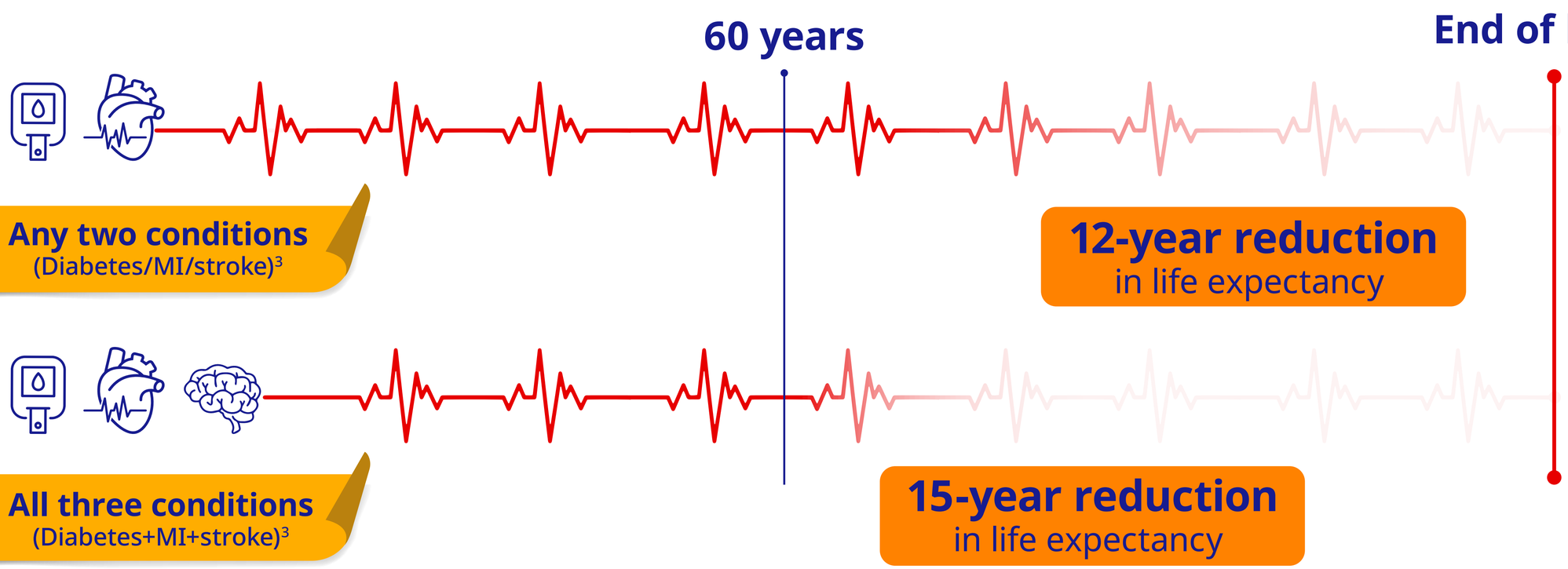
On the road with T2D and CVD, complications may arise[1]

T2D, Type 2 diabetes; CVD, Cardiovascular disease



*Among individuals with diabetes, stroke and MI.
ASCVD, atherosclerotic cardiovascular disease; PwD, people with diabetes; MI, myocardial infarction; CVD, cardiovascular disease;

Life expectancy is reduced in people living with diabetes with pre-existing ASCVD.[3]



Early screening and further management of cardiovascular risk in people with T2D is required to protect them from the risk of cardiovascular event[3]

ASCVD, atherosclerotic CVD; MI, myocardial infarction

Even with modern therapies, the road ahead could be full of residual cardio-vascular risks.[5-7]

Residual CV risk

- Obesity
- Inflammation
- Dyslipidemia
- Diabetes
- Thrombosis

CV, cardiovascular

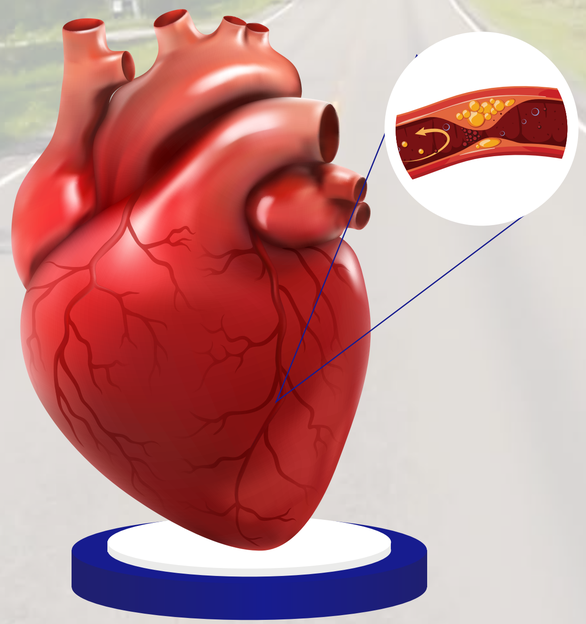
The 2023 ESC guidelines recommend GLP- 1 RA and/or SGLT2i with proven CV benefits for patients with T2D and ASCVD[8]

