University of Michigan Health Plan

DRUG DETERMINATION POLICY

Title: DDP-43 Non-Insulin Diabetic Agents

Effective Date: 8/27/25

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by UM Health Plans and may not be covered by all UM Health Plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact UM Health Plan Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

GLP-1 agonists, GLP-1/GIP agonists, DPP-4 inhibitors, and SGLT-2 inhibitors are traditional non-insulin drugs indicated for the treatment of diabetes. Select drugs from each class have been also approved to reduce the risk of major cardiovascular events in adults with type 2 diabetes and established cardiovascular disease or those with multiple cardiovascular risk factors; for adults with heart failure with reduced and preserved ejection fraction; and for adults with chronic kidney disease. These criteria were developed and implemented to ensure these drugs are used at the appropriate place in therapy and severity of the disease.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General Considerations

A. Appropriate medication use [must meet all listed below]

1. Diagnosis: meets standard diagnostic criteria that designates signs, symptoms, and test results to support specific diagnosis.

2. Food and Drug Administration (FDA) approval status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved use: Compendium support (UpToDate® LexiDrug™) for use of a drug for a non-FDA approved indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or internationally accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Required site-of-care as determined by the Health Plan (DDP-08 Site of Care for Administration of Parenteral Specialty Drugs).

C. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.

D. Adherence to requested medication required for re-approval [must meet one listed below]:

1. Medications processed on the medical benefit: consistent (at least 80% of days covered) utilization history documented in claims history or chart notes.

2. Medications processed on the pharmacy benefit: consistent (at least 80% of days covered) fill history electronically or verbally from the pharmacy.

E. Preferred agents.

1. Preferred agent by class.

a. GLP-1 and GLP-1/GIP agonists: Trulicity SQ (dulaglutide), Mounjaro SQ (tirzepatide), Victoza SQ, (liraglutide) Ozempic SQ, Rybelsus oral (semaglutide).

b. DPP-4 Inhibitors: Januvia oral (sitagliptin).

c. SGLT-2: Jardiance oral (empagliflozin), Farxiga oral (dapagliflozin).

F. Prior authorized agents [must meet both below]:

1. Prior authorized agents by class:

a. GLP-1: None

b. DDP-4: Alogliptin oral (generic)

c. SGLT-s: None

2. Other therapies: Trials of all preferred formulary agents in the same drug class are required unless contraindicated. Trials must result in an inadequate reponse after four consecutive months or use per medications or a severe adverse reaction.

G. Excluded Agents:

1. Excluded agents by class:

a. GLP-1 agonist: Adlyxine (lixisenatide) Byetta/Bydureon (exenatide).

b. DPP-4 Inhibitors: Nesina (alogliptin), Onglyza (saxagliptin), Tradjenta (linagliptin).

c. SGLT-2: Brenzavvy (bexagliflozin), Inpefa (sotagliflozin), Invokana (canagliflozin), Steglatro (ertugliflozin)

2. Trials of all preferred formulary agents are required unless contraindicated. Trials must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.

II. Type 2 Diabetes Mellitus [must meet all listed below]: Trulicity SQ (dulaglutide), Mounjaro SQ (tizepatide), Ozempic SQ (semiglutide), Rybelsus oral (semiflutide), Victoza (liraglutide); Januvia oral (sitagliptide); Jardiance oral (empagliflozin), Farxiga (dapagliflozin)

A. Diagnosis and severity:

1. Hgb A1c measured after three months of consistent use of metformin 2,000 mg/day, pioglitazone, glimepiride, glipizide, or glyburide [must meet one listed below]:

a. GLP-1 and GLP-1/GIP agonists: at least 6.5 percent.

b. DPP-4 Inhibitors and SGLT-2 inhibitors: 6.5 to 10 percent (these agents will not sufficiently decrease Hgb A1c if more than 10 percent).

B. Other Therapies:

1. HgbA1c >10%: Skip other therapies requirement for GLP-1 agents

2. A trial of metformin 1,000 mg twice daily is required unless contraindicated. Trial must result in an inadequate response after three consecutive months of use or a severe adverse reaction.

3. If metformin immediate release causes gastrointestinal side effects or is contraindicated, a trial of one drug below is required unless all are contraindicated. The trial must result in an inadequate response after three consecutive months of use or a severe adverse reaction.

a. Metformin extended release 500 mg, two tablets twice daily.

b. Thiazolidinediones: pioglitazone.

c. Sulfonylureas: glimepiride, glipizide, glyburide.

C. Prior authorized agents [must meet both listed below]:

1. Prior authorized agent by class.

a. GLP-1 agonist: none.

b. DPP-4 Inhibitors: Alogliptin oral (generic).

c. SGLT-2: none.

