/day	2000 mg/ day							
Drug Class: TZD (Thiazolidinediones) Actions: Regulates insulin responsive genes necessary for glucose and lipid metabolism; improves sensitivity to insulin in skeletal and adipose tissue Indications: Type 2 diabetes as monotherapy or in combination with any other agents; Actos is also approved for use with insulin **Note: Rosiglitazone is not listed on this chart due to restricted use by FDA. For more information, see:** http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm226976.htm													
pioglitazone (Actos)	15 mg 30 mg 45 mg	15-30 mg	Same	Increase by 15 mg 6-12 wks	15-45 mg/ day	45 mg/day (30 mg if on insulin)	1-1.5%	+	N/A	Do NOT use if ALT > 2.5X ULN	LFTs: prior to initiation then periodically	• weight gain, edema • heart failure symptoms, macular edema • increased fracture rate • increase risk of bladder cancer	• CHF III & IV or any symptomatic heart failure • Clinical evidence of liver disease or ALT > 2.5 ULN • Do not use rosiglitazone in combina-tion with insulin or nitrates (may increase risk of MI) • Use caution in females at high risk for fractures • Monitor for increase edema • May cause ovulation to resume in anovulatory, premenopausal women

DIABETES MELLITUS MEDICATIONS 2012

ORAL GLUCOSE-LOWERING AGENTS

RX	Avail. Dosage	Initial Dose	Initial Dose (elderly)	Dose Adjustment Schedule	Usual Maint. Dosage	Max. Effecttive Dose	A1C Lowering	Wt	Renal Dosing	Hepatic Dosing	Lab Monitoring	Common Side Effects	Contraindications/ Precautions
Drug Class: Meglitinides Actions: Augments glucose induced insulin output; more rapid onset of effect and shorter duration of action than sulfonylureas Indications: Type 2 diabetes as monotherapy or in combination with other oral agents; people with sulfa allergies; hypoglycemia on low doses of sulfonylureas													
repaglinide (Prandin)	0.5 mg 1 mg 2 mg	A1C < 8%: 0.5 mg w/ each meal A1c>8:1-2 mg w/each meal	Same (caution if Renal Dz)	Double after 1-2 wks	0.5-4 mg before meals	16 mg/day	1-1.5%	+/-	CrCl < 40 ml/min, start at 0.5 mg	Use Caution	N/A	• hypoglycemia • weight gain	• nateglinide: active metabolites, renal excretion • repaglinide: no active metabolites, minimal renal excretion, more effective than nateglinide in clinical trials
nateglinide (Starlix)	60 mg 120 mg	60-120 mg before meals	Same (caution if Liver Dz)	Increase by 60mg at each meal after 1-2 wks	60-120 mg before meals	120 mg TID	0.5-1%		N/A				
Drug Class: Alpha-glucosidase Inhibitors Actions: Slows absorption of carbohydrates; reduces post-prandial blood glucose Indications: Type 2 diabetes as monotherapy or in combination with sulfonylurea,metformin or insulin; post-prandial hyperglycemia													
acarbose (Precose)	25 mg 50 mg 100 mg	25 mg TID with meals	Same	Double current dosing regimen after 4-8 wks	25-100 mg TID **with meals**	Wt. < 60 kg = 50 mg TID Wt. > 60 kg = 100 mg TID	0.5-1%	0	Treat-ment not recom-mended if SCr > 2	N/A	Serum Transaminases q 3 mo. X 1 year	• flatulence • diarrhea • abdominal pain (less severe if titrated slowly)	• The mechanism of action shows the correction of hypoglycemia so treat hypoglycemia with glucose tablets • Chronic intestinal disease • Renal dysfunction • (creatinine > 2.0) (Glyset) • Cirrhosis (Precose)
miglitol (Glyset)					50-100 mg TID **with meals**	100 mg TID					N/A		
Drug Class: Dipeptidyl Peptidase 4 Inhibitors (DPP-IV) Actions: Increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner Indications: Type 2 diabetes as monotherapy or in combination with sulfonylureas, metformin, or TZDs													
sitagliptin (Januvia)	25 mg 50 mg 100 mg	100 mg daily	Same	If making adjustments, wait 4-6 wks	100 mg daily	100 mg daily	0.6-0.8%	0/-	CrCl 30-50 ml/min: 50 mg daily CrCl < 30 ml/min: 25 mg daily	N/A	BUN, Cr prior to initiation then yearly	• headache, naso- • pharyngitis, upper respiratory tract infection • rarely severe allergic reactions	• If using in combination with solfonuylurea and metglitinide, may need lower dose of sulfonylurea to prevent hypoglycemia • At the reduced doses suggested for stage 4 or worse CKD, the medications maybe ineffective; use with extreme caution, if at all in Stage 5 CKD.❖
saxagliptin (Onglyza)	2.5 mg 5 mg	2.5 or 5 mg daily (2.5 mg for renal impairment of if given with a CYP3A4/5 Inhibitor)	Same	N/A	5 mg daily	5 mg daily	0.5-0.8%	0	CrCl < 50 ml/min: 2.5 mg daily	N/A	BUN, Cr prior to initiation and then yearly		
linagliptin (Tradjenta)	5 mg	5 mg daily with or without food	Same	N/A	5 mg daily	5 mg daily	0.4% mono-therapy	0	No ad-justment needed	N/A	N/A	• nasopharyngitis 5.8%, monotherapy (placebo 5.5%-not statistically significant)	• If used with sulfonylurea or metglitinide, consider lowering dose to prevent hypoglycemia • Strong P-glycoprotein/CYP 3A4 inducer