Disease of 'PIPES'

people living with diabetes are at an increased risk of ASCVD[9]

Myocardial infarction

The benefits of GLP-1 RAs are owing to their effect on PIPES



Myocardial scarring

Disease of 'PUMPS'

people living with diabetes are at risk of myocardial disease[9]

Heart failure

*Pipes: Refers to coronary and cerebral arteries involved in atherosclerotic events.
†Pump: Refers to myocardial function, specifically the heart's ability to pump blood effectively.
ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; GLP-1RA, glucagon-like peptide-1 receptor agonist; PwDs, people with diabetes; SGLT2i, sodium-glucose cotransporter 2 inhibitors.

Stop the Ride from T2D CVD

to start the journey to a healthier future.

FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES

RYBELSUS®

semaglutide tablets

A GAME CHANGER. A LIFE CHANGER.



Not a real patient. The images of person depicted are for illustration purposes only.
T2D, type 2 diabetes; CVD, cardio vascular disease; BP, blood pressure, LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides.

Stop the Ride from

T2D ♥ CVD

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FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES

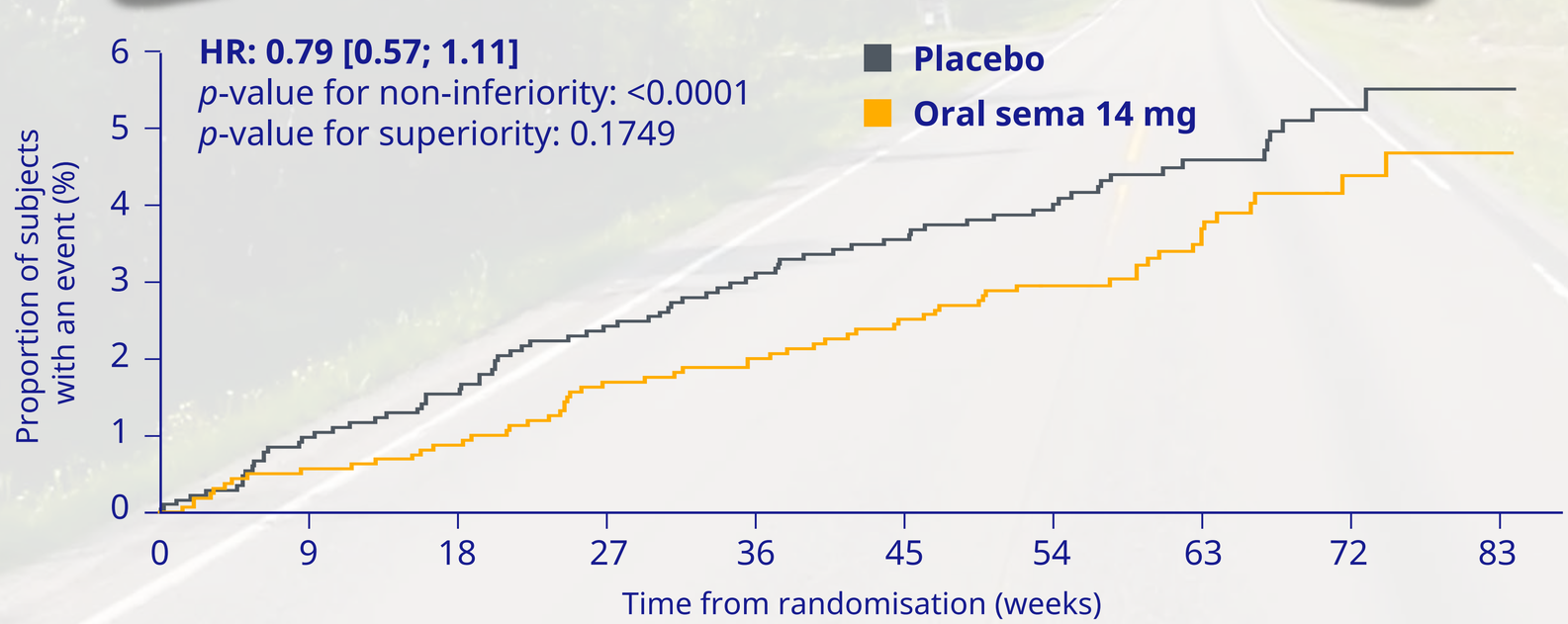
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Oral Semaglutide has established CV safety in T2D[10]

