DRUG DETERMINATION POLICY

Title: DDP-43 Non-Insulin and Adjunctive Diabetic Agents

Effective Date: 11/09/2021

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP 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 PHP 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, DPP-4 inhibitors, and SGLT-2 inhibitors are traditional non-insulin drugs indicated for the treatment of diabetes. GLP-1 inhibitors (e.g. Trulicity, Ozempic and Victoza) have been approved to reduce the risk of major cardiaovascular events in adults with type 2 diabetes and established cardiovascular disease. SGLT-2 inhibitors (e.g. Jardiance and Fargixa) have been approved for heart failure with reducted ejection fraction in those with type 2 diabetes. Fargixa has also been approved for heart failure with high ejection fraction in those with out type 2 diabetes and chronic kidney disease.These criteria were developed and implemented to ensure these drugs are used at the appropriate place in therapy and severity of disease.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Diabetes Mellitus Type II.

A. Diagnosis and severity: Hgb A1c measured after three months of consistent use of a preferred product [must meet one listed below]

1. Hgb A1c: measured after three months of consistent use of the preferred agent [must meet one listed below]:

a. GLP-1: at least 7 percent.

b. DPP-4 Inhibitors and SGLT-2 inhibitors: 7 to 9 percent (these agents will not sufficiently decrease Hgb A1c if more than 9 percent).

B. Preferred agents.

1. Metformin step therapy [must meet one or both listed below]:

a. Dosage regimen: 1000mg twice daily for three months.

b. Additional trial of metformin extended release (ER) if experiencing gastrointestinal side effects from metformin immediate release (IR).

2. Preferred agent by class.

a. GLP-1 agonist: Trulicity SQ (dulaglutide), Victoza SQ, (liraglutide) Ozempic SQ, Rybelus oral (semaglutide).

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

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

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

1. All preferred formulary agents in specific drug class are contraindicated; inadequate response after four months or significant adverse effects.

2. Prior authorized agent by class.

a. GLP-1 agonist: Adlyxin SQ (lixisenatide).

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

c. SGLT-2: none.

D. Excluded agents [must meet #1 listed below]:

1. All preferred formulary anti-diabetic agents are contraindicated; inadequate response after four-month trial or significant adverse effects.

2. Excluded agents by class.

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

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

c. SGLT-2: Invokana (canagliflozin), Steglatrooral (ertugliflozin).

E. Concomitant therapy: DPP-4 and GLP-1 combination doesn't confer additional benefit on HgbA1c

F. Dosage regimen: See Appendix I

G. Approval:

1. Initial: six months.

2. Reapproval: one year (reduced Hgb A1c).

II. Cardiovascular disease: Trulicity. Ozempic, Victoza

A. Age: at least 18 years

B. Diagnosis and severity [must meet both listed below]

1. Type 2 Diabetes Mellitus: no specific HgbA1c requirement

2. Established Cardiovascular disease or for Trulicity is also indicated for patients with multiple cardiovascular risk factors

C. Concomitant therapies: add on to standared therapies unless contraindicated

D. Dosage Regimen: See Appendix I

E. Approval: one year

III. Heart Failure with Reduced Ejection Fraction [must meet all listed below]: Jardiance, Farxiga

A. Age: at least 18 years

B. Diagnosis and severity

1. Heart failure [must meet both listed below]

a. Ejection fraction at or below 40 percent

b. NYHA functional class II through IV

2. Concomitant type 2 Diabetes Mellitus:

a. Only with Jardiance

b. HgbA1c: no specific HgbA1c requirement

C. Concomitant therapies: add on to standared therapies (e,g, ACE/ARB/ARNI; beta blocker and/or diuretcis) unless contraindicated

