Treat with Heart in mind: Manage CV Risks in PwDs

PwDs have **2-4** times increased **CV risks**[1]

Excess weight increases the risk of **CV event by 33%**[2]

~1/5 PWDs may experience their 1st **CV event** within **~5 years** of diagnosis.[3]

Not a real patient. The images of person depicted are for illustration purposes only.
Abbreviations: CV risk: Cardiovascular Risk, PwDs: People with Diabetes

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High Body Weight Complicates CV Risk in PwDs[2]

33%
increased risk of fatal/ non-fatal stroke[2]

49%
increased risk of fatal/ non-fatal coronary heart disease*[2]

71%
increased risk of all-cause mortality[2]

Abbreviation: CV: Cardiovascular, PwDs: People with Diabetes
*Nonfatal coronary heart disease was defined as nonfatal myocardial infarction, unstable angina, percutaneous coronary intervention and/or coronary artery bypass graft

Not a real patient. The images of person depicted are for illustration purposes only.
$compared to people with type 1 diabetes
Abbreviations: CV risk: Cardiovascular Risk, PwDs: People with Diabetes

Multifactorial intervention increased the survival rate by 7.9 years[4]

- Mortality: ↓**45%**
- Time to 1st CVD event: ↑**8.1 years**
- Survival: ↑**7.9 years**
- ↓**Microvascular complications**

STENOS-2
After 21 years of follow-up:
(mean 7.8 years of treatment)

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Abbreviation: CVD: Cardiovascular Disease

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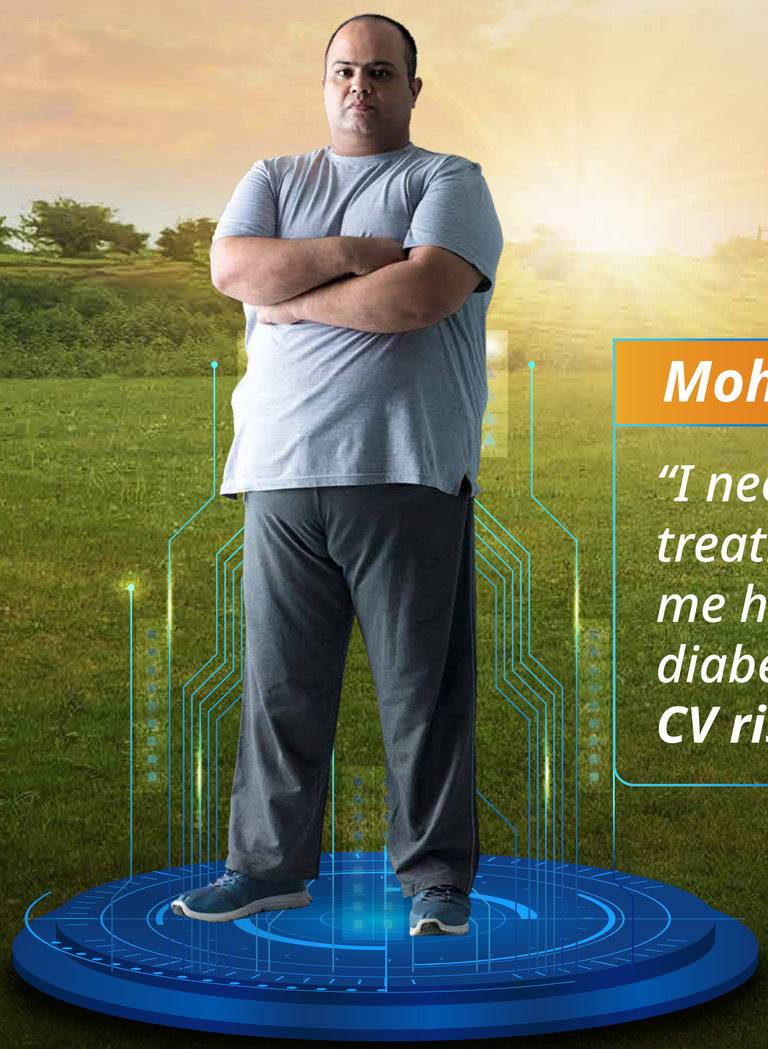
Abbreviation: CV - Cardiovascular

Diverse patient profiles, diverse stories

PwDs with evolving CV risk



Mohan, 47

*"I need a diabetes treatment plan to help me holistically manage diabetes, **CKD** and **CV risk factors**."*

