Dear Healthcare Professional,

At MPR, we strive to bring you important drug information in a concise and timely fashion. In keeping with this goal, we are pleased to bring you this PRESCRIBING ALERT announcing the FDA approval of a new product—Metozolv™ ODT (metoclopramide HCl) from Salix Pharmaceuticals, Inc.—for short-term therapy in adults with refractory GERD† and for relief of symptoms of diabetic gastroparesis.¹

Metozolv ODT is the first available orally disintegrating metoclopramide tablet.¹,² Metozolv ODT employs a unique delivery system compared with traditional metoclopramide, Zydis® technology, which combines the reliability of traditional metoclopramide with the convenience of a tablet that rapidly⁵ melts on the tongue.³ Two studies were conducted to assess patient preference for an orally disintegrating tablet compared with a conventional tablet. The majority of patients—91%—said that the use of orally disintegrating tablets was convenient or very convenient.⁴,c Nearly half of patients—42%—favored the ease of compliance with orally disintegrating tablets vs 7% who favored conventional tablets.⁵,d

In a bioequivalence study, Metozolv ODT was bioequivalent to Reglan® (metoclopramide) as determined by the 90% confidence interval for area under the curve and maximum concentration.¹,²

Adverse reactions, especially those involving the nervous system, may occur after stopping the use of Metozolv ODT. Patients may experience a withdrawal period after stopping that could include dizziness, nervousness, and/or headaches.¹

All prescription metoclopramide products, including Metozolv™ ODT, have a Boxed Warning. The Boxed Warning is below.

WARNING: TARDIVE DYSKINESIA

Treatment with metoclopramide can cause tardive dyskinesia, a serious movement disorder that is often irreversible. The risk of developing tardive dyskinesia increases with duration of treatment and total cumulative dose.

Metoclopramide therapy should be discontinued in patients who develop signs or symptoms of tardive dyskinesia. There is no known treatment for tardive dyskinesia. In some patients, symptoms may lessen or resolve after metoclopramide treatment is stopped.

Treatment with metoclopramide for longer than 12 weeks should be avoided in all but rare cases where therapeutic benefit is thought to outweigh the risk of developing tardive dyskinesia.

— Refractory GERD is symptomatic, documented gastroesophageal reflux that fails to respond to conventional therapy.
— Metozolv ODT disintegrates on the tongue in a median of 53.5 seconds (mean ± standard deviation, 76.8 ± 110.6 seconds).¹
— In a multicenter, observational, cross-sectional study of 734 men and women aged 18 years or older with lansoprazole orally disintegrating tablets.¹
— In a multicenter, open-label, sequential study of 60 men and women aged 18 years or older with carbidopa-levodopa tablets.⁵

Zydis is a registered trademark of Catalent Pharma Solutions.

(Please see Important Safety Information on the reverse side)
More information about the use of Metozolv ODT is available in the current edition of MPR.

For your reference, please see accompanying full Prescribing Information for METOZOLV ODT, including BOXED WARNING.

Sincerely,

Grace L. McBride
Editorial Director
MPR Custom Programs

REFERENCES
2. Data on File, Salix Pharmaceuticals, Inc.
3. Data on File, Catalent Pharma Solutions.

Important Safety Information

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METOZOLV™ ODT (metoclopramide HCl) is indicated as short-term therapy for adults with symptomatic, documented gastroesophageal reflux disease (GERD) who fail to respond to conventional therapy and for the relief of symptoms associated with acute and recurrent diabetic gastroparesis (diabetic gastric stasis) in adults. Therapy should not exceed 12 weeks in duration. METOZOLV ODT is contraindicated in patients with intestinal obstruction, hemorrhage, or perforation; pheochromocytoma; known sensitivity or intolerance to metoclopramide; epilepsy; or are receiving concomitant medications with extrapyramidal reactions. METOZOLV ODT should be used with caution in patients showing acute dystonic reactions, drug-induced Parkinsonism, or other extrapyramidal symptoms; neuroleptic malignant syndrome; with a prior history of depression; hypertension; congestive heart failure and ventricular arrhythmia. Patients may experience withdrawal symptoms after stopping the use of METOZOLV ODT.

In clinical studies, the most frequently reported adverse events (≥2% occurrence) were headache, nausea, fatigue, somnolence and vomiting.

Please see accompanying full Prescribing Information for METOZOLV ODT, including BOXED WARNING.
Company: Salix Pharmaceuticals, Inc.
Pharmacologic Class: Prokinetic
Active Ingredient: Metoclopramide (as monohydrochloride monohydrate) 5 mg, 10 mg in orally disintegrating tablets; Mint flavor
Indications: Symptomatic documented GERD. Symptomatic relief in acute and recurrent diabetic gastroparesis.
Adults: Take on empty stomach. GERD: 10-15 mg up to 4 times daily 30 minutes before meals and at bedtime up to 12 weeks. Diabetic gastroparesis: 10 mg 30 minutes before meals and at bedtime for 2 to 8 weeks. Renal impairment: reduce dose. ODT: Dissolve on tongue and swallow with or without liquid.
Children: Not recommended.
Contraindications: When stimulation of GI motility may be dangerous (eg, obstruction, perforation, or hemorrhage). Pheochromocytoma. Epilepsy. Concomitant drugs which may cause extrapyramidal reactions (eg, phenothiazines, haloperidol).
Interactions: Hypertensive crisis with MAOIs. Antagonized by anticholinergics and narcotics. Monitor insulin use; may diminish gastric and accelerate intestinal absorption of drugs or food. Avoid concomitant use of antidepressants, antipsychotics or neuroleptics associated with extrapyramidal symptoms or NMS.
Adverse Reactions: Restlessness, drowsiness, fatigue, extrapyramidal effects, parkinsonism, tardive dyskinesia, arrhythmias, motor restlessness, neuroleptic malignant syndrome, endocrine disturbances, hypo- or hypertension, arrhythmias, GI upset, hepatotoxicity (rare), incontinence, neutropenia, allergic reactions, visual disturbances.
How Supplied: Tabs 5 mg — 10 ct/card; 10 cards/box
10 mg — 10 ct/card; 10/box