❖ Based on expert opinion.

DIABETES MELLITUS MEDICATIONS 2012

INJECTABLE NON-INSULIN GLUCOSE-LOWERING AGENTS

RX	Avail. Dosage	Initial Dose	Dose Adjustment Schedule	Max. Dose	Meal Timing	A1C Lowering	Wt	Renal Dosing	Hepatic Dosing	Lab Monitoring	Stability	Common Side Effects	Contraindications/ Precautions
Drug Class: GLP-1 agonist Actions: stimulates the pancreas to increase insulin production and suppress glucagon secretion. Secondary actions include inhibition of gastric emptying and reduction of appetite and food intake. Indications: Type 2 diabetes as monotherapy or in combination with sulfonylureas, metformin, or TZDs. See individual drug insert recommendations for when it is appropriate to use with a specific type of basal insulin in adults with type 2 diabetes. Not approved for use with type 1 diabetes.													
exenatide (Byetta)	5 mcg per dose, 60 doses, 1.2 mL prefilled pen 10 mcg per dose, 60 doses, 2.4 mL prefilled pen	Type 2 DM: 5 mcg BID at any time within the 60-minute period before the 2 main meals of the day, approximately 6 hours or more apart	Type 2 DM: May be increased to 10 mcg BID after one month of therapy	10 mcg twice a day	Within 60 minute period before morning and evening meals	1%	-	Do not use if CrCl < 30 ml/min	N/A	Monitor INR for patients on warfarin	Store unused pen in refrigerator. After first use, may be kept at room temp (up to 77° F) for up to 30 days.	• nausea • other GI disturbance	• Severe gastro-esophageal reflux disorder (GERD) • Gastroparesis • Pancreatitis
exenatide extended-release (Bydureon)	2 mg single dose trays	2 mg every 7 days	None	2 mg/ week	Independent of meals	1.60%	-	Do not use if CrCl < 30 ml/min Use with caution if 30 - 50 CrCl	N/A	Monitor INR for patients on warfarin	Administor immediately after suspension	• nausea, other GI disturbance • Injection site nodules	• Avoid use in people with risk for pancreatitis, previous pancreatitis and or very elevated triglycerides • Avoid in people with risk for pancreatitis • Severe gastro-esophageal reflux disorder (GERD) • Gastroparesis • Pancreatitis • See Black Box Warning: Thyroid C-Cell Tumors, Medullary Thyroid Carcinoma (MTC) and Multiple Endocrine Neoplasia Syndrome Type 2- (MEN 2)
liraglutide (Victoza)	0.6 mg/mL 3 mL prefilled syringes	Type 2 DM: 0.6 mg subcuta-neously once a day for 1 week◎	Type 2 DM: Titrate to 1.2 mg after 1 week then may increase to 1.8 mg if 1.2 mg reveals no signifi-cant changes	1.8 mg one time daily	Independent of meals	1-1.5%	-	No dosage adjustment necessary. Caution w/ renal impairment N/A	No dosage adjustment necessary, caution w/ hepatic impairment	N/A	Store unused pen in refrigerator. After first use can be kept in refrigerator or room temp (up to 86° F) for up to 30 days. Keep pen cap on.	• nausea • other GI disturbance	
Drug Class: Amylin analogue Actions: slows gastric emptying, decreases glucagon secretion, centrally modulates appetite Indications: Type 1 & 2 diabetes as adjunct treatment to those who use meal-time insulin and fail to achieve postprandial glucose control Note: A specialist should prescribe Symlin due to the complexity of dosing guidelines.													
pramlintide (Symlin)	0.6 mg/mL 5 mL vials 1 mg/mL prefilled pens	Type 1 DM: 15 mcg immediately prior to major meals Type 2 DM: 60 mcg immediately prior to major meals ⌘	Type 1 DM: Titrate at 15 mcg increments to a maintenance dose of 30 or 60 mcg, as tolerated Type 2 DM: Increase to a dose of 120 mcg as tolerated ❖	120 mcg before major meals	Immediately before meals containing ≥ 250 kcal or ≥ 30 grams of carbo-hydrate	0.4 – 0.6%	0/-	N/A	N/A	N/A	Discard 28 days after first use. Open bottles may be refrigerated or kept at room temp.	• nausea	• Avoid combination with GLP-1 agonist • Gastroparesis

