

GLP-1 Agonist Medication Review

Extended Release GLP-1 Agonists			
Drug	Exenatide ER (Bydureon)	Albiglutide (Tanzeum)	Dulaglutide (Trulicity)
Approval Year	2012	2014	2014
Indication	<ul style="list-style-type: none"> • DM-2 • Not recommended for use: <ul style="list-style-type: none"> ○ In DM-1 and DKA ○ Severe renal impairment (< 30 mL/min) ○ In patients w/ pancreatitis ○ In patients with severe GI disorders ○ In pediatrics 	<ul style="list-style-type: none"> • DM-2 • Not recommended for use: <ul style="list-style-type: none"> ○ In DM-1 and DKA ○ In patients w/ pancreatitis ○ In patients with severe GI disorders ○ In pediatrics 	<ul style="list-style-type: none"> • DM-2 • Not recommended for use: <ul style="list-style-type: none"> ○ In DM-1 and DKA ○ In patients w/ pancreatitis ○ In pediatrics
A1c Reduction	~1.3%	~1%	~1.5%
MOA	Recombinant fusion protein that acts as GLP-1 receptor agonist - enhances glucose-dependent insulin synthesis/secretion, suppresses inappropriate glucagon secretion, slows gastric emptying		
Dosing	2 mg SQ once weekly	30 mg SQ once weekly Max: 50 mg SQ once weekly	0.75 mg SQ once weekly Max: 1.5 mg SQ once weekly
Dosing Adjustments	<ul style="list-style-type: none"> • Renal: Avoid use if CrCl < 30 ml/min 	<ul style="list-style-type: none"> • None listed 	<ul style="list-style-type: none"> • None listed
Most Common AEs	<ul style="list-style-type: none"> • GI: N/V, diarrhea, constipation, dyspepsia • Hypoglycemia (worst w/ SU) • Decreased appetite • Injection site reactions/"nodules" 	<ul style="list-style-type: none"> • URIs • GI: Diarrhea, nausea • Injection site reactions 	<ul style="list-style-type: none"> • GI: N/V, diarrhea, constipation, abdominal pain • Decreased appetite
PK	<ul style="list-style-type: none"> • SS achieved over 6 weeks • Elimination: renal • T_½: 2 weeks 	<ul style="list-style-type: none"> • SS achieved in 3-4 weeks • Metabolism: degradation to small peptides • T_½ : 5 days 	<ul style="list-style-type: none"> • SS achieved over 4-6 weeks • Metabolism: Degradation to amino acids by protein catabolism pathways • T_½ : 5 days
Contraindications	<ul style="list-style-type: none"> • Personal or family hx of medullary thyroid carcinoma (MTC) • Multiple endocrine neoplasia syndrome type 2 (MEN 2) 		
Warning & precautions	<ul style="list-style-type: none"> • Black Box: Risk of thyroid C-cell tumors • Pancreatitis (avoid use) • ESRD (avoid use) • Moderate renal dysfunction (use with caution) • Severe GI disease (avoid use) • Pregnancy category C 	<ul style="list-style-type: none"> • Black Box: Risk of thyroid C-cell tumors • Pancreatitis (avoid use) • Use with prandial insulins has not been studied • Pregnancy category C • Breastfeeding (no adequate data) 	<ul style="list-style-type: none"> • Black Box: Risk of thyroid C-cell tumors • Pancreatitis (avoid use) • H/o cardiac conduction abnormalities (in rare cases, causes tachycardia, PR interval prolongation, first degree AV block) • Severe GI disease (avoid use)

