NEW PACKAGING,
SAME RYBELSUS®

RYBELSUS® is making the switch from
blister packs to bottles in Fall of 2021

Indications and Usage

RYBELSUS® (semaglutide) tablets 7 mg or 14 mg is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.

Limitations of Use

- RYBELSUS® is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans
- RYBELSUS® has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis
- RYBELSUS® is not indicated for use in patients with type 1 diabetes

Important Safety Information

WARNING: RISK OF THYROID C-CELL TUMORS

- **In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether RYBELSUS® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined**
- **RYBELSUS® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of RYBELSUS® and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with RYBELSUS®**

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Please see additional Important Safety Information throughout and click https://www.novo-pi.com/rybelsus.pdf for Prescribing Information, including Boxed Warning.

RYBELSUS®
semaglutide tablets 7mg | 14mg

RYBELSUS® is changing from

BLISTER PACKS TO BOTTLES

Storage instructions for RYBELSUS® to work as planned:

Store tablets in the closed RYBELSUS® bottle until ready to take one

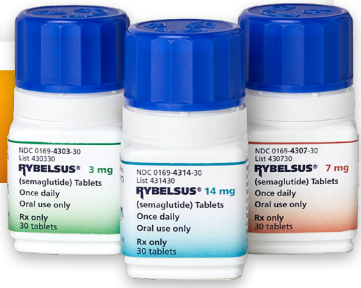
Do not use a pill organizer or other container to store RYBELSUS® tablets

Swallow tablet whole. Do not cut, crush, or chew

Important note: The RYBELSUS® blue cap is equipped with a drying agent to help protect the tablets from moisture, which helps preserve RYBELSUS®. Tablets should be kept in the RYBELSUS® bottle with the blue cap whenever the patient is not taking one.

Store at room temperature between 68°F–77°F (20°C–25°C).
Store in a dry place away from moisture.

KEEPING THE BLUE CAP TIGHT
helps the pills work right



Important Safety Information (cont'd)

Contraindications

- RYBELSUS® is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2), and in patients with a prior serious hypersensitivity reaction to semaglutide or to any of the excipients in RYBELSUS®. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with RYBELSUS®

Warnings and Precautions

- **Risk of Thyroid C-Cell Tumors:** Patients should be further evaluated if serum calcitonin is measured and found to be elevated or thyroid nodules are noted on physical examination or neck imaging
- **Pancreatitis:** Has been reported in clinical trials. Observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, discontinue RYBELSUS® and initiate appropriate management; if confirmed, do not restart RYBELSUS®

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RYBELSUS® semaglutide tablets 7mg | 14mg

SAME SUPERIOR EFFICACY

in 2 separate head-to-head studies

Superior A1C reduction[1]

RYBELSUS® vs Januvia®[1,2]

Added to metformin with or without sulfonylurea

26-week primary endpoint

-1.3% with RYBELSUS® 14 mg (Baseline: 8.3%, *P*<0.001)

-1.0% with RYBELSUS® 7 mg (Baseline: 8.4%, *P*<0.001)

-0.8% with Januvia® 100 mg (Baseline: 8.3%)

Superior A1C reduction[1]

RYBELSUS® vs Jardiance®[1,3]

Added to metformin

26-week primary endpoint

-1.3% with RYBELSUS® 14 mg (Baseline: 8.1%, *P*<0.001)

-0.9% with Jardiance® 25 mg (Baseline: 8.1%)

[a]**PIONEER 3: Head-to-head vs Januvia®[1,2]**
In a double-blind, double-dummy trial with a primary endpoint of mean change in A1C from baseline to 26 weeks, 1864 patients with type 2 diabetes on metformin alone or metformin with a sulfonylurea were randomized to RYBELSUS® 3 mg (n=466), RYBELSUS® 7 mg (n=465), RYBELSUS® 14 mg (n=465), or Januvia® 100 mg (n=467), all once daily.

[b]**PIONEER 2: Head-to-head vs Jardiance®[1,3]**
In an open-label trial with a primary endpoint of mean change in A1C from baseline to 26 weeks, 822 patients with type 2 diabetes on metformin were randomized to RYBELSUS® 14 mg (n=411) or Jardiance® 25 mg (n=410), both once daily.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

- **Diabetic Retinopathy Complications:** In a pooled analysis of glycemic control trials with RYBELSUS®, patients reported diabetic retinopathy related adverse reactions during the trial (4.2% with RYBELSUS® and 3.8% with comparator). In a 2-year trial with semaglutide injection involving patients with type 2 diabetes and high cardiovascular risk, more events of diabetic retinopathy complications occurred in patients treated with semaglutide injection (3.0%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline than among patients without a known history of diabetic retinopathy.
  Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy

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RYBELSUS®
semaglutide tablets 7mg | 14mg

SAME ONCE-DAILY ROUTINE

RYBELSUS® is a once-daily tablet that must be taken[1]:

On an **empty stomach** when the patient first wakes up

With a sip of plain water
(no more than 4 oz)

At least 30 minutes before the first food, beverage, or other oral medications of the day

