

Newer Diabetes Therapeutic Drug Classes and Insulin

The 2020 American Diabetes Association guidelines continue to recommend metformin as the preferred and most cost-effective first line agent in the treatment of type 2 diabetes (T2DM). Therapy should be initiated at diagnosis (or soon after) especially when lifestyle interventions are not expected to achieve HbA1c targets. If a patient remains above target and a second agent is needed the decision should be based on a patient's *cardiovascular status and risk independently of baseline A1C or individualized A1C target*. If not high risk or established ASCVD, CKD or HF and A1C above target consider the following: hypoglycemia, weight impact and or cost.

- For patients with established atherosclerotic cardiovascular disease (ASCVD), or indicators of high risk, a GLP-1 receptor agonist with cardiovascular benefit is preferred if possible
- For patients with heart failure or chronic kidney disease (CKD), an SGLT-2 is preferred if possible.
- For patients *without established CVD*, medication specific factors as well as insurance coverage, side effect profile, and patient preference should drive selection.
- Select SGLT-2 inhibitors and GLP-1RA have proven cardiovascular benefit for patients with T2DM and established CVD.
 - Cardiovascular outcome trials (CVOT) conducted have demonstrated CV non-inferiority and/or superiority; the primary outcome measured: 3-point MACE (major adverse CV events: CV death, MI, stroke)
 - CV effects appear to be *independent* of effects on HbA1c

Document Key:
PA: Prior Authorization, ST: Step Therapy, NC: Not Covered; 1: lowest Tier copay, 2: mid-Tier copay, 3: highest Tier copay; NTM=new to market Pricing and coverage verified as of 11/18/19.

Glucagon-like peptide-1 receptor agonists (GLP-1 RA)

	Trulicity (dulaglutide)	Victoza (liraglutide)	Ozempic (semaglutide)	Bydureon BCise pre-filled pen/pre-attached hidden needle (exenatide ER)	Adlyxin (lixisenatide)	Byetta (exenatide)	Rybelsus (semaglutide)
Common Dosing	0.75 - 1.5mg Once WEEKLY (No dosing restrictions)	1.2 - 1.8mg Once DAILY (No dosing restrictions)	0.25mg-0.5mg; 1mg Once WEEKLY (No dosing restrictions)	2 mg Once WEEKLY (No dosing restrictions)	10 -20 mcg Once DAILY (1 hr before 1 st meal of the day)	5 - 10 mcg Twice DAILY (≤60 min before the 2 largest meals)	3mg, 7mg, 14mg Once DAILY[^] ORAL Therapy
% A1c Reduction	1.5%	1.5%	1.4%	1.4%	1%	1%	1%
Cost/Month	\$730	\$ 891	\$ 741	\$ 792	\$ 744	\$ 350-\$874	NTM
Health Plan Coverage							
BCBS-MA	2/ST	NC	NC	2/ST	NC	2/ST	NTM
HPHC	2/ST	2/ST	2/ST	2/ST	NC	2/ST	NTM
FALLON	2/PA	2/PA	2/PA	3/PA	3/PA	3/PA	NTM
TUFTS	2	2	2	NC	NC	NC	NTM
MA Heath Tufts ACO (BIDCO/Lahey)	NC	2	2	NC	NC	NC	NTM
BMC-Lahey MAH- ACO	2/ST	2/ST	2/ST	2/ST	2/ST	2/ST	NTM

[^]Rybelsus- expected December 2019; Dosing: take at least 30 minutes before first food, beverage, or other oral medications of the day with max of 4 ounces of plain water only.

GLP-1 RA and Insulin Combination Products

Brand Name	Cost/month	BCBS-MA	HPHC	FALLON	TUFTS	MA Heath Tufts ACO (BIDCO/Lahey)	BMC-Lahey MAH-ACO	Comments
Xultophy (liraglutide/insulin degludec)	\$1005	NC	NC	3/PA	NC	NC	2/ST	-Each mL contains: 100 units of insulin degludec & 3.6 mg of liraglutide -A1c reduction of additional 1% vs. insulin
Soliqua (lixisenatide/insulin glargine)	\$675	NC	NC	3/PA	NC	NC	2/ST	-Each mL contains: 100 units of insulin glargine & 33 mcg of lixisenatide -A1c reduction of additional 0.5% vs. insulin