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	<ul style="list-style-type: none"> Breastfeeding 		<ul style="list-style-type: none"> Pregnancy category C Breastfeeding
Potential Drug Interactions	<ul style="list-style-type: none"> May slow rate of absorption of PO medications (slows gastric emptying) Use w/ insulins & insulin secretagogues (e.g., sulfonylurea) may increase the risk of hypoglycemia; dosage reduction may be required Warfarin (increase in INR, bleeding risk) 	<ul style="list-style-type: none"> May slow rate of absorption of PO medications (slows gastric emptying) Use w/ insulins & insulin secretagogues (e.g., sulfonylurea) may increase the risk of hypoglycemia; dosage reduction may be required 	<ul style="list-style-type: none"> May slow rate of absorption of PO medications (slows gastric emptying) Use w/ insulins & insulin secretagogues (e.g., sulfonylurea) may increase the risk of hypoglycemia; dosage reduction may be required
Other Counseling Points	<ul style="list-style-type: none"> Available as vial & syringe (reconstitution required) OR pen (twist to reconstitute, then "tap" 80+ times) Let sit at room temp for 15 minutes before reconstitution step Comes with special needle attachment (CANNOT use insulin pen needles) Take with or without meals If a dose is missed, take within 3 days (otherwise skip) Can store at room temp for up to 4 weeks Dose should be given immediately after reconstituting Copay card available (for private insurance, copay as low as \$25/mo x 24) 	<ul style="list-style-type: none"> Available as pen (30 or 50 mg, twist to reconstitute, then wait 15-30 minutes) Comes with special needle attachment (CANNOT use insulin pen needles) Take with or without meals If a dose is missed, take within 3 days (otherwise skip) Day of weekly administration can be changed as long as last dose given \geq 4 days ago Can store at room temp for up to 4 weeks Pen should be used within 8 hrs of reconstitution Copay card available (for uninsured or private insurance and < 65 yo, free x 12 months) 	<ul style="list-style-type: none"> Available as auto-inject pen (0.75 or 1.5 mg); no reconstitution required Needle included as part of pen Take with or without meals If a dose is missed, take within 3 days (otherwise skip) Day of weekly administration can be changed as long as last dose given > 3 days ago OK to keep at room temp for up to 14 days Copay card available (for private insurance, copay as low as \$25/mo x 24)

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Short Acting GLP-1 Agonists		
Drug	Exenatide (Byetta)	Liraglutide (Victoza)
Approval Year	2005	2010
Indication	<ul style="list-style-type: none"> • DM-2 • Not recommended for use: <ul style="list-style-type: none"> ○ In DM-1 and DKA ○ Severe renal impairment (< 30 mL/min) ○ In patients w/ pancreatitis ○ In patients with severe GI disorders ○ In pediatrics 	<ul style="list-style-type: none"> • DM-2 • Not recommended for use: <ul style="list-style-type: none"> ○ In DM-1 and DKA ○ In patients with severe GI disorders ○ In patients w/ pancreatitis ○ In pediatrics
A1c Reduction	~1%	~1.5%
MOA	Recombinant fusion protein that acts as GLP-1 receptor agonist - enhances glucose-dependent insulin synthesis/secretion, suppresses inappropriate glucagon secretion, and slows gastric emptying	
Dosing	5 mcg SQ BID Max: 10 mcg SQ BID	0.6 mg SQ once daily x 1 week, then 1.2 mg SQ once daily Max: 1.8 mg SQ once daily <i>For weight loss: 3 mg (Saxenda)</i>
Dosing Adjustments	<ul style="list-style-type: none"> • Renal: Avoid use if CrCl < 30 ml/min • Hepatic: None 	<ul style="list-style-type: none"> • Renal: Use caution with moderate-to-severe impairment • Hepatic: Use caution, limited experience
Most Common AEs	<ul style="list-style-type: none"> • GI: N/V (30%), diarrhea, constipation, dyspepsia • Headache • Hypoglycemia (worst w/ SU) • Decreased appetite • Injection site reactions 	<ul style="list-style-type: none"> • GI: N/V (25%), diarrhea, constipation, dyspepsia • Headache • Hypoglycemia (worst w/ SU) • Decreased appetite • Injection site reactions • <i>Increased HR (+ 10 bpm) – with Saxenda</i>
PK	<ul style="list-style-type: none"> • Time to peak level: 2.1 hrs • Elimination: urine • T_½: 2-4 hrs 	<ul style="list-style-type: none"> • Time to peak level: 8-12 hrs • Elimination: urine, feces • T_½ : 13 hrs
Contraindications	<ul style="list-style-type: none"> • Personal or family hx of medullary thyroid carcinoma (MTC) • Multiple endocrine neoplasia syndrome type 2 (MEN 2) 	<ul style="list-style-type: none"> • Personal or family hx of medullary thyroid carcinoma (MTC) • Multiple endocrine neoplasia syndrome type 2 (MEN 2) • Pregnancy (Saxenda)
Warning & precautions	<ul style="list-style-type: none"> • Black Box: Risk of thyroid C-cell tumors • Pancreatitis (avoid use) • ESRD (avoid use) • Moderate renal dysfunction (use with caution) • Severe GI disease (avoid use) 	<ul style="list-style-type: none"> • Black Box: Risk of thyroid C-cell tumors • Pancreatitis (avoid use) • Renal impairment and reports of severe GI side effects • CV effects - Increased HR (Saxenda)

