Pr RYBELSUS®
semaglutide tablets

INTRODUCING RYBELSUS®, THE FIRST AND ONLY ORAL GLP-1 RA*

RYBELSUS® (semaglutide tablets) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus:[1]

- **as monotherapy when metformin is considered inappropriate due to intolerance or contraindications**
- **in combination with other medicinal products for the treatment of diabetes (see clinical trials in the Product Monograph for patient populations and drug combinations tested)**

novo nordisk®

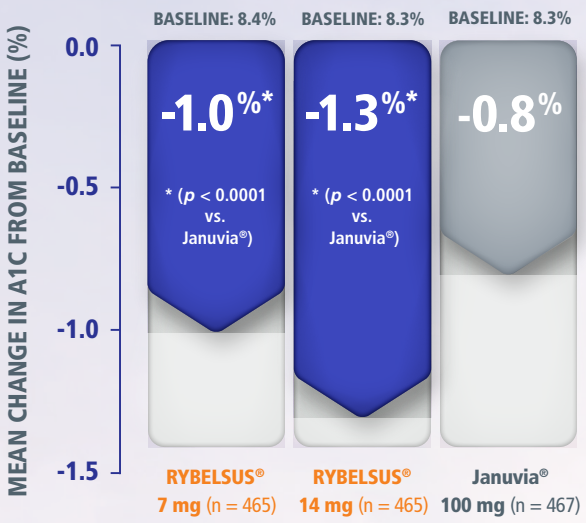
* Comparative clinical significance has not been established.
GLP-1 RA, glucagon-like peptide-1 receptor agonist.

Pr RYBELSUS®
semaglutide tablets

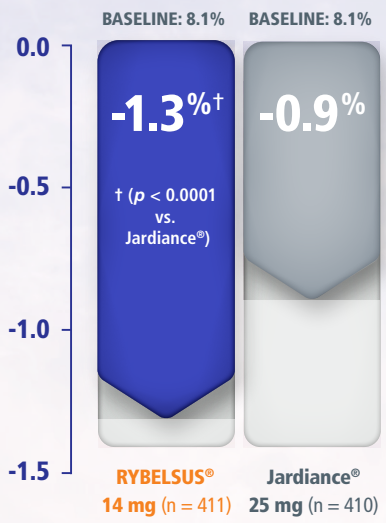
DEMONSTRATED A1C RESULTS ACROSS 3 DIFFERENT STUDIES[1-4]

Mean change in A1C from baseline at week 26

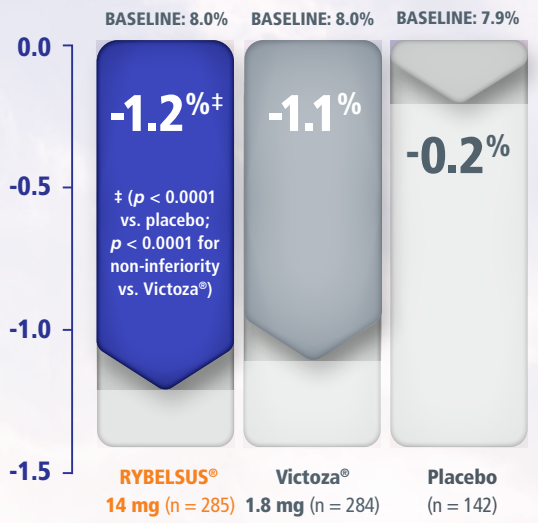
PIONEER 3 (vs. Januvia®)[2]
All + MET ± SU