Now available in orally disintegrating tablets

The first available orally disintegrating metoclopramide tablet
- Metozolv ODT features Zydis® technology
- Unique delivery system compared with traditional metoclopramide
- First available orally disintegrating metoclopramide tablet
- Rapidly melts on the tongue
- Makes it easy for people with difficulty swallowing to take their medication

Zydis is a registered trademark of Catalent Pharma Solutions.

Please see accompanying full Prescribing Information for METOZOLV ODT, including BOXED WARNING.

(continued on back)
The first available orally disintegrating metoclopramide tablet (continued)

- The convenience of orally disintegrating tablets appeals to patients\(^6\)
- Can be taken anywhere without liquid\(^2\)
- Your patients can now take Metozolv ODT in situations where they are not able to take regular metoclopramide tablets\(^7\)
- Does not require additional liquid that may add to gastric volume\(^2\)

Pharmacokinetics

- In a bioequivalence study, a single 10 mg dose of Metozolv ODT was compared to a 10 mg dose of metoclopramide tablets\(^2\)
- The randomized, two-arm, two-way crossover study was completed in 44 healthy adult (male and female) fasted subjects\(^2\)
- Metozolv ODT was bioequivalent to traditional metoclopramide tablets as determined by the 90% confidence interval for area under the curve and maximum concentration\(^2\)

Efficacy

- Numerous clinical studies have proven the efficacy of metoclopramide in diabetic gastroparesis and refractory GERD\(^8\text{-}14,b\)
- Metoclopramide has been clinically proven to help alleviate symptoms of diabetic gastroparesis\(^8\text{-}12\)
- Metozolv ODT treats the symptoms of diabetic gastroparesis and refractory GERD\(^2\)

Safety

- Safety profile equivalent to metoclopramide tablets\(^2\)
- Pregnancy category B\(^3\)

Approximately 35% to 40% of people are affected by GERD\(^15\)

- 20% of GERD patients continue to experience unmanageable reflux symptoms despite twice-daily proton pump inhibitor (PPI) therapy\(^15\)
- Metoclopramide decreases episodes of daytime and nighttime heartburn and vomiting\(^15\)

Gastroparesis occurs in up to 12% of patients with diabetes\(^16,17\)

- Diabetes is the second leading cause of gastroparesis\(^18\)
- 27% to 58% of people with type 1 diabetes exhibit delayed gastric emptying\(^18\)
- 30% of people with type 2 diabetes exhibit delayed gastric emptying\(^18\)
- Metoclopramide has been shown to increase the speed at which food moves through the digestive system\(^8\text{-}12\)

Please see accompanying full Prescribing Information for METOZOLV ODT, including BOXED WARNING.

(continued on next page)
Can your patients’ treatment be more convenient?

- Seven clinical studies demonstrate that patients prefer orally disintegrating tablets
  - 91% of patients said that the use of orally disintegrating tablets was convenient or very convenient
  - 42% of patients favored the ease of compliance with the dosing schedule of orally disintegrating tablets versus 7% who favored conventional tablets
  - 75% of patients who have difficulty swallowing preferred orally disintegrating tablets to conventional tablets

Metozolv ODT features Zydis® technology

- Zydis® technology allows Metozolv ODT to rapidly melt on the tongue
  - Thanks to Zydis® technology, patients can conveniently take Metozolv ODT when liquid is not available or if they have difficulty swallowing
  - Metozolv ODT, featuring Zydis® technology, works by releasing medicine in the mouth that travels with saliva, as it is swallowed, into the digestive system
  - 75% of subjects expressed a preference for the orally disintegrating Zydis® technology formulation compared with a conventional tablet

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Important Safety Information (continued)

patients with intestinal obstruction, hemorrhage, or perforation; pheochromocytoma; known sensitivity or intolerance to metoclopramide; epilepsy; or are receiving concomitant medications with extrapyramidal reactions. METOZOL V ODT should be used with caution in patients showing acute dystonic reactions, drug-induced Parkinsonism, or other extrapyramidal symptoms; neuroleptic malignant syndrome; with a prior history of depression; hypertension; congestive heart failure and ventricular arrhythmia. Patients may experience withdrawal symptoms after stopping the use of METOZOL V ODT.

In clinical studies, the most frequently reported adverse events (≥2% occurrence) were headache, nausea, fatigue, somnolence and vomiting.

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REFERENCES