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	<ul style="list-style-type: none"> • Pregnancy category C • Breastfeeding 	<ul style="list-style-type: none"> • Pregnancy category C (X with Saxenda) • Breastfeeding (no adequate data)
Potential Drug Interactions	<ul style="list-style-type: none"> • May slow rate of absorption of PO medications (slows gastric emptying) • Use w/ insulins & insulin secretagogues (e.g., sulfonylurea) may increase the risk of hypoglycemia; dosage reduction may be required • Warfarin (increase in INR, bleeding risk) 	<ul style="list-style-type: none"> • May slow rate of absorption of PO medications (slows gastric emptying) • Use w/ insulins & insulin secretagogues (e.g., sulfonylurea) may increase the risk of hypoglycemia; dosage reduction may be required
Other Counseling Points	<ul style="list-style-type: none"> • Available as prefilled multi-dose pens (5 or 10 mcg) – no mixing required • Requires separate Rx for pen needles (uses insulin pen needles) • Inject within 60 minutes of morning and evening meals • Take with or without meals • Copay card available, “MySavingsRx” through AstraZeneca (for private insurance, copay as low as \$25/mo x 12) 	<ul style="list-style-type: none"> • Available as prefilled multi-dose, ready-to-use pens (1.8 or 3 mg) – no mixing required • Requires separate Rx for pen needles (uses insulin pen needles) • Take with or without meals • Copay card available (for private insurance, copay as low as \$25/mo x 24)

Tables adapted from: PL Detail-Document, Comparison of GLP-1 Agonists. *Pharmacist’s Letter/Prescriber’s Letter*. August 2014.

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GLP-1 Agonist Comparison:

- A1c lowering: Trulicity/Victoza (1.5%) > Bydureon (1.3%) > Byetta/Tanzeum (1%)
 - Long-acting agents more likely to lower PP and fasting readings (short-acting, just PP)
- Weight loss (avg): Trulicity/Bydureon/Victoza (2.5 kg) > Byetta (2 kg) > Tanzeum (1 kg)
- Nausea: Byetta (30%) > Victoza (25%) >> Bydureon/Trulicity/Tanzeum (11-12%)
 - Dose-dependent, usually self-limiting (1-2 weeks)
 - Higher risk when used as combo-therapy
- Injection site reactions: Bydureon/Tanzeum (17-18%) > Byetta (12%) >> Victoza (2%) > Trulicity (0.5%)
- Price per month (cash, AWP): Victoza (\$600, 1.8mg dose) > Trulicity (\$500) > Bydureon/Byetta (\$450) > Tanzeum (\$330)

Other tips/information:

- Alternative to insulin for patients within 1-1.5% of A1c goal and already on 2-3 oral agents
 - Some studies suggest that adding to metformin may be MORE effective vs adding Lantus (if relatively close to goal A1c)
- Adding to basal insulin in place of mealtime insulin
 - Fewer injections, no weight gain (potential weight loss)
- **Pros**: PP coverage, modest weight loss (2-6 lbs on average), small reduction in SBP (up to 6 mmHg w/ long-acting agents), small improvement in lipids (seen in some studies), more effective (vs DPP4 inhibitors), once weekly dosing options available (vs insulins)
- **Cons**: injectable (no PO options), cost, GI side effects
 - To minimize nausea: eat smaller meals, avoid overeating, cut down on fat content, wear non-restrictive clothing (i.e. avoid tight waistband)
- Pancreatitis risk
 - No causality, but continued association; large observational studies do not show a risk
 - No link to pancreatic cancer
- MTC/C-cell hyperplasia
 - Rodents – increased incidence
 - Humans – no increased incidence to date
 - Possible mechanism: GLP-1 receptors on C-cell tumors
- Remember – use may require reduction in insulin and/or SU doses to avoid hypoglycemia
 - Most have not been studied for use with mealtime insulins