- Waiting less than 30 minutes or taking with food, beverages (other than plain water), or other oral medications will lessen the effect of RYBELSUS® by decreasing its absorption. Waiting more than 30 minutes to eat may increase the absorption of RYBELSUS®
- Swallow tablets whole. Do not cut, crush, or chew
- If a patient misses a dose of RYBELSUS®, they should skip the missed dose and go back to their regular schedule

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

- **Hypoglycemia:** Patients receiving RYBELSUS® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogue) or insulin. Inform patients using these concomitant medications of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia
- **Acute Kidney Injury:** There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis, in patients treated with GLP-1 receptor agonists, including semaglutide. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function when initiating or escalating doses of RYBELSUS® in patients reporting severe adverse gastrointestinal reactions
- **Hypersensitivity:** Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported in patients treated with RYBELSUS®. If hypersensitivity reactions occur, discontinue use of RYBELSUS®, treat promptly per standard of care, and monitor until signs and symptoms resolve. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 receptor agonist

Adverse Reactions

- The most common adverse reactions, reported in ≥5% of patients treated with RYBELSUS® are nausea, abdominal pain, diarrhea, decreased appetite, vomiting and constipation

SAME GRADUAL DOSE ESCALATION

Start patients on RYBELSUS® 3 mg once daily for 30 days, then increase the dose[1]

STARTING DOSE[1]

3 mg	Start RYBELSUS® with 3 mg once daily for 30 days

MAINTENANCE DOSES[1]

7 mg	After 30 days on the 3 mg dose, increase the dose to 7 mg once daily
14 mg	If additional glycemic control is needed after at least 30 days on the 7 mg dose, the dose can be increased to 14 mg once daily

The 3 mg dose is intended for treatment initiation and is not effective for glycemic control

Gradual dose escalation is designed to help patients adjust to therapy.

Provide patients with what they need to get started on RYBELSUS® with the digital Patient Starter Kit on the RYBELSUS® HCP website

Important Safety Information (cont'd)

Drug Interactions

- When initiating RYBELSUS®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia
- RYBELSUS® delays gastric emptying and has the potential to impact the absorption of other oral medications. Closely follow RYBELSUS® administration instructions when coadministering with other oral medications and consider increased monitoring for medications with a narrow therapeutic index, such as levothyroxine

Use in Specific Populations

- **Pregnancy:** Available data with RYBELSUS® are not sufficient to determine a drug-associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Based on animal reproduction studies, there may be risks to the fetus from exposure to RYBELSUS®. Use only if the potential benefit justifies the potential risk to the fetus

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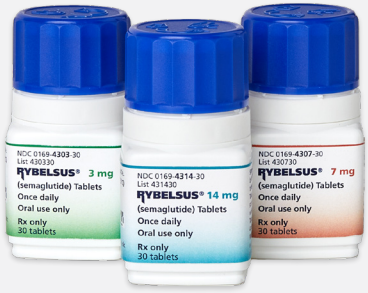
RYBELSUS® semaglutide tablets 7mg | 14mg

KEEPING THE BLUE CAP TIGHT

helps the pills work right

The **new RYBELSUS® bottle cap** is specifically designed to keep tablets protected from moisture, so they can work as intended to lower blood sugar.



RYBELSUS® 3 mg
NDC:
0169-4303-30
Package Presentation:
30 x 3 mg per bottle

RYBELSUS® 7 mg
NDC:
0169-4307-30
Package Presentation:
30 x 7 mg per bottle

RYBELSUS® 14 mg
NDC:
0169-4314-30
Package Presentation:
30 x 14 mg per bottle

PAY AS LITTLE AS **$10**

Patients could pay as little as $10 for a 30-day prescription[a]

Patients can text READY to 21848[b] to get the Savings Offer and helpful tips on how to start and stay on RYBELSUS®

[a]Commercially insured patients only. Eligibility and other restrictions apply.
[b]Message and data rates may apply. Tell patients to check with their mobile service provider. See Terms and Conditions of Use at RYBELSUS.com.

Important Safety Information (cont'd)

Use in Specific Populations (cont'd)

- **Lactation:** There are no data on the presence of semaglutide in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the unknown potential for serious adverse reactions in the breastfed infant due to the possible accumulation of salcaprozate sodium (SNAC), an absorption enhancer in RYBELSUS®, from breastfeeding and because there are alternative formulations of semaglutide that can be used during lactation, advise patients that breastfeeding is not recommended during treatment with RYBELSUS®
- Discontinue RYBELSUS® in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide
- **Pediatric Use:** Safety and efficacy of RYBELSUS® have not been established in pediatric patients (younger than 18 years)

References: 1. RYBELSUS® [package insert]. Plainsboro, NJ: Novo Nordisk Inc; April 2021. **2.** Rosenstock J, Allison D, Birkenfeld AL, et al. Effect of additional oral semaglutide vs sitagliptin on glycated hemoglobin in adults with type 2 diabetes uncontrolled with metformin alone or with sulfonylurea: the PIONEER 3 randomized clinical trial. *JAMA*. 2019;321(15):1466-1480. **3.** Rodbard HW, Rosenstock J, Canani LH, et al. Oral semaglutide versus empagliflozin in patients with type 2 diabetes uncontrolled on metformin: the PIONEER 2 trial. *Diabetes Care*. 2019;42(12):2272-2281.

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