D. Dosage regimen: See Appendix I

E. Exclusions.

1. Type 1 diabetes mellitus

2. Estimated Glomerular filtration rate (eGFR)

a. Glycemic control in adults with type 2 diabetes mellitus: Farxiga - eGFR below 45 mL/min/1.73 m2; Jardiance - below 30 mL/min/1.73 m2

b. Heart failure: eGFR at or below 25 mL/min/1.73m^2 or currently on dialysis

3. Concomitant medications: use with another SGLT-2 inhibitor

F. Approval.

1. Initial: 12 months

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

   a. Improvement in heart failure symptoms

   b. Improvement in glycemic control

III. Chronic Kidney Disease [meet all listed below]: Fargixa

A. Age ≥ 18 years

B. Diagnosis and severity [meet both listed belwo]

1. Estimated glomerular filtration rate: between 25 and 75 mL/min/1.73 m2

2. Albuminuria with urine albumin creatinine ratio [UACR] between 200 and 5000 mg per ram)

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

D. Dosage Regimen: See Appendix I

E. Exclusions.[one listed below]

1. Disease states [one listed below]

   a. Type 1 diabetes mellitus

   b. Polycystic kidney disease

2. Estimated Glomerular filtration rate [one listed below]

   a. Glycemic control in adults with type 2 diabetes mellitus: Farxiga - eGFR below 45 mL/min/1.73 m2; Jardiance - below 30 mL/min/1.73 m2

   b. Heart failure: eGFR at or below 25 mL/min/1.73m^2 or currently on dialysis

3. 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 eGFR decline

   b. No need for renal transplant or dialysis

   c. Improvement in glycemic control

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 accessed August 2021.
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.

6.0 Appendices:

See pages 6-8.

