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# Metoclopramide Nasal Spray

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## Related Coverage Resources

### INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

## Overview

This policy supports medical necessity review for **Gimoti™** (metoclopramide nasal spray).

## Coverage Policy

**Gimoti™ (metoclopramide nasal spray) for the relief of symptoms in adults with acute and recurrent diabetic gastroparesis is considered experimental, investigational or unproven.**

### Note:

*Gimoti is FDA approved for the relief of symptoms in adults with acute and recurrent diabetic gastroparesis; however, there is insufficient clinical efficacy data supporting this formulation for this use.*

## Conditions Not Covered

Gimoti (metoclopramide nasal spray) is considered experimental, investigational or unproven for ANY other use.

## Background

### Overview

Gimoti is a dopamine-2 (D2) antagonist indicated for the relief of symptoms in adults with acute and recurrent diabetic gastroparesis.<sup>1</sup>

### Limitations of Use:

Gimoti is not recommend for use in:

- Pediatric patients due to the risk of tardive dyskinesia (TD) and other extrapyramidal symptoms as well as the risk of methemoglobinemia in neonates.
- Moderate or severe hepatic impairment (Child-Pugh B or C), moderate or severe renal impairment (creatinine clearance less than 60 mL/minute), and patients concurrently using strong CYP2D6 inhibitors due to the risk of increased drug exposure and adverse reactions.

### Clinical Efficacy

Gimoti was approved using the 505(b)(2) New Drug Application approval pathway. The efficacy portion of the submission relied upon previous evaluations of oral metoclopramide. One unpublished Phase III study provides information on the efficacy of Gimoti in diabetic gastroparesis. It is notable that the FDA-approved strength of Gimoti (15 mg) differs from the strength of Gimoti (10 mg) used in the study below.

**Study 1** (unpublished) [n = 205] was a Phase III, multicenter, placebo-controlled, 4-week study which evaluated the efficacy of a lower dose of Gimoti (10 mg) in women with diabetic gastroparesis.<sup>2-4</sup>

The available data with Gimoti have several limitations. The data are not fully published and details regarding efficacy endpoints are very limited. Demonstration of efficacy relies on a post hoc analysis of a subgroup of patients; even in this selected subgroup, efficacy was not established at all time points. Additionally, the study dose used (10 mg), population (females only), and duration (only studied up to 4 weeks) are not reflective of the approved dose and labeled indication. Data are incomplete regarding baseline and concomitant medication use, therefore, it is unclear whether patients were using medications known to cause gastroparesis (e.g., glucagon-like peptide-1 [GLP-1] receptor agonists) or whether these were matched between treatment groups. A different gastroparesis symptom scale was used than what had been used in Phase II studies. Phase II data used a modified version of the Gastroparesis Cardinal Symptom Index – Daily Diary (GCSI-DD), evaluating nausea, bloating, early satiety, upper abdominal pain, based on discussion with the FDA.<sup>5</sup> The GCSI-DD used in the Phase II study ranges from 0 (no symptoms) to 5 (very severe), with a 1-point change considered clinically meaningful. It is unclear why the GSA was selected for the Phase III study rather than the GCSI-DD and what constitutes a meaningful change on this scale.

### Disease Overview

It is estimated that 34.2 million children and adults in the US have diabetes, which is 10.5% of the population.<sup>6,7</sup> Type 2 diabetes is the most common form of diabetes in the US accounting for 90% to 95% of cases, while type 1 diabetes is estimated to occur in approximately 5% of the cases. Microvascular complications associated with diabetes include chronic kidney disease, retinopathy, and neuropathy.<sup>8</sup> GI neuropathies may occur and can involve any portion of the GI tract, manifesting as esophageal dysmotility, gastroparesis, constipation diarrhea, and fecal incontinence. Based on epidemiological data, the risk of diabetic gastroparesis is estimated to be approximately 5% in patients with type 1 diabetes and 1% in patients with type 2 diabetes.<sup>9</sup> There is also a noted female predominance: diabetic gastroparesis rates have been reported as 9.6 per 100,000 individuals in males and 37.8 per 100,000 individuals in females.<sup>10</sup> Diabetic gastroparesis has been associated with other complications including retinopathy, neuropathy, and nephropathy, as well as poor glycemic control. Symptoms include nausea/vomiting, early satiety, bloating, and abdominal pain.<sup>9</sup> The American Diabetes Association (ADA) Standards of Care (2020) note that gastroparesis should be suspected in individuals with erratic glycemic control or with upper GI symptoms without another identified cause (e.g., gastric outlet obstruction, peptic ulcer disease).<sup>8</sup> The diagnostic gold standard for gastroparesis is measurement of gastric emptying using scintigraphy of digestible solids for 15-minute intervals over a 4-hour period after eating.<sup>8,9</sup>

## Guidelines

Gimoti is not specifically addressed in clinical practice guidelines, although metoclopramide is addressed more broadly. In the ADA Standards of Care (2020), it is noted that treatment for diabetic gastroparesis is very challenging.<sup>8</sup> Low-fiber, low-fat diets and small, frequent meals with a greater proportion of liquid calories may be useful. Additionally, medications which negatively impact GI motility should be withdrawn, including opioids, anticholinergics, tricyclic antidepressants, GLP-1 receptor agonists, Symlin® (pramlintide acetate for injection), and possibly dipeptidyl peptidase-4 inhibitors. Metoclopramide is the only medication approved by the FDA for treatment of gastroparesis. However, the level of evidence regarding benefit is noted to be weak. Given the risk for serious AEs, use of metoclopramide is not recommended beyond 12 weeks by the FDA or the European Medicines Agency.

## References

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