Sodium-glucose co-transporter 2 Inhibitors (SGLT-2 Inhibitors)

	Invokana (canagliflozin)	Farxiga (dapagliflozin)	Jardiance (empagliflozin)	Steglatro (ertugliflozin)
Starting dose (GFR > 60 mL/min)	100 mg once daily (in the morning)	5 mg once daily (in the morning)	10 mg once daily (in the morning)	5 mg once daily (in the morning)
Renal Dosing				
>60 ml/min	100-300mg daily	5-10mg daily	10-25mg daily	5-15 mg daily
45-60 ml/min	100mg daily	not recommended	10-25mg daily	not recommended
30-45 ml/min	not recommended	not recommended	not recommended	not recommended
<30 ml/min	contraindicated	contraindicated	contraindicated	contraindicated
Expected HbA1c reduction: 0.7%-1%				
Cost/month	\$480	\$480	\$480	\$270
Health Plan Coverage				
BCBS-MA	2/ST	NC	2/ST	NC
HPHC	2	3	2	3
FALLON	3/PA	2/PA	2/PA	3/PA
TUFTS	NC	NC	2	NC
MA Heath Tufts ACO (BIDCO/Lahey)	NC	NC	NC	2/ST
BMC-Lahey MAH-ACO	2/ST	2/ST	2/ST	2/ST

SGLT-2 Inhibitor **Combination** Products

Brand Name	Generic Components	Cost/month	BCBS-MA	HPHC	FALLON	TUFTS	MA Heath Tufts ACO (BIDCO/Lahey)	BMC-Lahey MAH-ACO
Invokamet, Invokamet XR	<i>canagliflozin + metformin (ER)</i>	\$480	2ST	2	3/PA	NC	NC	2/ST
Synjardy, Synjardy XR	<i>empagliflozin + metformin (ER)</i>	\$480	2 ST	NC	2/PA	2	NC	2/ST
Xigduo XR	<i>dapagliflozin + metformin (ER)</i>	\$480	NC	3/ST	2/PA	NC	NC	2/ST
Segluromet	<i>ertugliflozin + metformin</i>	\$300	NC	NC	3/PA	NC	2/ST	2/ST

Dipeptidyl peptidase-4 Inhibitors (DPP-4 Inhibitors)

	Tradjenta (linagliptin)	Januvia (sitagliptin)	Onglyza (saxagliptin)	Nesina (alogliptin)	
Initial Dose	5mg once daily	100mg once daily	2.5 - 5mg once daily	25mg once daily	
Renal impairment	No dose adjustment	≥30 - <45 ml/min : 50mg once daily <30 ml/min: 25mg once daily	≤45 ml/min: 2.5mg once daily	≥30 - <60 ml/min: 12.5 mg once daily <30 ml/min: 6.25mg once daily	
Expected HbA1c reduction: 0.5%-1%					
Cost/month	\$420	\$420	\$390	\$180(g)	\$360(b)
Health Plan Coverage					
BCBS-MA	NC	2/ST	2/ST	NC(g)	NC (b)
HPHC	2	2	NC	3 (g)	NC (b)
FALLON	2	3/PA	3/PA	1 (g)	NC (b)
TUFTS	NC	2	NC	1 (g)	NC (b)
MA Heath Tufts ACO (BIDCO/Lahey)	NC	NC	NC	1 (g)	NC (b)
BMC-Lahey MAH-ACO	2 ST	2 ST	2 ST	1 (g)	NC (b)

DPP-4 Inhibitors **Combination Products**

Drug Name	Cost/month	BCBS-MA	HPHC	FALLON	TUFTS	MA Heath Tufts ACO (BIDCO/Lahey)	BMC-Lahey MAH-ACO			
Kazano (alogliptin + metformin) (generic available)	\$180(g)/\$360(b)	NC (b&g)	NC (b&g)	NC (b)	1 (g)	NC (b)	1 (g)	NC (b)	1/PA (g)	2/ST
Oseni (alogliptin + pioglitazone) (generic available)	\$180(g)/\$720(b)									
Jentadueto, Jentadueto XR (linagliptin + metformin (ER))	\$420(g)/\$840 (b)	NC	2	NC	NC	NC	2/ST			
Kombiglyze XR (saxagliptin + metformin (ER))	\$420(g)/\$840 (b)	2/ST	NC	3/PA	NC	NC	2/ST			
Janumet, Janumet XR (sitagliptin + metformin (ER))	\$420(g)/\$840 (b)	2/ST	2	3/PA	2	NC	2/ST			

