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 or for the treatment of patients with diabetic ketoacidosis

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®

Please see additional Important Safety Information throughout. Please see inside pocket for Prescribing Information, including Boxed Warning.
Getting patients started on RYBELSUS®

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

**STARTING DOSE**

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

**MAINTENANCE DOSES**

- 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 their therapy¹

Proper administration is important

It’s important to remind your patients to take RYBELSUS® the right way, every day.

**RYBELSUS® IS A ONCE-DAILY ORAL TABLET THAT MUST BE TAKEN¹:**

- 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®

**Warnings and Precautions**

**Contraindications**

- RYBELSUS® is not indicated for use in patients with type 1 diabetes
- RYBELSUS® has not been studied in patients with a history of pancreatitis or for the treatment of patients with diabetic ketoacidosis

**Important Safety Information**

- It is unknown whether treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether semaglutide-induced rodent thyroid C-cell tumors has not thyroid carcinoma (MTC), in humans as human relevance of syndrome type 2 (MEN 2), and in patients with known or in patients with Multiple Endocrine Neoplasia or family history of medullary thyroid carcinoma (MTC)

**Blood Glucose Monitoring**

- Thyroid C-cell tumors, including medullary thyroid carcinomas, have been reported in diabetic patients treated with some medications that contain the hormone GLP-1, including RYBELSUS®

**Hypoglycemia**

- The risk of hypoglycemia is increased when semaglutide is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Patients may reduce the risk of hypoglycemia in this setting

**Diabetic Retinopathy Complications:**

- In a 2-year trial with patients reported diabetic retinopathy related adverse events in 1.2% of patients with a history of diabetic retinopathy at baseline than among patients without a known history of diabetic retinopathy.

**Pharmacokinetics**

- The peak plasma concentration of semaglutide after administration of 3 mg of RYBELSUS® is about 7 hours, and its elimination half-life is about 11 days in patients with type 2 diabetes

**Pharmacology**

- RYBELSUS® is a GLP-1 receptor agonist that is indicated to improve glycemic control in adults with type 2 diabetes

**Additional Important Safety Information**

- To the Possibilities
- The World’s First
Proper storage

- Patient should keep tablet in the blister pack until they are ready to take it.¹
- Push tablet out of the blister. Do not cut from the packaging.¹
- Swallow tablet whole. Do not cut, crush, or chew.¹

Important Safety Information

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 known hypersensitivity to semaglutide or to any of the components in 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®

Product information

Patients starting on RYBELSUS® may have received a starter kit containing a 30-day supply of the 3 mg dose along with a prescription for a 7 mg fill specifying use for at least 30 days. Once the patient has completed the pack of the 3 mg dose and the escalation to the 7 mg dose, their healthcare provider may decide to either refill the 7 mg or increase their dose to 14 mg, if additional glycemic control is needed.

### Dosage Form

<table>
<thead>
<tr>
<th>Strength</th>
<th>Trade Pack</th>
<th>NDC Number</th>
<th>SIG</th>
<th>Notes to Pharmacy</th>
<th>Dispense Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mg</td>
<td>Tablet</td>
<td>00169-4303-13</td>
<td>One pill daily on an empty stomach with up to 4 oz plain water. Swallow whole. Wait 30 min to eat, drink, or take other oral meds.</td>
<td>30 tablets (no refills needed for this dose)</td>
<td></td>
</tr>
<tr>
<td>7 mg</td>
<td>Tablet</td>
<td>00169-4307-13</td>
<td>One pill daily on an empty stomach with up to 4 oz plain water. Swallow whole. Wait 30 min to eat, drink, or take other oral meds.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 mg</td>
<td>Tablet</td>
<td>00169-4314-13</td>
<td>One pill daily on an empty stomach with up to 4 oz plain water. Swallow whole. Wait 30 min to eat, drink, or take other oral meds.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Important Safety Information

**Warnings and Precautions**
- 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.
Frequently asked questions

Patients taking RYBELSUS® may have questions. Below are some of the questions they may ask, with helpful answers you can provide.

Why do I need to take RYBELSUS® on an empty stomach?

Taking RYBELSUS® with food, beverages (other than plain water), or other oral medication interferes with its absorption in the stomach. This will lessen its effectiveness.¹

How strict must I be about taking RYBELSUS® with 4 oz of water?

Because of the way RYBELSUS® is absorbed, you should take it with no more than 4 oz of plain water. Anything more than that could impact the amount of RYBELSUS® that is absorbed.¹

Do I have to take RYBELSUS® in the morning, or at the same time every day?

For RYBELSUS® to work as intended, taking it on an empty stomach is what is important, which in most cases is when you first wake up.¹

What if I miss a dose of RYBELSUS®?

If you miss a dose, the missed dose should be skipped and the next dose should be taken the following day.¹

Can I take more than one RYBELSUS® pill at once?

No, just take 1 pill of the prescribed dose of RYBELSUS®. As a reminder, taking two 7 mg RYBELSUS® tablets to achieve a 14 mg dose is not recommended.¹

Can I take other pills with RYBELSUS®?

Because of the way RYBELSUS® is absorbed, the pill is intended to sit in the stomach by itself.² Taking multiple pills at the same time as RYBELSUS® may impact absorption and is not recommended.³

How should shift workers incorporate RYBELSUS® into their routine?

Talk to your doctor and/or healthcare provider about how RYBELSUS® can be incorporated into your daily routine. People with irregular schedules may take it upon waking on an empty stomach, regardless of the time.¹

Important Safety Information

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

- **Hypoglycemia:** The risk of hypoglycemia is increased when RYBELSUS® is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Patients may require a lower dose of the secretagogue or insulin to reduce the risk of hypoglycemia in this setting.