PIONEER 6: Cardiovascular outcome with oral Semaglutide



76 events
Rate: 3.7 events per 100 patient–years

61 events
Rate: 2.9 events per 100 patient–years

21%
MACE reductions[10] (non-significant)

51%
Reduction in[10] cardiovascular deaths

49%
Reduction in[10] all-cause deaths

GLP-1, glucagon-like peptide-1; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; CV, cardiovascular; HR, hazard ratio; MACE, major adverse cardiovascular event; PIONEER, Peptide Innovation for Early Diabetes Treat; sema, semaglutide; T2DM, type 2 diabetes mellitus.

T2D, type 2 diabetes; CVD, cardio vascular disease.

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Reduction of multiple residual risk factors[10]

↓37%

Inflammation and hsCRP with oral semaglutide vs. empagliflozin at 52 weeks.[11]

↓~50%

Oral semaglutide improved UACR at 3 months.[12]

↓5mm Hg

Reduction of systolic blood pressure.[10,*]

Reduction of lipid parameters LDL,TC, TG.[13]

*Baseline SBP was 135 mmHg.

CKD, chronic kidney, disease; eGFR, estimated glomerular filtration rate; ; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; T2D, type 2 diabetes; CVD, cardio vascular disease; TC, total cholesterol; TG, triglycerides; UACR, urine albumin-to-creatinine ratio.

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Significant HbA1c reduction

Up to **1.5%** reduction in HbA1c[14,*]

Clinically relevant weight loss

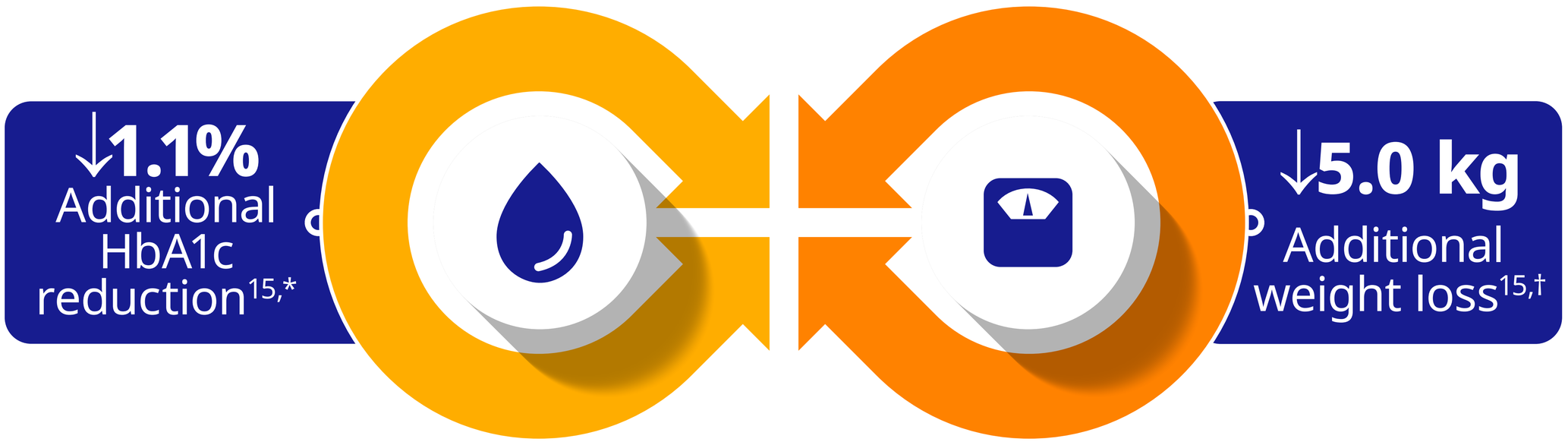
Up to **5 kg** of weight loss[15,†]

Targeting Residual Risk
Open

*Baseline HbA1c of 8.0%. †Baseline weight 92.9 kg
CVD, cardiovascular disease; HbA1c, glycated haemoglobin; T2D, type 2 diabetes.