PwDs with high insulin volume

Riya, 60

*"Lighten my load of **insulin** and help me control my diabetes."*

Not a real patient. The images of person depicted are for illustration purposes only.
Not a real case profile, depicted profile is for hypothetical purposes only
Abbreviation: CV: Cardiovascular, CKD: Chronic Kidney Disease, PwD: People with Diabetes

Optimise combination therapy *from the beginning by adding Rybelsus® for additional benefits[5,6]*

PwDs with evolving CV risk

"I need a diabetes treatment plan to help me holistically manage diabetes, CKD and CV risk factors"

Mohan, 47

- HbA1c – **8.7%**
- BMI: **28 kg/m²**
- **Comorbidities:** Dyslipidemia, Chronic Kidney Disease, Hypertension
- **Medication:** Metformin, ARBs, Statins & SGLT2is

Not a real patient. The images of person depicted are for illustration purposes only.
Not a real case profile, depicted profile is for hypothetical purposes only
Abbreviation: CV: Cardiovascular , CKD: Chronic Kidney Disease, SGLT2i: Sodium-glucose cotransporter-2 inhibitor, ARBs: Angiotensin receptor blockers,BMI: Body mass Index, HbA1c: glycated haemoglobin

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Unprecedented HbA1c reduction

Up to **1.5%** reduction in **HbA1c**[*7]

Unsurpassed weight loss

~20% achieved >10% **weight loss**[8]

Synergistic benefits of Rybelsus®>>>

Not a real patient. The images of person depicted are for illustration purposes only.
Not a real case profile, depicted profile is for hypothetical purposes only
*Baseline HbA1c of 8.0%,
Abbreviations: T2DM: Type 2 diabetes Mellitus, HbA1c: Glycated hemoglobin,

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Target Residual CVD Risk with Dual Therapy: Benefits of adding Oral semaglutide as combination with SGLT2is[9]

-1.1%
Additional HbA1c reduction*[9]

-5.0 kg
Additional weight loss*[9]

when added to metformin + SGLT2i*[9]

*Results are from a post-hoc analysis of PIONEER 4, a 52-week, double-blind, double-dummy trial in 711 adult patients with type 2 diabetes. Patients who entered the trial were either on metformin alone or metformin plus an SGLT-21. All patients were randomised to RYBELSUS 14 mg, liraglutide 1.8 mg, or placebo in PIONEER 4. Over the course of the thal, those patients who continued on a stable regimen with metformin plus an SGLT-21 demonstrated a slight increase (0.4%) in HOA, compared to a-1.1% reduction

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Not a real case profile, depicted profile is for hypothetical purposes only
*Baseline HbA1c of 8.0%,
Abbreviations: T2DM: Type 2 diabetes Mellitus, HbA1c: Glycated hemoglobin,

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Consistent CV Safety

21% MACE reduction[@~#10]

51% CV death[10]

49% all cause death[10]

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Not a real case profile, depicted profile is for hypothetical purposes only
Abbreviations: CV: Cardiovascular, MACE: Major Adverse Cardiovascular Events
@Hazard ratio, 0.79 (95% CI, 0.57-1.11), ~non significant, #Results were not significant for the primary outcome of MACE reduction.

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Reduction of multiple cardio-metabolic risk factors

5mm Hg
Systolic blood pressure~[10]

Reduces
UACR
& **eGFR decline**[10,12]

LDL, TC, TG
Lipid Profile#[11]

37%
reduction in **hsCRP**[13]

Not a real patient. The images of person depicted are for illustration purposes only.
Not a real case profile, depicted profile is for hypothetical purposes only
Abbreviations: CVD: Cardiovascular Disease, LDL: Low-density Lipoprotein, SBP: Systolic Blood Pressure, TC: Total Cholesterol, TG: Triglycerides, hsCRP: high-sensitivity C-reactive protein, UACR: urine albumin-to-creatinine ratio, eGFR: estimated glomerular filtration rate
~Baseline SBP – 135 mmHg, #non Significant

64% PwDs *with combination OAD therapy and high-dose insulin still fail to achieve treatment*[5,6,9,10,14]

PwDs with high insulin volume

"Lighten my load of insulin and help me control my diabetes"

Riya, 60

- HbA1c – **8.9%,** eGFR: 60 ml/min/1.73m²
- BMI: **28 kg/m²**
- **Medication:** High dose **insulin**

Not a real patient. The images of person depicted are for illustration purposes only.