b = brand g = generic

SGLT-2 Inhibitor/DPP-4 Inhibitor **Combination Products**

Brand Name	Cost/month	BCBS-MA	HPHC	FALLON	TUFTS	MA Heath Tufts ACO (BIDCO/Lahey)	BMC-Lahey MAH-ACO
Glyxambi (linagliptin + empagliflozin)	\$510	2/ST	NC	3/PA	3	NC	2/ST
Steglujan (ertugliflozin + sitagliptin)	\$660	NC	NC	3/PA	NC	NC	2/ST
Qtern (dapagliflozin + saxagliptin)	\$480	NC	PA	3/PA	NC	NC	2/ST

Insulin Products

Long Acting Insulin											
Product	Onset	Peak	Duration	Stability (In-use at room temp)	Cost (10mL vial/ box=5 pens)	Health Plan Coverage					
						BCBS-MA	HPHC	FALLON	Tufts	MA Heath Tufts ACO (BIDCO/Lahey)	BMC-Lahey MAH-ACO
Lantus (insulin glargine)	~ 1 hr	none	10.8 to > 24 hrs.	Vial & Pen: 28 days	\$272/\$405	2	2	2	2	NC	NC
Basaglar (insulin glargine recombinant)	~ 1 hr	none	24 hrs.	Pen: 28 days	\$405	2	3/PA	3/PA	NC	2	2
Levemir (insulin detemir)	1-2 hrs.	6-8 hrs.	7.6 to >24hrs.	Vial & Pen: 42 days	\$300/\$450	NC	2	3/PA	NC	NC	NC
Toujeo (insulin glargine U-100) & Toujeo Max (insulin glargine U-300)	> 6 hrs.	12-16 hrs	> 24 hrs.	Pen: 28 days	\$373 Max: \$498 (box/2 pens)	2	2	2	2	NC	NC
Tresiba (insulin degludec U-100 & U-200)	~ 1 hr	~ 9 hrs.	> 24 hrs.	Pen: 56 days (do not refrigerate once open)	U-100: \$495 U-200: \$585 (box/3 pens)	NC	4/PA	3/PA	NC	2	NC
Rapid Acting Insulin											
Humalog (insulin lispro U-100 & U-200)	15-30 mins	30-150 min	3-6.5 hrs.	Vial & Pen: 28 days	U-100 (Vial & Pen) \$260 U-200 Pen: \$480 (box/2 pens)	2	2	2	2	NC	NC
Novolog (insulin aspart)	10-20 mins	40-50 mins	3-5 hrs.		\$270/\$540	NC	3/PA	3/PA	NC	NC	NC
Apidra (insulin glulisine)	25 mins	~ 45 mins	4-5.5 hrs.		\$270/\$525	NC	NC	3/PA	NC	NC	NC
Fiasp (insulin aspart)	16-20 mins	90-130 min	5-7 hrs.		\$280/\$540	NC	NC	3/PA	NC	NC	NC
Admelog (insulin lisproU-100)	15-30 mins	30-150 min	3-6.5 hrs.		\$130/\$240	NC	NC	3/PA	NC	2	2
Biphasic Premixed Insulin											
Humalog Mix 75/25 (75% insulin lispro protamine, 25% insulin lispro)	15-30 mins	1-6.5 hrs.	Up to 24 hrs.	Vial: 28 days, Pen: 10 days	\$270/\$510	2	2	2	2	2	NC
Humalog Mix 50/50 (50% insulin lispro protamine, 50% insulin lispro)	15-30 mins	0.8-4.8 hrs.	22+ hrs.	Vial: 28 days, Pen: 10 days	\$270/\$510	2	2	2	2	2	NC
Novolog Mix 70/30 (70% insulin aspart protamine, 30% insulin aspart)	10-20 mins	1-4 hrs.	Up to 24 hrs.	Vial: 28 days, Pen: 14 days	\$290/\$540	NC	3/PA	3/PA	NC	2	2
Humulin 70/30 (70% NPH, 30% Regular)	~30 mins	1.5-6.5 hrs.	18-24 hrs.	Vial: 31 days, Pen: 10 days	\$150/\$450	2	2	2	2	2	2
Novolin 70/30 (ReliOn) (70% NPH, 30% Regular)	30 mins	2-12 hrs.	Up to 24 hrs.	Vial: 42 days	ReliOn~\$25	NC	3/PA	2	NC	2	2
Intermediate Acting Insulin											
Humulin N (isophane human insulin)	1-2 hrs.	6.5 hrs.	4-12 hrs.	Vial: 31 days, Pen: 14 days	\$178/\$570	2	2	2	2	2	2
Novolin N (ReliOn) (isophane human insulin)	90 mins	16-24+ hrs.	Up to 24 hrs.	Vial: 42 days	ReliOn~\$25	NC	3/PA	3/PA	NC	2	2
Short Acting Insulin											
Humulin R (human regular insulin U-100 & U-500)	~ 30 mins	Dose dependent U-100: ~ 3 hrs. U-500: 4-8 hrs.	Dose dependent U-100: ~ 8 hrs. U-500: 13-24 hrs.	U-100 Vial: 31 days U-500 Vial: 40days U-500 Pens: 28 days	U-100 (vial) \$178 U-500 \$1780 (20 mL vial)/ \$550 (box/2 syringes)	2	2	2	2	2	2
Novolin R (ReliOn) (human regular insulin)	~ 30 mins	1.5-3.5 hrs.	~ 8 hrs.	Vial: 42 days	ReliOn~\$25	NC	3/PA	3PA	NC	2	2

