This program applies to Medicaid. It is implemented with auto-grandfathering.

Step Therapy only applies to the MN Medicaid Preferred Drug List (PDL) preferred drugs: Farxiga, Invokana, and Jardiance.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

**FDA APPROVED INDICATIONS AND DOSAGE**

**FDA Indications**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Important limitations for use</th>
<th>Dosage and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invokana® canagliflozin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus</td>
<td>Not recommended in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis</td>
<td>Recommended starting dose is 100 mg per day; May be increased to 300 mg once daily in patients tolerating 100 mg dose who have an eGFR* (\geq 60) mL/min/1.73m(^2). Dose should remain 100 mg once daily in patients with eGFR of 45 to &lt;60 mL/min/1.73m(^2); Should not be initiated in patients with an eGFR &lt;45 mL/min/1.73m(^2)</td>
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<td><strong>Invokamet™</strong></td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are not adequately controlled on a regimen containing metformin or canagliflozin or in patients already being treated with both canagliflozin and metformin.</td>
<td>Not for treatment of type 1 diabetes or diabetic ketoacidosis.</td>
<td>Take twice daily with meals, with gradual dose escalation to reduce the gastrointestinal side effects due to metformin. Do not exceed a daily dose of metformin 2,000 mg and canagliflozin 300 mg; Invokamet is limited to canagliflozin 50 mg twice daily in patients with an eGFR of 45 to less than 60 mL/min/1.73 m². Assess renal function before initiating Invokamet. Do not initiate or continue Invokamet if creatinine levels are greater than or equal to 1.5 mg/dL for males or 1.4 mg/dL for females, or if eGFR is below 45 mL/min/1.73 m².</td>
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<td></td>
<td>Canagliflozin is indicated to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes and established cardiovascular disease.</td>
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<td><strong>Invokamet XR™</strong></td>
<td>Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both canagliflozin and metformin is appropriate.</td>
<td>Not recommended in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.</td>
<td>Up to 2 tablets once daily, individualize based on patient’s regimen.</td>
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<td>Canagliflozin is indicated to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes and established cardiovascular disease.</td>
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<tr>
<td><strong>Farxiga™</strong> dapagliflozin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus</td>
<td>Not recommended in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis</td>
<td>Recommended starting dose is 5 mg once daily, taken in the morning, with or without food. In patients tolerating Farxiga 5 mg once daily who require additional glycemic control, the dose can be increased to 10 mg once daily. Should not be initiated in patients with an eGFR &lt;60 mL/min/1.73m²</td>
</tr>
</tbody>
</table>
| **Jardiance®** empagliflozin| Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus  
To reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease | Not for treatment of type 1 diabetes or diabetic ketoacidosis | Recommended dose is 10 mg once daily, taken in the morning, with or without food. Dose may be increased to 25 mg once daily. Assess renal function before initiating Jardiance. Do not initiate Jardiance if eGFR is below 45 mL/min/1.73 m². Discontinue Jardiance if eGFR falls persistently below 45 mL/min/1.73 m² |
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<td>Segluromet™</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in</td>
<td>Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis</td>
<td>Maximum recommended dose is 7.5 mg ertugliflozin/1,000 mg metformin twice daily</td>
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<td>(ertugliflozin /</td>
<td>adults with type 2 diabetes mellitus who are not adequately controlled on</td>
<td></td>
<td>Assess renal function before initiating:</td>
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<td>metformin)</td>
<td>a regimen containing ertugliflozin or metformin, or in patients who are</td>
<td></td>
<td>• Do not use in patients with an estimated glomerular filtration rate (eGFR) below 30 mL/minute/1.73 m².</td>
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<td></td>
<td>already treated with both ertugliflozin and metformin</td>
<td></td>
<td>• Initiation is not recommended in patients with an eGFR of 30 to less than 60 mL/minute/1.73 m².</td>
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<td></td>
<td>• Continued use is not recommended in patients with an eGFR persistently between 30 and less than 60 mL/min/1.73 m².</td>
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<tr>
<td>Steglatro™ ertugliflozin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus</td>
<td>Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis</td>
<td>Recommended starting dose is 5 mg once daily, taken in the morning, with or without food.增加剂量至每日15 mg在耐受ertugliflozin且需要额外的血糖控制。</td>
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<td>Assess renal function before initiating ertugliflozin and periodically thereafter:</td>
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<td></td>
<td>• Do not use in patients with an estimated glomerular filtration rate (eGFR) below 30 mL/minute/1.73 m².</td>
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<td>• Initiation is not recommended in patients with an eGFR of 30 to less than 60 mL/minute/1.73 m².</td>
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<td>• Continued use is not recommended in patients with an eGFR persistently between 30 and less than 60 mL/min/1.73 m².</td>
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| **Synjardy® empagliflozin/metformin** | Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus who are not adequately controlled on a regimen containing empagliflozin or metformin, or in patients already being treated with both empagliflozin and metformin. Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. However, the effectiveness of Synjardy on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established. | Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.                                                                                                                         | Individualize the starting dose of SYNJARDY based on the patient’s current regimen.  
The maximum recommended dose is 12.5 mg empagliflozin/1000 mg metformin twice daily.  
Take twice daily with meals, with gradual dose escalation to reduce the gastrointestinal side effects due to metformin.  
Assess renal function before initiating SYNJARDY. Do not initiate or continue SYNJARDY if creatinine levels are greater than or equal to 1.5 mg/dL for males or 1.4 mg/dL for females, or if eGFR is below 45 mL/min/1.73 m². |
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<tbody>
<tr>
<td>Synjardy XR® empagliflozin/metformin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both empagliflozin and metformin hydrochloride is appropriate. Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. However, the effectiveness of Synjardy XR on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established.</td>
<td>Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis</td>
<td>Individualize the starting dose of Synjardy XR based on the patient’s current regimen. The maximum recommended total daily dose is 25 mg empagliflozin and 2000 mg metformin hydrochloride. Take once daily with a meal in the morning, with gradual dose escalation to reduce the gastrointestinal side effects due to metformin. Assess renal function before initiating. SYNJARDY XR is contraindicated in patients with an eGFR below 45 mL/min/1.73 m².</td>
</tr>
<tr>
<td>Xigduo XR™ dapagliflozin/metformin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both dapagliflozin and metformin is appropriate.</td>
<td>Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis</td>
<td>Individualize the starting dose based on the patient’s current regimen. Administer once daily in the morning with food. Do not exceed a daily dose of 10 mg dapagliflozin / 2000 mg metformin.</td>
</tr>
</tbody>
</table>