PIONEER 2 (vs. Jardiance®)[3]
Both + MET; open label



PIONEER 4 (vs. Victoza® and placebo)[4]
All + MET ± SGLT2i

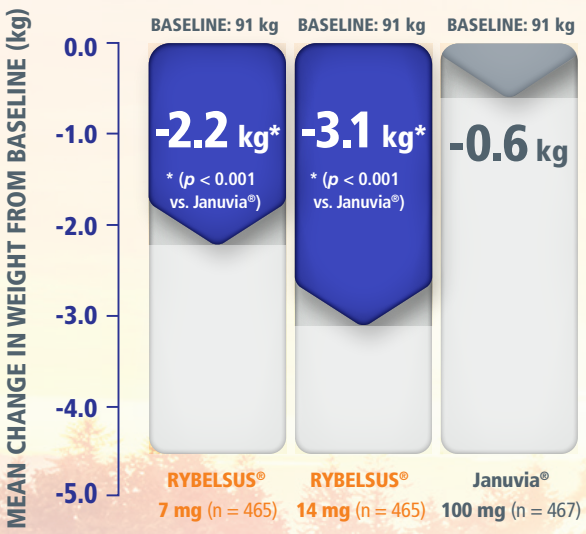


At week 52, the mean changes from baseline for A1C were -1.2% (RYBELSUS® 14 mg), -0.9% (Victoza® 1.8 mg), and -0.2% (placebo).

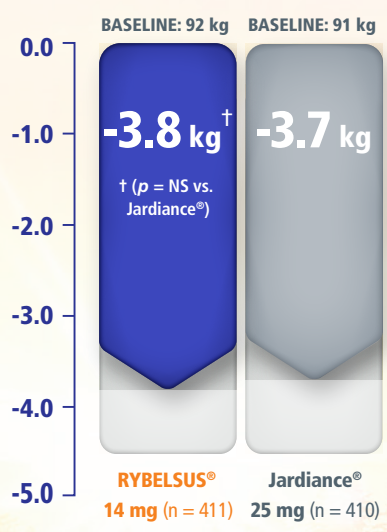
DEMONSTRATED WEIGHT RESULTS ACROSS 3 DIFFERENT STUDIES (2° ENDPOINT)[1-4]

Mean change in weight from baseline at week 26

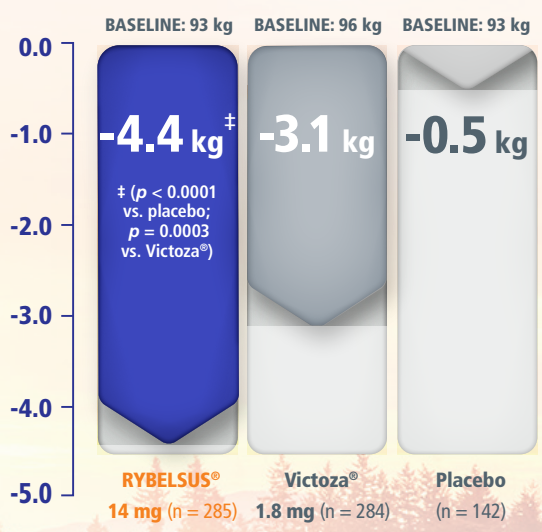
PIONEER 3 (vs. Januvia®)[2]
All + MET ± SU



PIONEER 2 (vs. Jardiance®)[3]
Both + MET; open label



PIONEER 4 (vs. Victoza® and placebo)[4]
All + MET ± SGLT2i



At week 52, the mean changes from baseline in body weight were -4.3 kg (RYBELSUS® 14 mg), -3.0 kg (Victoza® 1.8 mg), and -1.0 kg (placebo).

RYBELSUS® is not indicated for weight reduction.

Adapted from the RYBELSUS® Product Monograph[1]; Pratley RE, et al., 2019,[4] see back for study design (PIONEER 4); Rodbard H, et al., 2019,[3] see back for study design (PIONEER 2); Rosenstock J, et al., 2019,[2] see back for study design (PIONEER 3).
MET, metformin; NS, non-superiority; SGLT2i, sodium-glucose cotransporter-2 inhibitor; SU, sulfonylurea.

Pr RYBELSUS® semaglutide tablets

HELP PATIENTS START ONCE-DAILY RYBELSUS®[1]

STARTING DOSE

3 mg Start with 3 mg once daily for 30 days

MAINTENANCE DOSES

7 mg Increase dose to 7 mg once daily, for at least 30 days, and then maintain dose

14 mg If additional glycemic control is needed after at least 30 days on the 7 mg dose, you may increase the maintenance dose to 14 mg

This regimen is intended to mitigate gastrointestinal symptoms during dose escalation.

No dose adjustment of RYBELSUS® is recommended based on age, sex, race, ethnicity, upper gastrointestinal disease, or hepatic and renal impairment.