References:

Copy Tier estimates are based on:

- **BCBS-MA:** Standard formulary, 3-tier plan <https://provider.bluecrossma.com/ProviderHome/portal/home/pharmacy/lut/p/z1/ZHBbslwDlafptfYJG0VdksPo0wLEFKh5DK1JUCnpgnSUF5YdsBpsE2XyzbvzJv0FCDRithvpQuNq0RePrrYxf1yJOK-eUll9wgdN5uMZwLkaYRbD5E0BNCEXWNGGIkwUF-f9a9Lf9h8I5GP8BuQPktLfmO8gKxLTc6VJkjomHMWxSwOl6TM54uHoi0ZP4C0ag-ssuRkvbVH57r-KcAAO2uGeuf7ZXNSITV9rwtSGR3g8muSGq28zlj3-ZTvwKpPHeT3ONDpLMvxLWqGmXgHPwJaiA!!/dz/d5/L2dBISEvZ0FBIS9nQSEh/>
- **HPHC:** 3 tier value plan (note: multiple plans with differences exist including 3& 4 Tier Premium Plans and 3-5 Tier Value Plans) https://www.harvardpilgrim.org/portal/page?_pageid=253,41644&_dad=portal&_schema=PORTAL
- **FALLON:** 3 tier plan <https://www.fchp.org/en/members/Pharmacy/online-drug-formulary.aspx>
- **Tufts:** MA large group 4 tier commercial plans (note: other plans exist, minor differences) <https://formularysearch.caremark.com/FormularySearch/servlet/FdmsFormularyServlet?com=tufts&menu=1&formulary=5>
- **THHP:** Tufts Health Public Plan-2019 Together Health Plan Accountable Care Organization & Lahey Mass Health ACO Drug List <https://client.formularynavigator.com/Search.aspx?siteCode=1908057560>
- **BMC:** Boston Medical Center MassHealth MCO/ACO: <https://www.bmchp.org/I-Am-A/Member/Get-Prescriptions/Drug-Finder/MassHealth>

National Average Drug Acquisition Cost Website: <https://data.medicaid.gov/Drug-Pricing-and-Payment/NADAC-as-of-2019-05-15/rt4v-78r4>; accessed November 8, 2019.

Lexicomp: <http://online.lexi.com/action/home>, accessed November 8, 2019.

UptoDate: <https://www.uptodate.com/contents/search>, accessed November 15, 2019. **Pharmacist's Letter:** PL Detail-Documents, Drugs for Type 2 Diabetes. Pharmacist's Letter/Prescriber's Letter. July 2019. Compare Cardiovascular Benefits of SGLT2 Inhibitors for Type 2 Diabetes, January 2019.