Please see Important Safety Information throughout. Please see inside pocket for Prescribing Information, including Boxed Warning.
Help patients save on RYBELSUS®

Your eligible patients may obtain a digital savings offer via either text message or an online download.

**PAY AS LITTLE AS $10 FOR A 30-DAY PRESCRIPTION.**

TO GET YOUR OFFER:
Text® READY to 21848 or go to SaveOnR.com

*Commercially insured patients only. Eligibility and other restrictions apply.
*Message and data rates may apply. Check with your mobile service provider.
*Message frequency will be based on your selection. Text HELP to 21848 for help.
Text STOP to 21848 to quit. See Terms of Use & Conditions at RYBELSUS.com.

Call 1-888-401-0112 if you need assistance processing the RYBELSUS® Savings Card. Available Monday through Friday, 8:00 am–8:00 pm ET

**Pharmacy Connect**
Help line for the RYBELSUS® Savings Card

**Rybel Suz® Connect Program**
Patients can sign up for text messages with reminders, helpful information, and motivational messages! Text® READY to 21848 to get started

**Rybel Suz®. com**
Provides patients with more tips on incorporating RYBELSUS® into their wake-up routine, product information, and customer support

**1-833-ASK-A-CDE**
Offers patient one-on-one live support from a Certified Diabetes Educator, if they need it. Call 1-833-ASK-A-CDE (275-2233) Monday through Friday, 9:00 am–6:00 pm ET

*Message and data rates may apply. Check with your mobile service provider. See Terms of Use & Conditions at RYBELSUS.com.

**All RYBELSUS® support program resources are available in Spanish.**

**Support tools can help patients with their treatment**

Patients may ask you about support services available to them when they are taking RYBELSUS®. Included below are the different resources that are available, and how patients can access them.

- **RYBELSUS® Connect Program**
- **RYBELSUS®. com**
- **1-833-ASK-A-CDE**

**General Instructions for Pharmacists:**
If you receive a rejection due to a Managed Care Restriction (e.g., PA, Step Edit, or NDC Block) and the pharmacy system allows, continue processing with valid Other Coverage Code (OCC) of 03 or 08. Each pharmacy may have its own set of practice management systems and procedures. If the General Instructions do not apply, contact the RYBELSUS® Pharmacy Connect team.

PA=prior authorization.

Please see Important Safety Information throughout.
Please see inside pocket for Prescribing Information, including Boxed Warning.

RYBELSUS® is a registered trademark of Novo Nordisk A/S.
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All other trademarks, registered or unregistered, are the property of their respective owners.
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Common side effects with RYBELSUS®

- The most common side effects with RYBELSUS® may include nausea, stomach (abdominal) pain, diarrhea, decreased appetite, vomiting, and constipation. Nausea, vomiting, and diarrhea are most common during dose escalation.
- If a patient experiences nausea while taking RYBELSUS®, advise them to talk to their healthcare provider.

No dosage adjustment recommended for:
- Hepatic impairment

In patients with different degrees of hepatic impairment, no clinically relevant change in semaglutide pharmacokinetics (PK) was observed.

- Patients aged ≥65

No overall differences in safety or efficacy were detected between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

- Renal impairment

In patients with renal impairment, including end-stage renal disease (ESRD), no clinically relevant change in semaglutide PK was observed.

Please see Important Safety Information below regarding acute kidney injury.

Here are some general nausea tips you can share with your patients that may be helpful:
- Slowly eat smaller, more frequent meals
- Eat foods that are light and bland, like saltine crackers or plain bread
- Avoid fried, greasy, or sweet foods
- Drink clear or ice-cold drinks

Important Safety Information

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.

Important Safety Information

Warnings and Precautions
- 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 with GLP-1 receptor agonists, including semaglutide. 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.
In separate head-to-head studies
Superior A1C reduction vs 2 of the most-prescribed oral antidiabetic therapies, Januvia® and Jardiance® 1,4,a,b

26-WEEK PRIMARY ENDPOINT

<table>
<thead>
<tr>
<th>RYBELSUS® vs Januvia® (p&lt;0.001 for both comparisons)</th>
<th>RYBELSUS® vs Jardiance® (p&lt;0.001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1.3% with RYBELSUS® 14 mg (Baseline: 8.3%)</td>
<td>-1.3% with RYBELSUS® 14 mg (Baseline: 8.1%)</td>
</tr>
<tr>
<td>-1.0% with RYBELSUS® 7 mg (Baseline: 8.4%)</td>
<td>-0.9% with Jardiance® 25 mg (Baseline: 8.1%)</td>
</tr>
<tr>
<td>-0.8% with Januvia® 100 mg (Baseline: 8.3%)</td>
<td></td>
</tr>
</tbody>
</table>

Study Designs

1 PIONEER 3: Head-to-head vs Januvia®
In a double-blind, double-dummy trial with a primary endpoint of change in A1C at 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.1,5

2 PIONEER 2: Head-to-head vs Jardiance®
In an open-label trial with a primary endpoint of change in A1C at 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.1,6

Important Safety Information

Drug Interactions

• The risk of hypoglycemia may be lowered by a reduction in the dose of concomitantly administered secretagogues or insulin
• RYBELSUS® delays gastric emptying and has the potential to impact the absorption of other oral medications. Closely follow RYBELSUS® administration instructions when co-administering 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

Use in Specific Populations

• 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)


Please see Important Safety Information throughout.
Please see inside pocket for Prescribing Information, including Boxed Warning.