Target Residual CVD risk with Dual Therapy:

Benefits of adding oral Semaglutide in combination with SGLT2is



When added to metformin +/- SGLT2i*

*Baseline HbA1c of 8.0%. †Baseline weight 92.9 kg
CVD, cardiovascular disease; HbA1c, glycated haemoglobin; T2D, type 2 diabetes; SGLT2i, sodium-glucose cotransporter 2 inhibitors.

*Baseline HbA1c of 8.0%. †Baseline weight 92.9 kg
CVD, cardiovascular disease; T2D, type 2 diabetes.

ADA 2025 Guidelines recommend: Combination Treatment[16]

SGLT2i



GLP- 1 RA

If HbA1c is above goal, if the person is on **GLP-1 RA**, consider adding an **SGLT2i** with proven CVD benefit or vice versa

MoA of combination therapy

Open

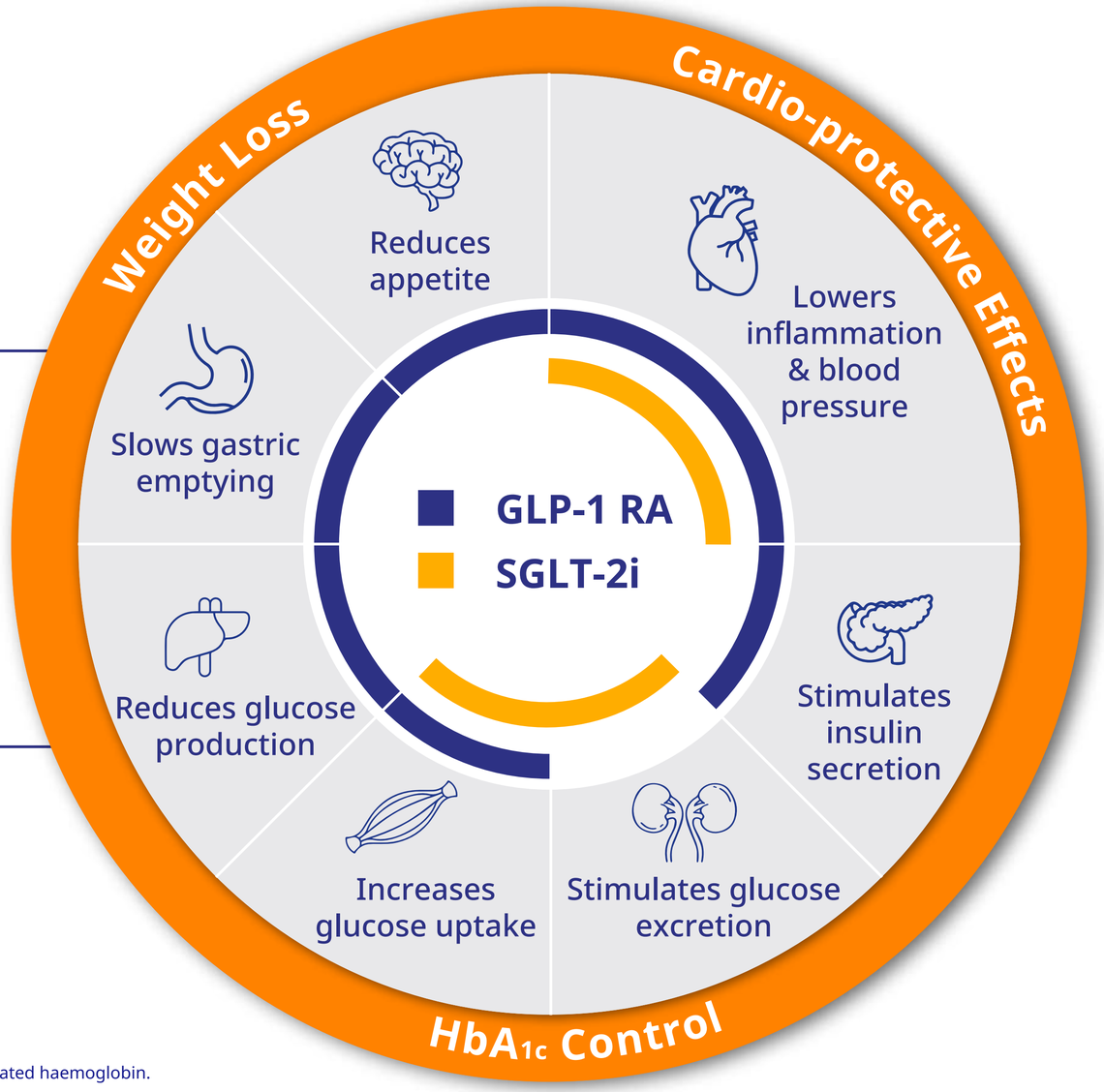
Benefits of Combination Therapy

Open

ASCVD, atherosclerotic cardiovascular disease; T2DM, type 2 diabetes mellitus; CV, cardiovascular; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose cotransporter 2 inhibitors; HbA1c, glycated haemoglobin.

