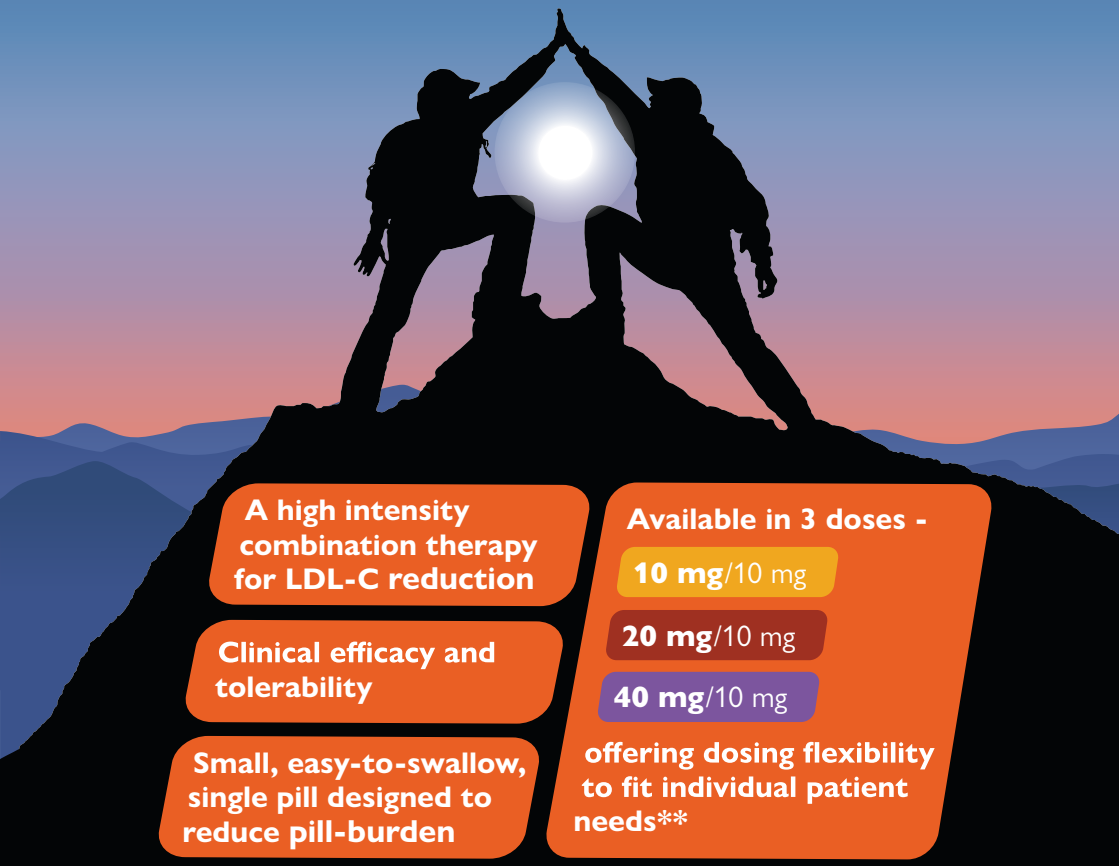
FOR HEALTHCARE PROFESSIONALS ONLY

SUVEZEN™
Rosuvastatin + Ezetimibe

COMBINING POWER AND CONFIDENCE AGAINST LDL-C*



A high intensity combination therapy for LDL-C reduction

Clinical efficacy and tolerability

Small, easy-to-swallow, single pill designed to reduce pill-burden

Available in 3 doses -

10 mg/10 mg

20 mg/10 mg

40 mg/10 mg

offering dosing flexibility to fit individual patient needs**

* LDL-C - low density lipoprotein cholesterol goal:

** Each film coated tablet contains 10mg 20mg or 40mg of rosuvastatin (as rosuvastatin calcium) respectively, and 10mg ezetimibe.