7.0 Revision History:

Original Effective Date: 11/09/2021

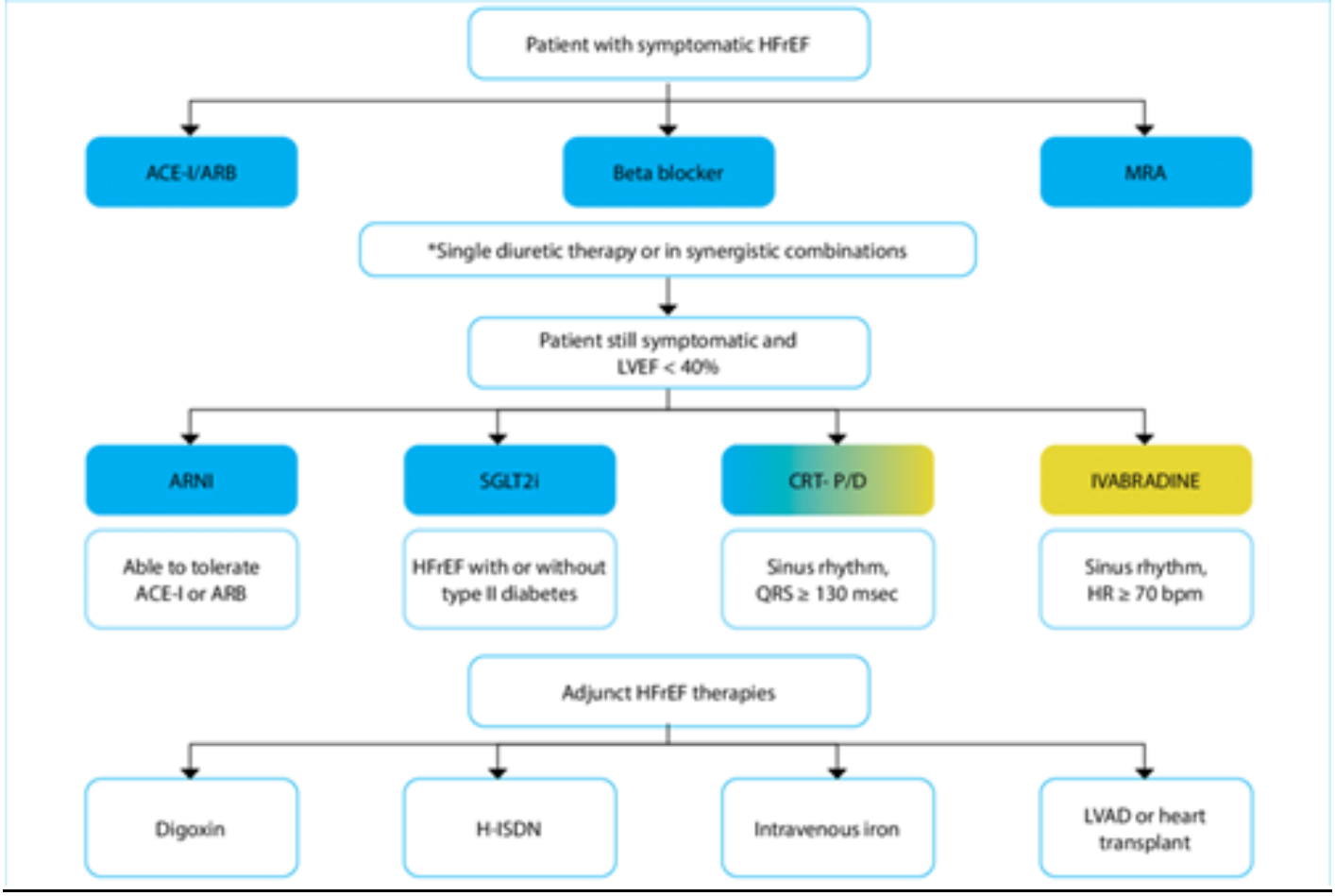
Next Review Date: 09/22/2022

Revision Date	Reason for Revision
10/20	Annual review, put formulary status of each agent/dosage in a table and simplified other critiera, 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

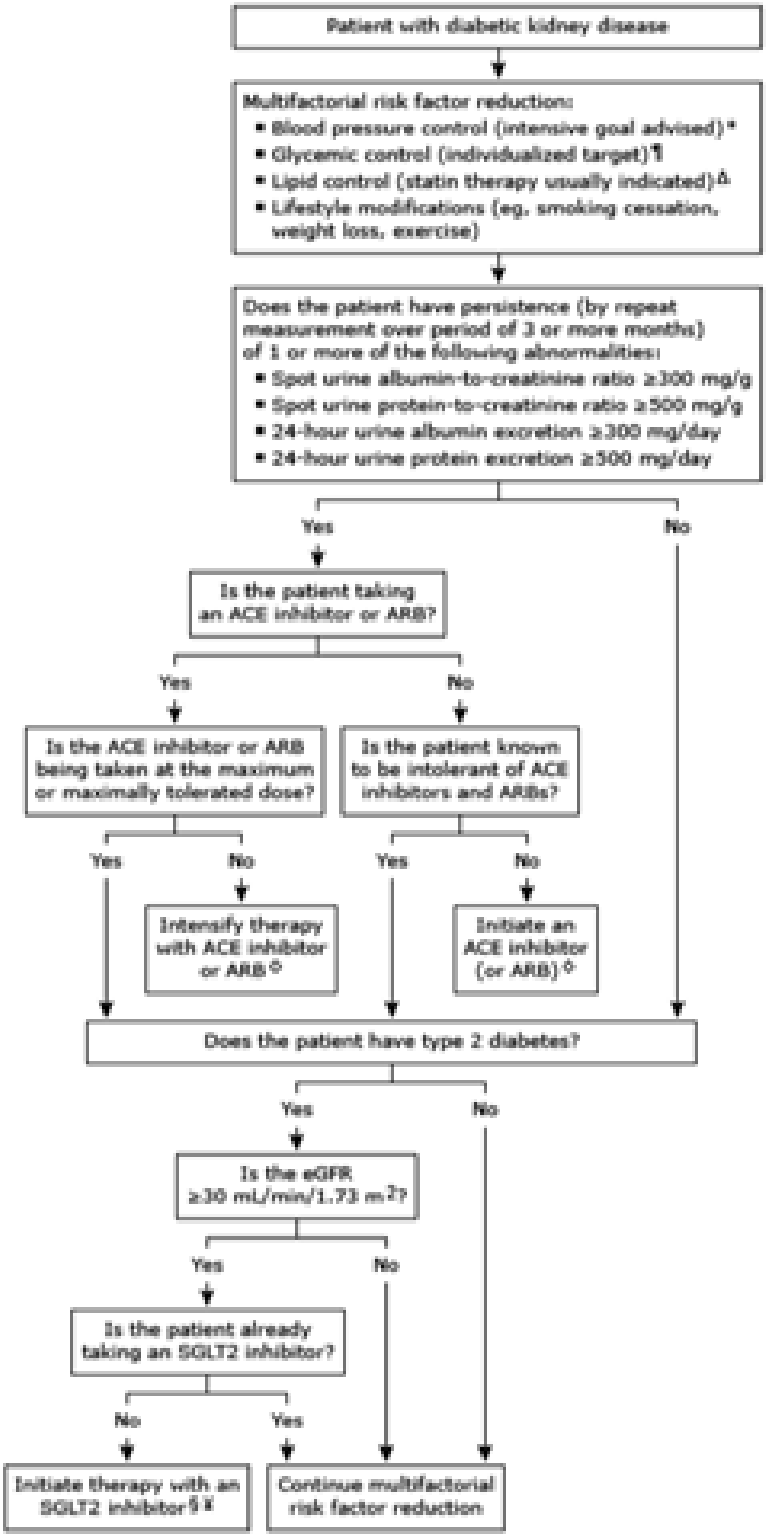
Appendix I. Dosage regimen.