Not a real case profile, depicted profile is for hypothetical purposes only

Abbreviation: CV: Cardiovascular, CKD: Chronic Kidney Disease, PwDs: People with Diabetes, BMI: Body mass Index, HbA1c:Glycated hemoglobin, eGFR: Estimated Glomerular Filtration Rate, ARBs: Angiotensin receptor blockers

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Unprecedented HbA1c reduction

Up to **1.5%** reduction in **HbA1c**[*7]

Unsurpassed weight loss

Up to **5kg** weight loss[^9]

Unveil the benefits of Rybelsus®>>>

Not a real patient. The images of person depicted are for illustration purposes only. Not a real case profile, depicted profile is for hypothetical purposes only

Abbreviations: T2DM: Type 2 diabetes Mellitus, HbA1c: Glycated hemoglobin, CVD: Cardiovascular Disease, MACE: Major Adverse Cardiovascular Events

*Baseline HbA1c of 8.0%, ^Baseline weight - 92.9 kg

FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES

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Benefits of adding oral semaglutide in PwDs on insulin[15]

1.2%
Additional HbA1c reduction of 1.2%*[15]

4.2 kg
No weight gain and weight loss of 4.2 kg^[15]

20%
Insulin sparing effect - reduction of total daily insulin dose[15]

Low risk of severe **hypoglycemic** episodes compared to placebo[15]

*Baseline HbA1c: 8.2%, ^Baseline weight: 85.9 kg
Abbreviation: HbA1c: glycated haemoglobin, PwDs: People with diabetes

Unveil the benefits of Rybelsus®>>>

Not a real patient. The images of person depicted are for illustration purposes only. Not a real case profile, depicted profile is for hypothetical purposes only
Abbreviations: T2DM: Type 2 diabetes Mellitus, HbA1c: Glycated hemoglobin, CVD: Cardiovascular Disease, MACE: Major Adverse Cardiovascular Events
*Baseline HbA1c of 8.0%, ^Baseline weight - 92.9 kg †Baseline waist circumference: 104.5 cm, @Hazard ratio, 0.79 (95% CI, 0.57-1.11), ~non significant, #Results were not significant for the primary outcome of MACE reduction.

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Broad range of patients[16]

65 years old elderly individuals

Individual with **hepatic** impairment

Individual with **renal** impairment*

*eGFR up to 15 ml/min/1.73 m2 body surface area

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Systematic dose escalation for Rybelsus®[16]

- Start with **3mg** once-daily for 1 month
- Increase dose to **7mg** once-daily, for at least 1 month, then maintain dose
- If additional glycemic control is needed, you may increase the maintenance dose to **14 mg**

Taking Rybelsus® tablets

- Take on an empty stomach upon waking
- Take with a sip of water (up to 120 mL)
- Wait at least 30 minutes before eating, drinking or taking any other oral medication

Strike out the side effects of Rybelsus®>>>

References: 1. Hussain M, et al. N Engl J Med. 2019;381:841-851. Supplementary appendix. 2. Dahl K, et al. Diabetes Obes Metab. 2021;23(7):1594-1603

FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES

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How to deal with GI symptoms after taking Rybelsus®?

Ease the symptoms of nausea by including foods like[17]

- Crackers
- Ginger root
- Apples
- Ginger-based drinks
- Mint

after 30 minutes of dosage.

References: 1. Hussain M, et al. N Engl J Med. 2019;381:841-851. Supplementary appendix. 2. Dahl K, et al. Diabetes Obes Metab. 2021;23(7):1594-1603

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FOR PEOPLE WITH UNCONTROLLED TYPE 2 DIABETES

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A GAME CHANGER. A LIFE CHANGER.

Up to **1.5%** unprecedented HbA1c reduction*[7]

Up to **5kg** unsurpassed weight loss^[9]

21% MACE reduction†$~[10]

Not a real patient. The images of person depicted are for illustration purposes only.
Abbreviation: HbA1c: Glycated hemoglobin, MACE: Major Adverse Cardiovascular Events
*Baseline HbA1c of 8.0%, ^Baseline weight - 92.9 kg, †Hazard ratio, 0.79 (95% CI, 0.57-1.11), ~non significant, $Results were not significant for the primary outcome of MACE reduction.)

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Abbreviated prescribing information

For the use only of registered medical practitioner or a hospital or a laboratory.
Abbreviated prescribing information (and not full package insert)
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. Patients treated with Rybelsus® in combination with a sulfonylurea or insulin may have an increased risk of hypoglycaemia. 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. **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. BIO/IMP/23/000116 dated 19 Jan 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, Plot No.32, 47 - 50, EPIP Area, Whitefield, Bangalore - 560 066 India (Effective from 27 Oct 2023 our registered office premise has been relocated to 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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