The distinctive mode of action of GLP-1 RAs that targets multiple organs is complemented by SGLT-2i[20]

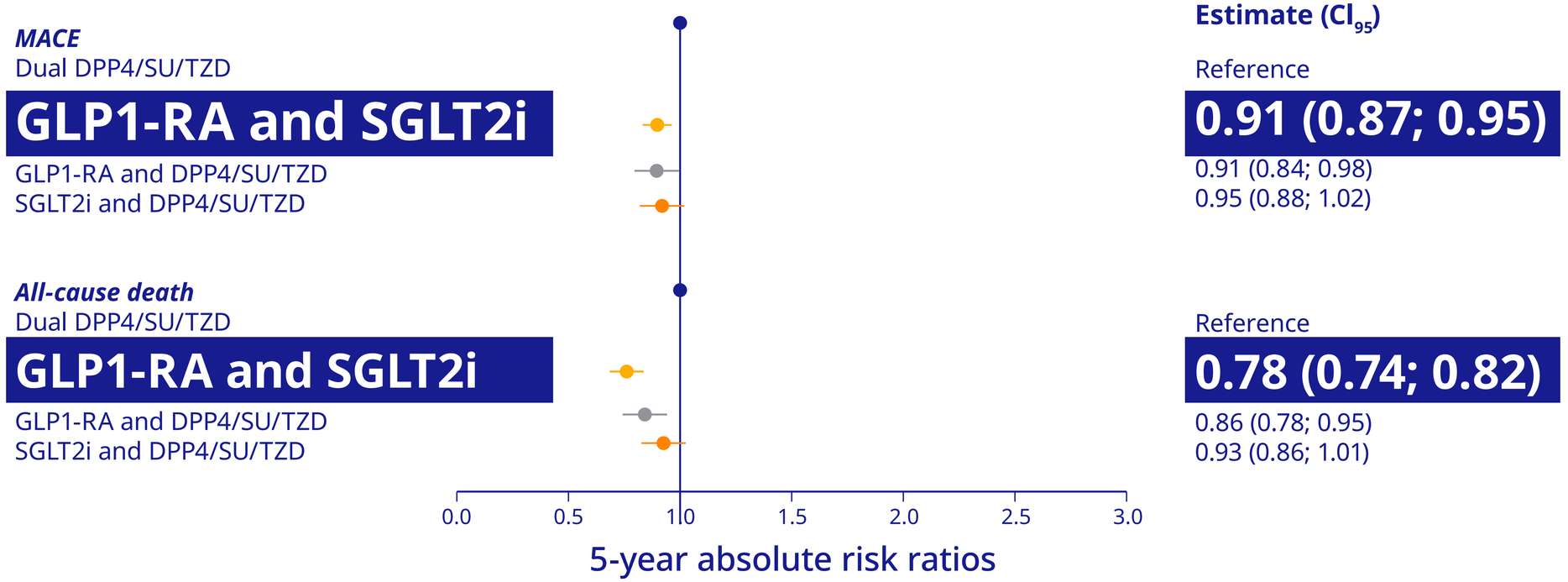
The complementary modes of action of GLP-1 RA and SGLT-2i may lead to improved long-term outcomes



GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose cotransporter 2 inhibitors; HbA1c, glycated haemoglobin.

Benefit of Dual Therapy with GLP-1 RA and SGLT2i on Cardiovascular outcomes in Type 2 Diabetes[17]

5-Year absolute risk ratio: Significantly lower risk of **MACE (9%)** and **all-cause death (22%)**



DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose co-transporter-2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione MACE: major cardiovascular events.

The Therapeutic Benefits of GLP-1RAs and SGLT2is Combination[17,18]

Better myocardial salvage post MI[19]

Addressing the residual risk[20]



Reduction in risk of eGFR decrease of >50%[18]

Reduction in MACE & all cause death[17]

Lower risk of end stage renal disease[18]

More CVD free life years[17]

CVD, cardiovascular disease; eGFR, estimated glomerular filtration Rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; MACE, major adverse cardiovascular events; MI, myocardial infarction; SGLT2i, sodium–glucose cotransporter-2 inhibitor.



Anand,
Diagnosis: Atherosclerotic Cardiovascular Disease (ASCVD)

"Help me streamline my type 2 diabetes care and reduce my cardiovascular events."