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LDL-C goal achievement

Achievement of the low-density lipoprotein cholesterol (LDL-C) goals in patients at ***high risk*** of coronary heat disease **presents a challenge.**[1] There is a gap between guideline recommended LDL cholesterol goals and what is achieved in real world practice.[2]

The European Society of Cardiology (ESC) / European Atherosclerosis Society (EAS) 2019 dyslipidaemia guidelines propose, based on recent studies, **a CV-risk based approach and recommend LDL-C goals**, which are particularly relevant to ***high*** and ***very-high risk*** patients.[3]

Risk category	2019
Very high risk	<1.4 mmol/L **and** ≥50% ↓ from baseline
High risk	<1.8 mmol/L **and** ≥50% ↓ from baseline
Moderate risk	<2.6 mmol/L
Low risk	<3.0 mmol/L

References

1. Ballantyne M *et al.* Efficacy and Safety of Rosuvastatin 40 mg Alone or in Combination With Ezetimibe in Patients at High Risk of Cardiovascular Disease (results from the EXPLORER Study) Am J Cardiol. 2007;99(5):673-80
2. Ray K *et al.* EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care: the DA VINCI study. Eur J Prev Cardiol. 2021; 28(11):1279-1289
3. Mach F, *et al.* 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2019;0:1-78
4. Jones PH, *et al.* Effects of rosuvastatin versus atorvastatin, simvastatin, and pravastatin on non-high-density lipoprotein cholesterol, apolipoproteins, and lipid ratios in patients with hypercholesterolemia: additional results from the STELLAR trial. Clin Ther. 2004;26(9):1388-99.
5. Collins R, Reith C, Emberson J, *et al.* Interpretation of the evidence for the efficacy and safety of statin therapy. Lancet. 2016;388(10059):2532-61.
6. Suvezen Summary of Product Characteristics
7. Krahenbuhl S, *et al.* Unmet needs in LDL-C lowering: when statins won't do! Drugs. 2016;76(12):1175-90 6.

SUVEZEN
Rosuvastatin + Ezetimibe

A high-intensity single pill statin combination for LDL-C reduction

Rosuvastatin:
The most potent statin, producing a larger reduction in LDL-C than older statins.[4,5]

+

Ezetimibe:
To inhibit cholesterol absorption[6]

Dual inhibition, providing complementary action against cholesterol[6]

Rosuvastatin:
Highly effective HMG-CoA reductase inhibition, preventing cholesterol synthesis[7]

DUAL Inhibition

Ezetimibe:
Highly effective in inhibiting cholesterol absorption[7]

Results from pharmacokinetic/ pharmacodynamic studies do not always correlate with clinical efficacy. The safety profile is consistent with the known profiles of the two components.

LDL-C: low density lipoprotein cholesterol;
HMG-CoA: hydroxy-methyl-glutaryl-coenzyme A.

Therapeutic Indications:

Primary Hypercholesterolaemia/Homozygous Familial Hypercholesterolaemia (HoFH)

Suvezen is indicated as adjunct to diet for treatment of primary hypercholesterolaemia (heterozygous familial and non-familial) or homozygous familial hypercholesterolaemia in adult patients who are not appropriately controlled with statin alone, who are adequately controlled with rosuvastatin and ezetimibe given concurrently at the same dose level as in the fixed combination, but as separate products.

Prevention of Cardiovascular Events Suvezen is indicated as substitution therapy in adult patients who are adequately controlled with rosuvastatin and ezetimibe given concurrently, at the same dose level as in the fixed dose combination, but as separate products to reduce the risk of cardiovascular events in patients with coronary heart disease (CHD) and a history of acute coronary syndrome (ACS).

Clinical efficacy and tolerability

Improved LDL-C reductions following the addition of ezetimibe to statin monotherapy has been demonstrated, with a tolerability profile that is comparable to that of the individual components[1]

Convenient

A small, easy-to-swallow, single pill combination, **reducing pill burden**

To be taken once per day; at the same time; with or without meals; as part of a low-fat dietary regimen[6]

Flexibility of dose range to suit individual patient needs[6]

Each film coated tablet contains 10mg, 20mg or 40mg of rosuvastatin (as rosuvastatin calcium) respectively, and 10mg ezetimibe.

Prescribing Information: Suvezen (rosuvastatin/ezetimibe) film-coated tablets

Please refer to the Summary of Product Characteristics (SmPC) for full prescribing details.