2. Other Therapies: Trials of all preferred formulary agents in the same drug class are required unless all are contraindicated. Trials must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.

D. General Exclusions:

1. Type 1 diabetes mellitus.

2. Use of these agents for weight loss without underlying type 2 diabetes.

3. Concomitant therapy: DPP-4 and GLP-1 (or GLP-1/GIP) combination doesn't confer additional benefit on Hgb A1c.

E. Dosage regimen: See Appendix I.

F. Approval:

1. Initial: six months.

2. Re-approval: one year; reduced Hgb A1c.

III. Cardiovascular disease [meet all listed below]: Trulicity (dulaglutide), Ozempic (semaglutide), Victoza (liraglutide), Jardiance (empagliflozin), Farxiga (dapagliflozin)

A. Age: at least 18 years.

B. Diagnosis and severity [must meet one listed below]:

1. Type 2 Diabetes Mellitus with Established Cardiovascular disease.

2. Trulicity (dulaglutide) and Farxiga (dapagliflozin) only: Type 2 Diabetes Mellitus with multiple cardiovascular risk factors [must meet both listed below]:

a. Age [must meet one listed below]:

i. Men ≥55 years.

ii. Women ≥60 years.

b. Additional cardiovascular risk factor [must meet one listed below]:

i. Dyslipidemia.

ii. Hypertension.

iii. Current tobacco use.

C. Other therapies: add on to standard therapies unless contraindicated.

D. Dosage Regimen: See Appendix I

E. Approval: one year.

IV. Heart failure [meet all listed below]: Jardiance (empagliflozin), Farxiga (dapagliflozin)

A. Age: at least 18 years.

B. Diagnosis and severity.

1. Heart failure.

a. Farxiga (dapagliflozin) only: NYHA functional class II through IV.

C. Other therapies: add on to standard therapies (e.g., ACE/ARB/ARNI; beta blocker and/or diuretics) unless contraindicated.

D. Dosage regimen: See Appendix I.

E. Exclusions:

1. Type 1 diabetes mellitus.

F. Approval.

1. Initial: 12 months.

2. Re-approval: 12 months if improvement in heart failure symptoms.

V. Chronic Kidney Disease [meet all listed below]: Jardiance (empagliflozin), Farxiga (dapagliflozin)

A. Age: at least 18 years.

B. Diagnosis and severity [meet pertinent table row below]:

Creatinine Clearance	Other factors	Comments
>45 ml/min per 1.73m^2	Albumin Creatinine Ratio ≥ 200mg/g (≥ 20mg/mmol) or Heart failure	Only one factor needed
20-45 ml/min per 1.73m^2	None	Continue therapy even if CrCl <20ml/min per m^2

C. Other therapies: add on to standard therapies (e.g., ACE or ARB) unless contraindicated.

D. Dosage Regimen: See Appendix I

E. Exclusions.

1. Disease states:

   a. Type 1 diabetes mellitus.

   b. Polycystic kidney disease.

2. Concomitant medications:

   a. Use with another SGLT-2 inhibitor.

   b. Requiring or with a recent history of immunosuppressive therapy for kidney disease.

F. Approval:

1. Initial: 12 months.

2. Re-approval: 12 months [must meet all listed below]:

   a. Reduced incidence of sustained estimated glomerular filtration rate decline.

   b. No need for renal transplant or dialysis.

4.0 Coding:
None.

5.0 References, Citations & Resources:

1. https://care.diabetesjournals.org/content/42/Supplement_1/S61 accesssed 11/19.
2. Lexicomp Lexicomp Online® Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Trulicity, Victoza, Ozempic, Januvia, Jardiance, Farxiga, Adlyxin, Alogliptin, Mounjaro accessed July 2025.

3. Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomized controlled trials. Lancet 2020; 396:121.
4. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation 2017; 136:e137.
5. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med 2020; 383:1436.
6. ACE/ACE, "Consensus Statement on the Comprehensive Type 2 Diabetes Management Algorithm - 2020 Executive Summary," January 2020
7. ADA, "Standards of Medical Care in Diabetes - 2021," January 2021
8. Endocrine Society, "Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline," May 2019
9. ESC, "Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure," September 2021
10. KDIGO, "KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease," October 2020
11. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int 2024; 105:S117.
12. Perkovic V, Badve S. *UpToDate*. (Glassock R, Nathan D, Forman J, eds.). Wolters Kluwer; 2024:Treatment of diabetic kidney disease. Accessed October 3, 2024. https://www.uptodate.com/contents/treatment-of-diabetic-kidney-disease
13. Pharmacological Approaches to Glycemic Treatmennt: Satndards of Care in Diabetes-2023. Diabetes Care 2023;46(supplement 1):S140-S157.