◎ May be given at any time of day independent of meals

⌘ Reduce preprandial, rapid-acting or short-acting, insulin dosages, including fixed-mix insulins by 50%

❖ Dose titrations should occur only when **no** clinically significant nausea has been seen for 3 days

INSULIN© THERAPY 2012

CLASS	INSULIN TYPE	BRAND	FORMULATIONS	ONSET of Action	PEAK	DURATION of Action	BASAL/ BOLUS	MEAL TIMING	APPEARANCE
Rapid Acting	Lispro	Humalog✣	Vials, cartridges, pens	5-15 min	1-2 hours	2-4 hours	Bolus	15 min before or immediately after	Clear
	Aspart	Novolog	Vials, cartridges, pens			2-4 hours		5-10 min before	
	Glulisine	Apidra	Vials, pen			2-4 hours		Within 15 min before or within 20 min after starting a meal	
Short Acting	Regular	Humulin R✣	Vials	30-60 min	2-4 hours	4-6 hours	Bolus	30 min before meals	Clear
		Novolin R	Vials						
Intermediate Acting	NPH	Humulin N✣	Vials, cartridges	1-2 hours	4-8 hours	10- 20 hours	Basal	Within 15 min before meals when mixed with rapid-acting insulin; 30 min before meals when mixed with regular insulin	Cloudy
		Novolin N	Vials						
	Detemir	Levemir	Vials, pen	1-2 hours	6-8 hours	Dose-dependent #	Basal	N/A	Clear
Long Acting	Glargine	Lantus	Vials, pens	1-2 hours★	Flat◆	~24 hours ⏏			
	Detemir	Levemir	Vials, pen	1-2 hours	6-8 hours	Dose-dependent #	Basal	N/A	
Combination	70 NPH/30 Regular	Humulin 70/30✣	Vials, pens	30-60 min		10-16 hours		Approximately 30 min before meals	Cloudy
		Novolin 70/30	Vials						
	70 aspart protamine/30 insulin aspart	Novolog Mix 70/30	Vials, cartridges, pens	10-20 min				Within 15 min of meal	
	75 lispro protamine/25 lispro	Humalog Mix 75/25	Vials, pens	Less than 30 min		15-18 hours			
High Strength U-500 Insulin	Regular	Humulin RU-500⌘	Vials	30 min	2-4 hours	6.5-8 hours	Basal/ Bolus	Varies⌘	Clear

⊙ The time course of action (onset of action, peak, duration of action) of any insulin may vary in different individuals or at different times in the same individual and can sometimes be dependent on dose. Time periods indicated should be considered a general guide only. Time may vary based on initial and subsequent doses. Consult with insulin package insert for additional information.

⌘ U-500 is a high-strength concentration of insulin (5-fold higher concentration than U-100 insulin) and typically used in people with very high insulin resistance; consultation with a diabetes specialist is recommended. See Section 4: Glycemic Control for more information related to U-500 use and precautions.

◆ Some people may have a peak at 10-14 hours and the duration may be <24 hours.

Dose response studies indicate an approximate duration of action of 6-12 hours for Detemir dose of <0.4 units/kg and duration of action of 20-24 hours for Detemir dose of ≥0.4 units/kg.

★ A 4-5 hour onset of action with initial dosing may occur based on expert opinion.

⏏ Some people may benefit from a BID dose schedule.

✣ Available in Humulin®/ReliOn® insulin manufactured for Walmart by Eli Lilly