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: Januvia, Janumet, Jentadueto, Kombiglyze XR, Onglyza, and Tradjenta.

**FDA APPROVED INDICATIONS AND DOSAGE**

**FDA Indications**\(^{2-11,13,14,15}\)

<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><strong>DPP-4 Inhibitors</strong></td>
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</tbody>
</table>
| Januvia® sitagliptin | Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus | • Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.  
• Has not been studied in patients with a history of pancreatitis. | 25 mg, 50 mg, 100 mg; 1 dose per day, maximum daily dose of 100 mg |
| Nesina® alogliptin | Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus | • Should not be used in patients with type 1 diabetes or diabetic ketoacidosis. | 6.25 mg, 12.5 mg, 25 mg; 1 dose per day, maximum daily dose of 25 mg |
| Onglyza® saxagliptin | Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus | • Should not be used in patients with type 1 diabetes or diabetic ketoacidosis. | 2.5 mg, 5 mg; 1 dose per day, maximum daily dose of 5 mg |
| Tradjenta® linagliptin | Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus | • Should not be used in patients with type 1 diabetes or diabetic ketoacidosis.  
• Has not been studied in combination with insulin | 5 mg; 1 dose per day, maximum daily dose of 5 mg |
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<tr>
<td><strong>DPP-4 Inhibitor Combinations</strong></td>
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</tr>
<tr>
<td>Glyxambi® empagliflozin/linagliptin</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 linagliptin is appropriate</td>
<td>• Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.</td>
<td>10 mg/5 mg, 25 mg/5 mg; one dose per day, maximum daily dose of 25 mg/5 mg</td>
</tr>
<tr>
<td>Janumet® sitagliptin/ metformin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus who are not adequately controlled on metformin or sitagliptin alone or in patients already being treated with the combination of sitagliptin and metformin</td>
<td>• Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.</td>
<td>50 mg/500 mg – 100 mg/1000 mg per day; two doses per day, maximum daily dose of 100 mg/2000 mg</td>
</tr>
<tr>
<td>Janumet® XR sitagliptin/ metformin (extended-release)</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 sitagliptin and metformin extended-release is appropriate</td>
<td>• Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. • Has not been studied in patients with a history of pancreatitis.</td>
<td>50 mg/500 mg, 50 mg/1000 mg, 100 mg/1000 mg; one dose per day, maximum daily dose of 100 mg/2000 mg</td>
</tr>
<tr>
<td>Jentadueto® linagliptin/ 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 linagliptin and metformin is appropriate</td>
<td>• Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. • Has not been studied in combination with insulin.</td>
<td>2.5 mg/500 mg, 2.5 mg/850 mg, 2.5 mg/1000 mg; two doses per day, maximum daily dose of 5 mg/2000 mg</td>
</tr>
<tr>
<td>Jentadueto XR® linagliptin/ metformin ER</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 linagliptin and metformin is appropriate</td>
<td>• Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. • Has not been studied in patients with a history of pancreatitis.</td>
<td>2.5 mg/1000 mg, 5 mg/2000 mg; one dose per day, maximum daily dose of 5 mg/2000 mg</td>
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<tr>
<td>Kazano™ alogliptin/ metformin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus</td>
<td>• Should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.</td>
<td>12.5 mg/500 mg, 12.5 mg/1000; two doses per day, maximum daily dose of 25 mg/2000 mg</td>
</tr>
<tr>
<td>Kombiglyze XR™ saxagliptin/ 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 saxagliptin and metformin is appropriate</td>
<td>• Should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. • Has not been studied in combination with insulin</td>
<td>2.5 mg/1000 mg, 5 mg/500 mg, 5 mg/1000 mg; one dose per day, maximum daily dose of 5 mg/2000 mg</td>
</tr>
<tr>
<td>Oseni™ alogliptin/ pioglitazone</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus</td>
<td>• Should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.</td>
<td>12.5 mg/15 mg, 12.5 mg/30 mg, 12.5 mg/45 mg, 25 mg/15 mg, 25 mg/30 mg, 25 mg/45 mg; one dose per day, maximum daily dose of 25 mg/45 mg</td>
</tr>
<tr>
<td>Qtern® dapagliflozin/ saxagliptin</td>
<td>Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin</td>
<td>• Not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. • Should only be used in patients who tolerate 10 mg dapagliflozin</td>
<td>10 mg/5 mg; one dose per day, maximum daily dose of 10 mg/5 mg</td>
</tr>
<tr>
<td>Steglujan™ Ertugliflozin/sitagliptin</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 ertugliflozin and sitagliptin is appropriate</td>
<td>• Not for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. • Has not been studied in patients with a history of pancreatitis</td>
<td>5mg/100 mg, 15mg/100 mg; one dose per day, maximum daily dose of 15 mg/100 mg</td>
</tr>
</tbody>
</table>
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.\textsuperscript{1,12} Two-drug combinations should be used if metformin fails to achieve A1c target after approximately 3 months.\textsuperscript{1,12} 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{1,12}

For additional clinical information see the Prime Therapeutics Formulary Chapters 4.6H: Combination Antidiabetic Agents and 4.6K: Dipeptidyl Peptidase-4 (DPP-4) Inhibitors.

REFERENCES

DPP-4 Inhibitors and Combinations Step Therapy – 1-Step Edit

OBJECTIVE
The intent of the DPP-4 (dipeptidyl peptidase-4) Inhibitors 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 DPP-4 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 one of the agents. 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
Glyxambi® (empagliflozin/linagliptin)
Januvia® (sitagliptin)
Janumet® (sitagliptin/metformin)
Janumet® XR (sitagliptin/metformin extended-release)
Jentadueto® (linagliptin/metformin)
Jentadueto XR® (linagliptin/metformin ER)
Kazano™ (alogliptin/metformin)
Kombiglyze XR™ (saxagliptin/metformin ER)
Nesina® (alogliptin)
Onglyza® (saxagliptin)
Oseni™ (alogliptin/pioglitazone)
Qtern® (dapagliflozin/saxagliptin)
Steglujan™ (ertugliflozin/sitagliptin)
Tradjenta® (linagliptin)

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 agent
   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.