6.0 Appendices:

See pages 8-9

7.0 Revision History:

Original Effective Date: 09/09/2025

Next Review Date: 11/01/2026

Revision Date	Reason for Revision
10/20	Annual review, put formulary status of each agent/dosage in a table and simplified other criteria, formatting, replace abbreviations; added diagnosis of DM-2; clarified metformin trial
8/21	Annual review; formatting, listed preferred/non-preferred and excluded meds outside table; added cardiovascular disease, heart failure and kidney disease indications as well as 2 algorithms
4/22	Off-cycle review ; format changes, removed Jardiance from heart failure , Removed GFR exclusions from Farxiga and included in dosage table; clarified metformin ER dosing requirement ; clarify heart failure with reduced or preserved ejection fraction
10/22	Annual review: Clarified cardiovascular indication for Jardiance and Farxiga; added Mounjaro, included general exclusion section under DM; removed DM reference in heart failure section
3/23	Off-cycle review; clarified multiple cardiovascular risk factors for Farxiga and Trulicity; added Jardiance to CKD indication section; removed ejection fraction requirement in heart failure indication; revised purpose
8/23	Annual review; added general consideration section and moved some exclusions to it. Added 5 references. Updated formatting and other therapies language. Adlyxine (lixisenatide) and Brenzavvy (bexagliflozin) added to excluded agents section. Clarified other therapies for diabetes indication.
8/24	Annual review; Deleted monitoring and Patient Safety Table, changed Renal failure diagnosis and severity section,. Added references; Cahnged Hgb A1cv

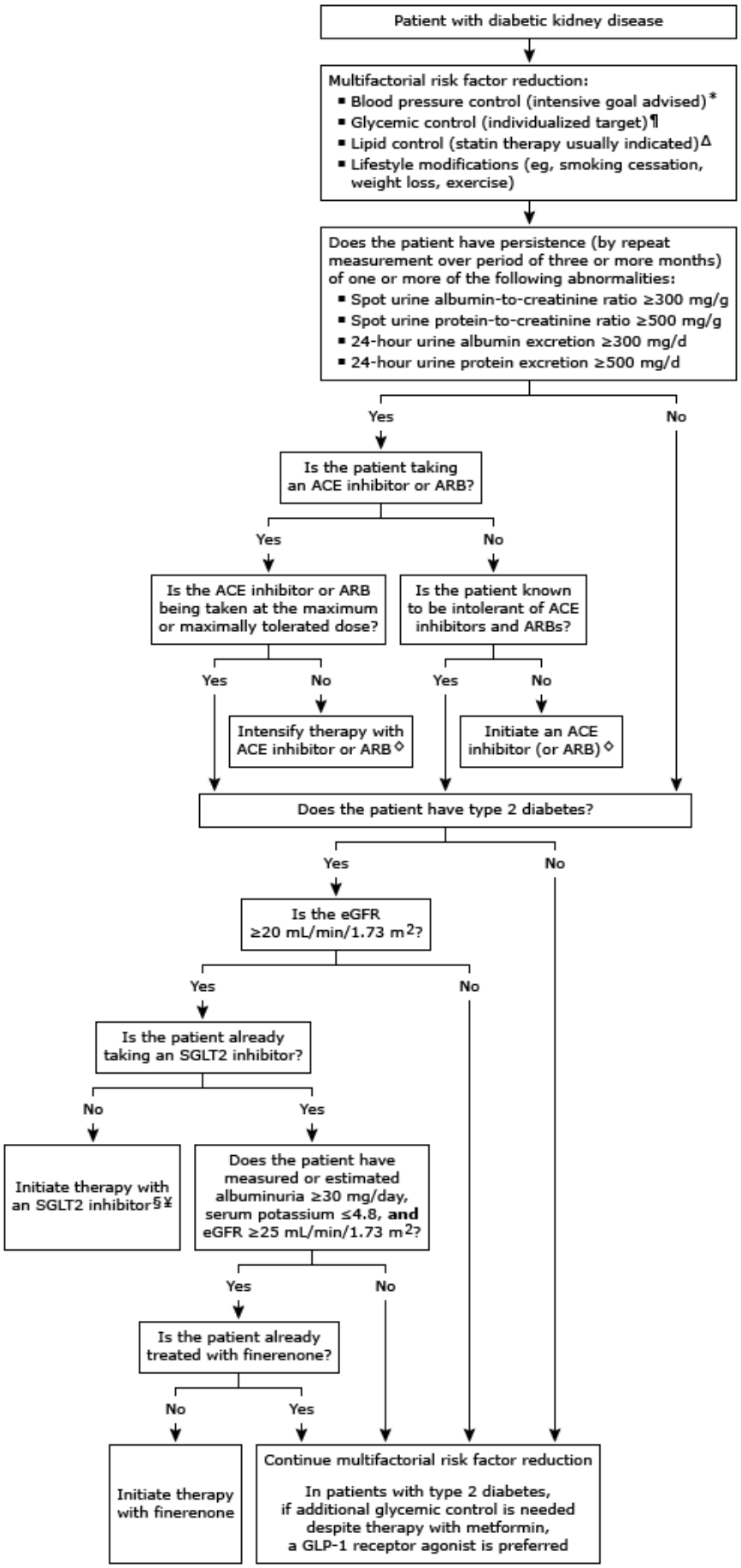
Revision Date	Reason for Revision
	level to 6.5% in DM section
11/24	Off-cycle review; removed need for other therpies for GLP1s if HgbA1c >10%, added reference
7/25	Off cycle review, Annual review schedule revised, updated references