Presentations: Suvezen 10mg/10mg, 20mg/10mg and 40mg/10mg: Each film-coated tablet contains 10mg; 20mg or 40mg of rosuvastatin (as rosuvastatin calcium) respectively, and 10mg ezetimibe. **Indication:** Primary Hypercholesterolaemia/Homozygous Familial Hypercholesterolaemia (HoFH) - Suvezen is indicated as adjunct to diet for treatment of primary hypercholesterolaemia (heterozygous familial and non-familial) or homozygous familial hypercholesterolaemia in adult patients who are not appropriately controlled with statin alone, who are adequately controlled with rosuvastatin and ezetimibe given concurrently at the same dose level as in the fixed combination, but as separate products. Prevention of Cardiovascular Events - Suvezen is indicated as substitution therapy in adult patients who are adequately controlled with rosuvastatin and ezetimibe given concurrently, at the same dose level as in the fixed dose combination, but as separate products to reduce the risk of cardiovascular events in patients with coronary heart disease (CHD) and a history of acute coronary syndrome (ACS). **Dosage and Administration:** The patient should be on and continue, an appropriate lipid-lowering diet, during treatment with Suvezen. Suvezen is not suitable for initial therapy. When Suvezen is indicated for patients not controlled by statin alone, the dose of Suvezen should be individualized according to the target lipid levels and the patient's response. When Suvezen is indicated for patients who are adequately controlled with rosuvastatin and ezetimibe given concurrently at the same dose level as in the fixed combination, but as separate product, treatment initiation or dose adjustment if necessary should only be done with the monocomponents and after setting the appropriate doses the switch to the fixed dose combination of the appropriate strength is possible. Patient should use the strength corresponding to their previous treatment. The recommended dose is one Suvezen tablet daily. To be administered at any time of the day, with or without food. The tablet should be swallowed whole with a drink of water. If co-administered with bile acid sequestrant (BAS), administration of Suvezen should occur either ≥2 hours before or ≥4 hours after administration of a BAS. **Special populations:** *Paediatric (<18 years):* Safety and efficacy has not been established. *Elderly (>70 years):* Starting dose of 5 mg rosuvastatin is recommended. The combination is not suitable for initial therapy. *Hepatic impairment: Mild:* No dosage adjustment is required. *Moderate/Severe:* Treatment with Suvezen is not recommended. *Renal impairment: Mild:* No dose adjustment is necessary. *Moderate (creatinine clearance <60 ml/min):* The recommended start dose is rosuvastatin 5mg. *Race:* The recommended start dose is rosuvastatin 5 mg for patients of Asian ancestry due to increased systemic exposure. The fixed dose combination is not suitable for initial therapy. Monocomponent preparations should be used to start the treatment or to modify the dose. Suvezen 40 mg/10 mg tablets are contraindicated in these patients. *Genetic polymorphisms:* In patients who are known to have specific types of genetic polymorphisms that can lead to increased rosuvastatin exposure, a lower daily dose of Suvezen is recommended. *Dosage in patients with pre-disposing factors to myopathy:* The recommended start dose is rosuvastatin 5mg in patients with pre-disposing factors to myopathy. Suvezen 40 mg/10 mg tablets are contraindicated in some of these patients. *Concomitant therapy:* The risk of myopathy (including rhabdomyolysis) is increased when Suvezen is administered concomitantly with certain medicinal products that may increase the plasma concentration of rosuvastatin (e.g. ciclosporin and certain protease inhibitors including combinations of ritonavir with atazanavir, lopinavir, and/or tipranavir). Whenever possible, alternative medications should be considered, and, if necessary,consider temporarily discontinuing Suvezen therapy. In situations where co-administration of these medicinal products with Suvezen is unavoidable, the benefit and the risk of concurrent treatment and rosuvastatin dosing adjustments should be carefully considered. **Contraindications:** Hypersensitivity to the active substances or excipients. Pregnancy, breast-feeding and in women of childbearing potential not using appropriate contraceptive measures. Active liver disease or any serum transaminase elevations which are unexplained, persistent or exceeding 3x the upper limit of normal (ULN). Severe renal impairment (creatinine clearance <30ml/min); myopathy or receiving concomitant ciclosporin. 