Category	Drug Name	Dosage Regimen	COMMENTS
GLP-1 Agonist	Trulicity SQ (dulaglutide)	0.75mg once weekly; up to 1.5mg once weekly.	Preferred, step therapy
	Victoza SQ (liraglutide)	0.6mg once daily for one week, then 1.2mg once daily	Preferred, step therapy
	Ozempic SQ Rybelus oral (semaglutide)	SQ: 0.25mg weekly for 4 weeks then increase to 0.5mg weekly for at least 4 weeks; maximum dose 1mg once weekly. Oral: 3mg for 30 days, then 7mg daily for 30 days (may increase to 14mg if inadequate control)	Preferred, step therapy
	Adlyxin SQ (lixisenatide)	10mcg once daily times 14 days, then increase to 20mcg once daily.	Non-preferred, PA required
	Byetta/Bydureon (exenatide)		Excluded
DPP-4 Inhibitors	Januvia oral (sitagliptin)	100mg once daily.	Preferred, step therapy
	Alogliptin oral (generic)	25mg once daily	Non-preferred, PA required
	Nesina (alogliptin), Tradjenta (linagliptin), Onglyza (saxagliptin).		Excluded
SGLT-2 Inhibitors	Jardiance oral (empagliflozin)	Diabetes: 10mg once daily; up to 25mg once daily	Preferred, step therapy
	Farxiga oral (dapagliflozin)	Diabetes: 5mg once daily; up to 10mg once daily Heart failure: 10mg daily	Preferred, Step therapy
	Invokana oral (canagliflozin), Steglatrooral oral (ertugliflozin).		Excluded

Appendix II - Algorithm for Heart Failure with Reduced Ejection Fraction



Appendix III - Algorithm for Management of Diabetic Kidney Disease



Appendix IV - Monitoring and Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
GLP-1 agents Trulicity (dulaglutide) Victoza (liraglutide) Ozempic (semaglutide) Adlyxin (lixisenatide)	• Endocrine/Metabolic: increased amylase (Ozempic: 10-13%), hypoglycemia (Ozempic: 16%) • Cardiovascular: increased heart rate (Victoza: 34%) • Central Nervous System: headache (Victoza: 14%) • Gastrointestinal: increased lipase (Ozempic: 22-34%) nausea/vomitting (6-39%), diarrhea (9-21%), abdominal pain (Ozempic: 6-11%), constipation (Victoza 19%) • Local: injection site reaction (Victoza: 3-14%)	• Labs: HbA1c, trglyceride • Renal: renal fuction • Gastrointestinal: signs and symptoms of pancreatitis or gallbladder disease • Psyche (Victoza): worsening depression, suicidal ideation, change in behavior	None needed
DPP-4 Inhibitors Januvia (sitagliptin)	• Respiratory: nasopharyngitis (5%)	• Labs: HbA1c, serum glucose • Renal: renal function • Cardiovascular: signs and symptoms of heart failure	None needed
SGLT-2 Inhibitors Jardiance (empagliflozin) Farxiga (dapagilflozin)	• Gentourinary: urinary tract infection (UTI) (6-9%), • Respiratory: nasopharyngitis (6%)	• Labs: HbA1c, LDL • Renal: renal function • Volume status (blood pressure, hematocrit, electrolytes • Infections: genetic mycotic infections, UTI	None needed