Age: 42 years

BMI: 30 kg/m2

HbA1c: 7.8 %,
BP: 150/90 mmHg
(Hypertensive)

History: MI 1 year back
Lifestyle: Sedentary lifestyle

Comorbidities: Dyslipidaemia, Obesity, Coronary Artery Disease (CAD), Hypertension (HTN), T2D

Medication: Metformin, Rosuvastatin, Telmisartan, Aspirin, Empagliflozin

Not a real patient. All images are for representation purpose only.
BMI, body mass index; HbA1c, glycated haemoglobin; T2D, type 2 diabetes; MI, myocardial infarction.

Stop the Ride from
T2D ♥ CVD
to start the journey to a healthier future.

FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES
RYBELSUS®
semaglutide tablets
A GAME CHANGER. A LIFE CHANGER.

Benefits of adding oral Semaglutide in patients with T2D



21%
reduction in MACE (non-significant)[10]

51%
reduction in CV death[10]

Up to **37%**
reduction in CRP levels[21]

Additional benefits when combined with SGLT2i therapy[15]

MACE, Major adverse cardiovascular events
CVD, cardiovascular disease; MI, myocardial infarction; SGLT2i, sodium–glucose cotransporter-2 inhibitor; T2D, type 2 diabetes; CRP, C-reactive protein; CV, cardiovascular.
Not a real patient. All images are for representation purpose only.

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How to deal with GI side effects after taking Rybelsus®[22]



Nausea +



Vomiting +



Diarrhea +



Constipation +

CVD, cardiovascular disease; T2D, type 2 diabetes; GI, gastrointestinal

Nausea



Eat crackers, apples, mint, ginger-based drinks 30 min after GLP-1 RA[22]



Avoid strong smells[22]

GLP-1RA, glucagon-like peptide-1 receptor agonist.

Vomiting



Generous hydration[22]



More frequent meals in small amounts[22]

Diarrhea



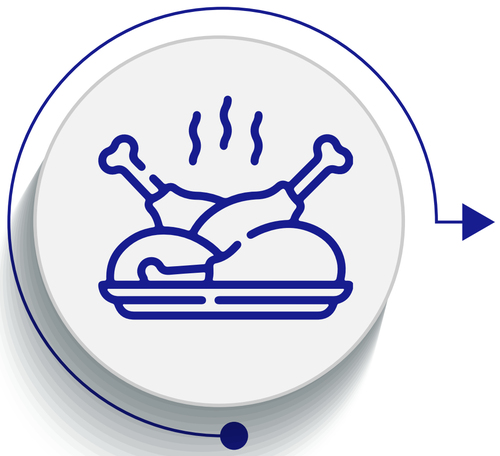
Generous hydration (water, lemon, bicarbonate)[22]



No: Sports drinks[22]



No: High fibre content foods (gradually restore them upon improvement)[22]

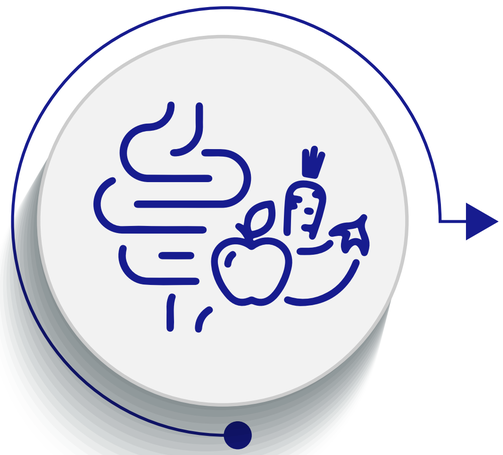


Yes: Chicken broth, rice, carrots, ripe peeled fruit, baked fruit[22]



No: Dairy products, laxatives, coffee, alcohol, soft drinks, very cold/hot foods, products with ol-ending sweeteners[22]