40mg/10mg dose contraindicated in patients with predisposing factors for myopathy/rhabdomyolysis; such factors include: Moderate renal impairment (creatinine clearance <60ml/min), hypothyroidism, personal or family history of hereditary muscular disorders, previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate, alcohol abuse, situations where an increase in plasma levels of rosuvastatin may occur, Asian patients, concomitant use of fibrates. **Precautions and Warnings:** *Skeletal muscle effects:* have been reported in rosuvastatin-treated patients with all doses and in particular with doses >20mg. As with other HMG-CoA reductase inhibitors, reporting rate for rhabdomyolysis is associated with use at doses >40mg. Post-marketing experience with ezetimibe, cases of myopathy and rhabdomyolysis have been reported. If myopathy is suspected based on muscle symptoms or is confirmed by a creatine phosphokinase (CPK) level, Suvezen and any of these other agents that the patient is taking concomitantly should be immediately discontinued. All patients starting therapy with Suvezen should be advised of the risk of myopathy and told to report promptly any unexplained muscle pain, tenderness or weakness, particularly if associated with malaise or fever. In few cases, statins have been reported to induce de novo or aggravate pre-existing myasthenia gravis or ocular myasthenia. Suvezen should be discontinued in case of aggravation of symptoms. Recurrences when the same or a different statin was (re-) administered have been reported. *Creatine kinase (CK) measurement:* CK should not be measured following strenuous exercise or in the presence of a plausible alternative cause of CK increase. If CK levels are significantly elevated at baseline (>5x ULN) a confirmatory test should be carried out within 5 – 7 days. If the repeat test confirms a baseline CK >5x ULN, treatment should not be started. *Patients with predisposing factors for myopathy/rhabdomyolysis:* Caution should be exercised in these patients. Risk: benefit of treatment should be considered and clinical monitoring is recommended. CK levels should be measured in these patients. Therapy should be discontinued if CK levels are markedly elevated (>5x ULN) or if muscular symptoms are severe and cause daily discomfort. If symptoms resolve and CK levels return to normal, then consideration should be given to re-introducing treatment at the lowest dose. *Immune-mediated necrotising myopathy (IMNM):* Clinically characterised by proximal muscle weakness and elevated serum CK, has been reported very rarely during or after treatment with statins, including rosuvastatin, despite discontinuation of statin treatment. In clinical trials an increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with fibric acid derivatives. Suvezen should not be used in any patient with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders; or uncontrolled seizures). *Liver effects:* In controlled coadministration trials in patients receiving ezetimibe with statin, consecutive transaminase elevations ≥3x ULN have been observed. It is recommended that liver function tests be carried out prior to, and 3 months following, the initiation of treatment. Rosuvastatin should be discontinued or the dose reduced if the level of serum transaminases is >3x ULN. The reporting rate for serious events is higher at the 40mg dose. In patients with secondary hypercholesterolaemia caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with rosuvastatin. *Liver disease and alcohol:* As with other HMG-CoA reductase inhibitors, rosuvastatin should be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease. *Renal effects:* Proteinuria has been observed in patients treated with higher doses of rosuvastatin and was transient or intermittent in most cases. Proteinuria has not been shown to be predictive of acute or progressive renal disease. An assessment of renal function should be considered during routine follow-up of patients treated with a dose of 40mg. *Diabetes mellitus:* Some evidence suggests that statins raise blood