Appendix I. Dosage regimen.

Category	Drug Name	Dosage Regimen	COMMENTS
GLP-1 and GLP-1/GIP Agonists	Trulicity SQ (dulaglutide)	0.75 mg once weekly; up to 4.5 mg once weekly.	Preferred, step therapy
	Victoza SQ (liraglutide)	0.6 mg once daily for one week, then 1.2 mg once daily; up to 1.8 mg once daily.	Preferred, step therapy
	Mounjaro SQ (tirzepatide)	2.5 mg once weekly for 4 weeks, then increase to 5 mg once weekly. May increase the dose in 2.5 mg/week increments every 4 weeks. Maximum dose 15 mg once weekly.	Preferred, step therapy
	Ozempic SQ Rybelus oral (semaglutide)	SQ: 0.25 mg weekly for 4 weeks, then increase to 0.5mg weekly for at least 4 weeks; maximum dose 2 mg once weekly. Oral: 3 mg for 30 days, then 7mg daily for 30 days (may increase to 14 mg if inadequate control)	Preferred, step therapy
	Adlyxin SQ (lixisenatide)		Excluded
	Byetta/Bydureon (exenatide)		Excluded
DPP-4 Inhibitors	Januvia oral (sitagliptin)	100 mg once daily.	Preferred, step therapy
	Alogliptin oral (generic)	25 mg once daily	Non-preferred, PA required
	Nesina (alogliptin), Tradjenta (linagliptin), Onglyza (saxagliptin).		Excluded
SGLT-2 Inhibitors	Jardiance oral (empagliflozin)	Diabetes: 10 mg once daily; up to 25 mg once daily. Heart Failure: 10 mg once daily.	Preferred, step therapy
	Farxiga oral* (dapagliflozin)	Diabetes: 5 mg once daily; up to 10 mg once daily Heart failure: 10 mg once daily	Preferred, Step therapy
	Invokana oral (canagliflozin), Steglatrooral oral (ertugliflozin).		Excluded

**Use not recommended with glomerular filtration rate (eGFR) <25 mL/minute/1.73 m^2.*

Appendix II. Algorithm for Management of Diabetic Kidney Disease[12]



ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; eGFR: estimated glomerular filtration rate; SGLT2: sodium-glucose cotransporter 2; Glucagon-like peptide 1 (GLP-1).

* More (versus less) intensive blood pressure goals are typically recommended in patients with diabetes. Refer to UpToDate content on treatment of hypertension in diabetic patients and on goal blood pressure in adults.

¶ Glycemic control targets are typically individualized, but an A1c goal of <7% is frequently recommended. Refer to UpToDate content on glycemic control in patients with type 1 and type 2 diabetes.

Δ Most patients with diabetic kidney disease are at high cardiovascular risk and therefore should be treated with statin therapy. Refer to UpToDate content on low-density lipoprotein cholesterol lowering for primary and secondary, and on medical care of diabetic patients.

◊ After adjusting the patient's therapy and measuring the response at an appropriate time interval, this algorithm can be used again to make further adjustments to the therapeutic regimen (if not already maximized).

§ SGLT2 inhibitors significantly increase the risk of genital infections.

¥ SGLT2 inhibitors reduce the risk of kidney disease progression and end-stage kidney disease in patients with diabetic kidney disease, regardless of the degree of proteinuria. However, patients with severely increased albuminuria (albumin-to-creatinine ratio ≥300 mg/g) are at higher risk for kidney disease progression and end-stage kidney disease and therefore derive a greater absolute benefit from therapy with SGLT2 inhibitors. Patients with normoalbuminuria or moderately increased albuminuria have a lower absolute risk for progression and therefore derive a smaller absolute benefit. Thus, for some patients at lower absolute risk for progression, the benefits and harms of taking an SGLT2 inhibitor may be more closely balanced.