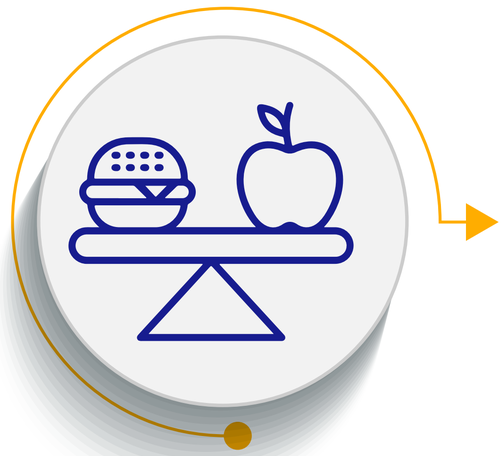
Constipation



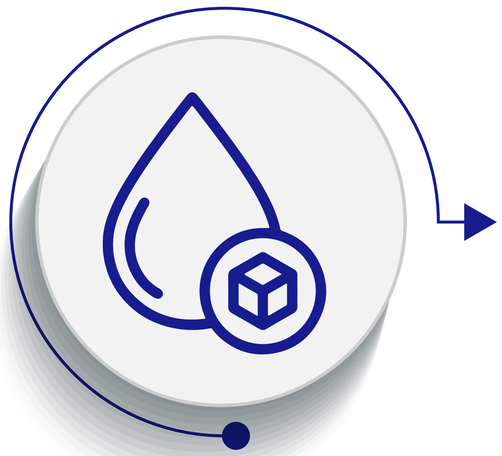
Enough fiber in diet[22]



Increase physical activity[22]



Healthy, balanced diet[22]



Generous hydration (water, sugar-free liquids)[22]

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FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES

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Systematic dose escalation for Rybelsus®[23]

Start with **3 mg** once-daily for 1 month

Increase dose to **7 mg** once-daily, then maintain dose for 1 month

If additional glycaemic control is needed, you may increase the maintenace dose to **14 mg**

Taking Rybelsus® tablets



Take on an empty stomach upon waking up



Take with a sip of water (up to 120 mL)



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

T2D, type 2 diabetes; CVD, cardiovascular disease.

References:

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23. Rybelsus. Prescribing information. Novo Nordisk. 2024.

Abbreviated prescribing information

Disclaimer: For the use only of registered medical practitioner or a hospital or a laboratory.
Abbreviated prescribing information (and not full package insert)
Rybelsus® aPI
Generic Name: Semaglutide Tablets
Brand Name: Rybelsus® 3 mg tablets, Rybelsus® 7 mg tablets and Rybelsus®14 mg tablets.