glucose and in some patients, at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment. Patients at risk (fasting glucose 5.6 – 6.9mmol/l, BMI >30kg/m^2, raised triglycerides, hypertension) should be monitored both clinically and biochemically according to national guidelines. *Interstitial lung disease:* Exceptional cases have been reported with some statins, especially with long term therapy. Presenting features can include dyspnoea, non-productive cough and deterioration in general health (fatigue, weight loss and fever). If it is suspected, statin therapy should be discontinued. *Severe cutaneous adverse reactions:* Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS), which could be life-threatening or fatal, have been reported with rosuvastatin. If signs and symptoms suggestive of this reaction appears, Suvezen must be discontinued immediately and an alternative treatment should be considered. Treatment with Suvezen must not be restarted at any time. *Protease inhibitors:* Increased systemic exposure to rosuvastatin has been observed in subjects receiving rosuvastatin concomitantly with various protease inhibitors in combination with ritonavir. Consideration should be given both to the benefit of lipid lowering by use of Suvezen in HIV patients receiving protease inhibitors and the potential for increased rosuvastatin plasma concentrations when initiating and up titrating rosuvastatin doses in patients treated with protease inhibitors. The concomitant use with certain protease inhibitors is not recommended unless the dose of rosuvastatin is adjusted. *Fibrates:* The safety and efficacy of ezetimibe administered with fibrates have not been established. If cholelithiasis is suspected in a patient receiving Suvezen and fenofibrate, gallbladder investigations are indicated and therapy should be discontinued. *Anticoagulants:* If Suvezen is added to warfarin, another coumarin anticoagulant, or fluindione, the International Normalised Ratio (INR) should be appropriately monitored. *Fusidic acid:* Suvezen must not be co-administered with systemic formulations of fusidic acid or within 7 days of stopping fusidic acid treatment. In patients where the use of systemic fusidic acid is considered essential, statin treatment should be discontinued throughout the duration of fusidic acid treatment. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving fusidic acid and statins in combination. The patient should be advised to seek medical advice immediately if they experience any symptoms of muscle weakness, pain or tenderness. Statin therapy may be reintroduced seven days after the last dose of fusidic acid. In exceptional circumstances, where prolonged systemic fusidic acid is needed, e.g., for the treatment of severe infections, the need for co-administration of Suvezen and fusidic acid should only be considered on a case by case basis and under close medical supervision. *Suvezen contains lactose and sodium:* Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. This medicine is essentially 'sodium-free'. **Interactions:** *Contraindicated combinations:* Ciclosporin. *Not-recommended combinations:* Fibrates and other lipid-lowering products, protease inhibitors, transporter protein inhibitors and fusidic acid. *Other possible interactions:* Cytochrome P450 enzymes, antacids, colestyramine, anticoagulants, Vitamin K antagonists, clopidogrel, ticagrelor, erythromycin, oral contraceptive/hormone replacement therapy. Concomitant use of 10 mg rosuvastatin and 10 mg ezetimibe resulted in a 1.2-fold increase in AUC of rosuvastatin in hypercholesterolaemic subjects. A pharmacodynamic interaction, in terms of adverse effects, between rosuvastatin and ezetimibe cannot be ruled out. When coadministering rosuvastatin with other medicinal products known to increase exposure to rosuvastatin, doses should be adjusted (see SmPC for full details). The maximum daily dose should be adjusted so that the expected rosuvastatin exposure would not likely exceed that of a 40mg daily dose of rosuvastatin taken without interacting medicinal products. **Fertility, Pregnancy and Breastfeeding:** No clinical data are available on the use of ezetimibe during pregnancy. Potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. If a patient becomes pregnant during use of Suvezen, treatment should be discontinued immediately. Animal studies have shown excretion of medicinal product through breast milk. However, there are no data in humans. No clinical trial data on the effects of fertility in humans. **Adverse Reactions:** Adverse drug reactions previously reported with one of the individual components (ezetimibe or rosuvastatin) may be potential undesirable effects with Suvezen. *Common:* diabetes mellitus, headache, dizziness, constipation, nausea, abdominal pain, diarrhoea, flatulence, myalgia, ALT and/or AST increased, asthenia and fatigue. *Uncommon:* decreased appetite, paraesthesia, hot flush, hypertension, cough, dyspepsia, gastroesophageal reflux disease, nausea, dry mouth, gastritis, pruritus, rash, urticaria, arthralgia, muscle spasms, neck pain, back pain, muscular weakness, pain in extremity, ALT and/or AST increased, blood CPK increased, gamma-glutamyltransferase increased, liver function test abnormal, chest pain, pain, asthenia, oedema peripheral. *Rare:* thrombocytopenia, hypersensitivity reactions including angioedema, pancreatitis, increased hepatic transaminases, myopathy (including myositis), rhabdomyolysis, lupus-like syndrome and muscle rupture. *Very rare:* polyneuropathy, memory loss, jaundice, hepatitis, arthralgia, haematuria, gynaecomastia. *Not known:* thrombocytopenia, hypersensitivity (including rash, urticaria, anaphylaxis and angioedema), depression, peripheral neuropathy, sleep disturbances (including insomnia and nightmares), dizziness, paraesthesia, myasthenia gravis, ocular myasthenia, cough, dyspnoea, diarrhoea, pancreatitis, constipation, hepatitis, cholelithiasis, cholecystitis, Stevens Johnson syndrome, erythema multiforme, drug reaction with eosinophilia and systemic symptoms, immune-mediated necrotising myopathy, tendon disorders (sometimes complicated by rupture), myalgia, myopathy/rhabdomyolysis, oedema, asthenia. **Prescribers should consult the SmPC in relation to other adverse reactions. Legal Category:** POM. **Marketing Authorisation Numbers:** 10mg/10mg: PA0540/193/001; 20mg/10mg: PA0540/193/002; 40mg/10mg: PA0540/193/003. **Marketing Authorisation Holder:** Sanofi-Aventis Ireland Ltd. T/A SANOFI, Citywest Business Campus, Dublin 24, Ireland. **Further information is available from:** Sanofi, 18 Riverwalk, Citywest Business Campus, Dublin 24 or contact IEmedinfo@sanofi.com **Date of Preparation:** February 2024

Adverse events should be reported. Reporting forms and information can be found at www.hpra.ie;
email: medsafety@hpra.ie
Adverse events should also be reported to Sanofi Ireland Ltd.
Tel: 01 403 5600. Alternatively, send via email to
IEPharmacovigilance@sanofi.com

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