Patients can take RYBELSUS® according to the following instructions:

Take on an empty stomach upon waking

Swallow tablet whole with no more than half a glass of water (up to 120 mL)

Patients can be counselled to swallow the tablet whole with a sip of water

A larger volume of water is likely to decrease the amount of RYBELSUS® absorbed

Wait at least 30 minutes before eating, drinking, or taking any other oral medication

Waiting < 30 minutes is likely to decrease the amount of RYBELSUS® absorbed

- Tablets should not be split, crushed, or chewed
- Tablets must be stored in their original blister packing to protect them from moisture and light

Missed dose: If a dose is missed, the missed dose should be skipped, and the next dose should be taken the following day.

For management of a suspected drug overdose, contact your regional poison control centre.

Please see the Product Monograph for complete dosing, administration, and overdosage information.

Clinical use:
RYBELSUS® is not indicated for use in type 1 diabetes or for the treatment of diabetic ketoacidosis. RYBELSUS® is not indicated for use in pediatric patients. Greater sensitivity of some older individuals cannot be ruled out. Therapeutic experience in patients ≥ 75 years of age is limited.

Contraindications:
- Personal or family history of medullary thyroid carcinoma (MTC), or Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
- Pregnancy or breastfeeding

Most serious warnings and precautions:
Risk of thyroid C-cell tumours: In both genders of rats and mice, semaglutide caused treatment-dependent thyroid C-cell tumours at clinically relevant exposures. It is unknown whether semaglutide causes thyroid C-cell tumours in humans. Patients should be counselled regarding the risk and symptoms of thyroid tumours.

Relevant warnings and precautions:
- Hypoglycemia with concomitant use of insulin secretagogues or insulin
- Driving and operating machinery
- CV effects: increased heart rate; PR interval prolongation
- Pancreatitis
- Hypersensitivity
- Diabetic retinopathy: In patients with history of disease, monitor for worsening
- Renal insufficiency: Severe GI adverse reactions warrant monitoring of renal function; acute renal failure and worsening of chronic renal failure have been reported
- Fertility
- Hepatic impairment

For more information:
Please consult the Product Monograph at RYBELSUSPM-E.ca for more information relating to adverse reactions, drug interactions, and dosing information, which have not been discussed in this advertisement.

The Product Monograph is also available by calling us at 1-800-465-4334.

CV, cardiovascular; GI, gastrointestinal.

References: 1. RYBELSUS® (semaglutide tablets) Product Monograph. Novo Nordisk Canada Inc., 2020. **2.** Rosenstock J, et al. Effect of additional oral semaglutide versus 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. *A 78-week, double-blind trial to compare the efficacy and safety of RYBELSUS® vs. Januvia®. A total of 1864 patients with type 2 diabetes were randomized to receive RYBELSUS® 3 mg (n = 466), RYBELSUS® 7 mg (n = 465), RYBELSUS® 14 mg (n = 465), or sitagliptin 100 mg (n = 467) once daily, all in combination with metformin alone or metformin and sulfonylurea. The primary endpoint was change in A1C from baseline to week 26.* **3.** Rodbard HW, 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. *A 52-week, open-label trial (26-week primary endpoint) to compare the efficacy and safety of RYBELSUS® vs. Jardiance®. A total of 821 patients with type 2 diabetes were randomized to receive RYBELSUS® 14 mg (n = 411) once daily or empagliflozin 25 mg (n = 410) once daily, both in combination with metformin.* **4.** Pratley R, et al. Oral semaglutide versus subcutaneous liraglutide and placebo in type 2 diabetes (PIONEER 4): A randomised, double-blind, phase 3a trial. *Lancet.* 2019;394(10192):39-50. *A 52-week, double-blind trial to compare the efficacy and safety of RYBELSUS® vs. Victoza®. A total of 711 patients with type 2 diabetes were randomized to receive RYBELSUS® 14 mg once daily (n = 285), liraglutide 1.8 mg subcutaneous injection (n = 284) once daily, or placebo (n = 142) once daily, all in combination with metformin or metformin and an SGLT2 inhibitor. The primary endpoint was change in A1C from baseline to week 26.*

Novo Nordisk Canada Inc., Tel: (905) 629-4222 or 1-800-465-4334. www.novonordisk.ca

CA20RYB00013E

Pr RYBELSUS® semaglutide tablets