Presentation: Rybelsus® 3 mg, 7 mg and 14 mg tablets for once-daily oral use. Each tablet contains 3, 7 or 14 mg semaglutide. Tablet for once daily oral use. Indication: RYBELSUS® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. **Limitations of Use:** • RYBELSUS® has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. [see section 4.4 Special Warnings and Precautions] •RYBELSUS® is not indicated for use in patients with type 1 diabetes mellitus. Description: The semaglutide drug products are white to light yellow oval shaped tablets. The primary packaging is a blister card composed of coloured forming foil and non-coloured lid foil. The colour of the forming foil is unique for each tablet strength: green for 3 mg tablets, red for 7 mg tablets and blue for 14 mg tablets. The blister card contains 10 identical cavities, each containing 1 tablet. Batch specific information is printed on each blister card. The secondary packaging consists of an outer sales carton. **Dosing and administration:** Posology The starting dose of Rybelsus® is 3 mg once daily. After 1 month, the dose should be increased to a maintenance dose of 7 mg once daily. If additional benefits are needed after at least one month on the 7 mg dose, the dose can be increased to a maintenance dose of 14 mg once daily. Rybelsus® can be used as monotherapy or in combination with one or more glucose-lowering medicinal products. When Rybelsus® is used in combination with metformin and/or a sodium-glucose co-transporter 2 inhibitor (SGLT2i) or thiazolidinedione, the current dose of metformin and/or SGLT2i/thiazolidinedione can be continued. When Rybelsus® is used in combination with a sulfonylurea or insulin, a reduction in the dose of sulfonylurea or insulin should be considered to reduce the risk of hypoglycaemia. **Missed dose:** If a dose is missed, the missed dose should be skipped, and the next dose should be taken the following day. **Method of administration:** Rybelsus® is a tablet for once-daily oral use. Rybelsus® should be taken on an empty stomach. Rybelsus® should be swallowed whole with up to half a glass of water equivalent to 120 ml. Do not split, crush or chew the tablet. Wait at least 30 minutes before the first meal or drink of the day or taking other oral medicinal products. Waiting less than 30 minutes may decrease the absorption of semaglutide. **Special Population:** Elderly (≥65 years old): No dose adjustment is required based on age. Gender: No dose adjustment is required based on gender. Race and ethnicity: No dose adjustment is required based on race and ethnicity. Patients with hepatic impairment: No dose adjustment is required for patients with hepatic impairment. Patients with renal impairment: No dose adjustment is required for patients with renal impairment. Children and adolescents: The safety and efficacy of Rybelsus® in children and adolescents below 18 years have not been studied. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Special warnings and precautions:** Rybelsus® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Gastrointestinal effects: Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions that can cause dehydration, which in rare cases can lead to a deterioration of renal function. Acute pancreatitis: Acute pancreatitis has been observed with the use of GLP-1 receptor agonists. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Rybelsus® should be discontinued; if confirmed, Rybelsus® should not be restarted. Caution should be exercised in patients with a history of pancreatitis. In the absence of other signs and symptoms of acute pancreatitis, elevations in pancreatic enzymes alone are not predictive of acute pancreatitis. Hypoglycaemia: Insulin and sulfonylurea are known to cause hypoglycaemia. When it is used in combination with a sulfonylurea or insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines. The risk of hypoglycaemia can be lowered by reducing the dose of sulfonylurea or insulin when initiating treatment with Rybelsus®. Diabetic retinopathy: Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. Long-term glycaemic control decreases the risk of diabetic retinopathy. Patients with a history of diabetic retinopathy should be monitored for worsening and treated according to clinical guidelines. Heart failure: There is no therapeutic experience in patients with congestive heart failure New York Heart Association (NYHA) class IV. Pregnancy and lactation: Studies in animals have shown reproductive toxicity. There are limited data from the use of semaglutide in pregnant women. Therefore, Rybelsus® should not be used during pregnancy. Women of childbearing potential are recommended to use contraception when treated with Rybelsus®. If a patient wishes to become pregnant, or pregnancy occurs, Rybelsus® should be discontinued. Rybelsus® should be discontinued at least 2 months before a planned pregnancy due to the long half-life. In lactating rats, semaglutide, salcaprozate sodium and/or its metabolites were excreted in milk. As a risk to a breast-fed child cannot be excluded, Rybelsus® should not be used during breast-feeding. **Drug Interaction:** Interaction with other medicines: In vitro studies have shown very low potential for semaglutide to inhibit or induce CYP enzymes, and to inhibit drug transporters. Semaglutide delays gastric emptying which may influence the absorption of other oral medicinal products. No clinically relevant drug-drug interaction with semaglutide was observed based on the evaluated medicinal products. Therefore, no dose adjustment is required for medicinal products when taken with Rybelsus®. Effects of Rybelsus® on other medicinal products: Total exposure (AUC) of thyroxine (adjusted for endogenous levels) was increased by 33% following administration of a single dose of levothyroxine. Maximum exposure (Cmax) was unchanged. Monitoring of thyroid parameters should be considered when treating patients with semaglutide at the same time as levothyroxine. No clinically relevant change in AUC or Cmax of warfarin, digoxin, oral contraceptives (containing ethinylestradiol and levonorgestrel), metformin, furosemide or rosuvastatin was observed when concurrently administered with semaglutide. Effects of other medicinal products on semaglutide: No clinically relevant change in AUC or Cmax of semaglutide was observed when taken with omeprazole. Interaction with food: Concomitant intake of food reduces the exposure of semaglutide. **Undesirable Effects:** In 10 phase 3a trials, 5,707 patients were exposed to Rybelsus® alone or in combination with other glucose-lowering medicinal products. The duration of the treatment ranged from 26 weeks to 78 weeks. The most frequently reported adverse reactions in clinical trials were gastrointestinal disorders, including nausea, diarrhoea and vomiting. In general, these reactions were mild or moderate in severity and of short duration. Other undesirable effects being delayed gastric emptying, dysgeusia and dizziness **Shelf life:** 3 mg: 24 months; 7 mg: 30 months; 14 mg: 30 months. Storage Keep this medicine out of the sight and reach of children. Do not use this medicine after the expiry date which is stated on the blister and carton. The expiry date refers to the last day of that month. Do not store above 30°C. Store in the original package to protect from moisture and light. Keep the tablet in the blister until you are ready to take it. Removing it too soon can prevent it from working as planned. Do not use this medicine if you notice that the package is damaged or shows signs of being open.

Disclaimer: The abbreviated package insert is updated from the CDSCO approved package insert (F. No.- 4-40/Novo Nordisk/PAC-R-Semaglutide/2023-BD dated 22 July 2024). Rybelsus® is a registered trademark owned by Novo Nordisk A/S and registered in Denmark. **Imported by:** Novo Nordisk India Private Limited, Bangalore

*The full prescribing information can be obtained at no cost from Novo Nordisk. For full prescribing information please contact +91-080-40303200 or write to us at INAgree@novonordisk.com or reach us at Novo Nordisk India Private Limited, NXT Tower -2, Floor 1 & 2, Embassy Manyata Business Park, Nagavara Village, Kasaba Hobli, Bangalore-560045).

Note: For detailed information on this product, please refer to full package insert*.

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