* estimated glomerular filtration rate

**CLINICAL RATIONALE**

Both the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) recommend metformin as the optimal non-insulin first-line drug in type II diabetes mellitus.8,9 Two-drug combinations should be used if metformin fails to achieve A1c target after approximately 3 months.8,9 The choice of the second agent (sulfonylurea, thiazolidinedione, dipeptidyl peptidase-4 inhibitors, sodium-glucose cotransporter 2 inhibitor, basal insulin, glucagon-like peptide 1 agonist) is based upon...
patient and drug characteristics, with the goal of improving glycemic control while minimizing side effects.\textsuperscript{8,9}

REFERENCES
12. Segluromet prescribing information. Merck Sharp & Dohme Corp. 12/2017
SGLT-2 Inhibitors and Combinations Step Therapy – 1-Step Edit

OBJECTIVE
The intent of the SGLT-2 (sodium-glucose co-transporter 2) Inhibitor Step Therapy (ST) program is to ensure appropriate selection of patients based on product labeling and/or clinical guidelines and/or clinical studies. Appropriate patients for SGLT-2 inhibitor therapy are those who are concurrently receiving or have tried an agent containing metformin or sulfonylurea, or insulin. The step edit allows continuation of therapy with one of these agents when a patient is currently receiving the requested agent. Patients without prerequisite agents in claims history or patients who are unable to take prerequisite agents due to documented intolerance, FDA labeled contraindication, or hypersensitivity will be reviewed when patient-specific documentation has been provided.

TARGET AGENTS
- Invokana® (canagliflozin)
- Invokamet™ (canagliflozin/metformin)
- Invokamet XR™ (canagliflozin/metformin ER)
- Farxiga™ (dapagliflozin)
- Jardiance® (empagliflozin)
- Segluromet™ (ertugliflozin/metformin)
- Steglatro™ (ertugliflozin)
- Synjardy® (empagliflozin/metformin)
- Synjardy XR® (empagliflozin/metformin ER)
- Xigduo XR™ (dapagliflozin/metformin)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Target Agents will be approved when ONE of the following is met:
1. The patient’s medication history includes use of one or more of the following antidiabetic agents; an agent containing metformin or sulfonylurea, or insulin in the past 90 days
   OR
2. There is documentation that the patient is currently using the requested SGLT-2 inhibitor containing product
   OR
3. The prescriber states the patient is using the requested agent AND is at risk if therapy is changed
   OR
4. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least one of the following agents: metformin, sulfonylurea, or insulin

Length of approval: 12 months

NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents.
Step Therapy Supplement Program
Summary

This program applies to Medicaid.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT
OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

2. BOTH of the following
   a. The patient’s medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
      i. Evidence of a paid claim(s) within the past 999 days
      OR
      ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days
   AND
   b. ONE of the following:
      i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
      OR
      ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)

OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria