For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

ROZUCOR B

1. **Generic Name**

   Bempedoic Acid and Rosuvastatin Tablets (180 mg+10 mg) (180 mg +20 mg).

2. **Qualitative and quantitative Composition:**

ROZUCOR B 10

Each film coated tablet contains:

Bempedoic Acid…….180 mg

Rosuvastatin Calcium I.P.

Eq. to Rosuvastatin……..10 mg

Excipients…….…….q.s.

Colors: Titanium dioxide IP, Ferric oxide yellow USP-NF, Ferric oxide red USP-NF

The Excipients used are Microcrystalline Cellulose, Pre gelatinised starch, Povidone, Isopropyl alcohol, Sodium Starch Glycolate, Purified Talc, Calcium Stearate, Lactose Monohydrate, Ferric oxide yellow, Ferric oxide red, Crospovidone, Magnesium Sterate and Instacoate Aqua Pink.

ROZUCOR B 20

Each film coated tablet contains:

Bempedoic Acid……...180 mg

Rosuvastatin Calcium I.P.

Eq. to Rosuvastatin…….20 mg

Excipients…….q.s.

Colors: Ferric Oxide Yellow USP-NF and Titanium Dioxide IP

The Excipients used are Microcrystalline Cellulose, Pregelatinised Starch, Povidone, Isopropyl alcohol, Sodium Starch Glycolate, Purified Talc, Calcium Sterate, Lactose Monohydrate, Ferric oxide yellow, Crospovidone, Magnesium Stearate, Instacoat Aqua Yellow.

3. **Dosage form and strength**

Dosage form: Film-coated tablets.

Strength: Bempedoic Acid and Rosuvastatin Tablets (180 mg+10 mg) (180 mg +20 mg)

4. **Clinical particulars**

4.1. Therapeutic indication

ROZUCOR B 10/ ROZUCOR B 20 is indicated for the treatment of hypercholesterolemia.

4.2. Posology and method of administration

Posology

The recommended dose is one tablet daily. Each film-coated tablet contains a fixed dose of Bempedoic Acid and Rosuvastatin.

If you miss a dose of Bempedoic Acid and Rosuvastatin Tablets, take it as soon as possible. However, if it is almost time for your next dose, skip the missed dose and go back to your regular schedule. Do not double the dose.

Special populations

Renal impairment

No dosage adjustment is necessary in patients with mild or moderate renal impairment. There are limited data available in patients with severe renal impairment (defined as estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m2), and patients with end-stage renal disease (ESRD) on dialysis have not been studied. Additional monitoring for adverse reactions may be warranted in these patients when Bempedoic Acid is administered.

There is limited information in patients with severe renal impairment; in a single dose study, the bempedoic acid AUC was increased by 2.4-fold in patients (n=5) with severe renal impairment (eGFR < 30 mL/min/1.73 m2) compared to those with normal renal function. Clinical studies of bempedoic acid did not include patients with ESRD on dialysis.

Hepatic impairment

No dosage adjustment is necessary in patients with mild or moderate hepatic impairment.

No data are available in patients with severe hepatic impairment (Child-Pugh C). Periodic liver function tests should be considered for patients with severe hepatic impairment

The pharmacokinetics of bempedoic acid and its metabolite (ESP15228) was studied in patients with normal hepatic function or mild or moderate hepatic impairment (Child-Pugh A or B) following a single dose (n=8/group). Compared to patients with normal hepatic function, the bempedoic acid mean Cmax and AUC were decreased by 11% and 22%, respectively, in patients with mild hepaticimpairment and by 14% and 16%, respectively, in patients with moderate hepatic impairment.

This is not expected to result in lower efficacy. Therefore, no dose adjustment is necessary in patients with mild or moderate hepatic impairment.

Bempedoic acid was not studied in patients with severe hepatic impairment (Child-Pugh C).

Elderly (≥ 65 years)

No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients. However, greater sensitivity of some older individuals cannot be ruled out.

Paediatric population

The safety and effectiveness of the medication have not been established in pediatric patients.

Pregnancy

Discontinue the medication when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus.

Method of administration

Bempedoic Acid and Rosuvastatin Tablets should be given orally once daily with or without food.

4.3. Contraindications

In patients with hypersensitivity to Bempedoic acid or Rosuvastatin or to any of the excipients.

- in patients with active liver disease including unexplained, persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3 times the upper limit of normal (ULN).
- In patients with severe renal impairment (creatinine clearance <30 ml/min).
- In patients with myopathy.
- In patients receiving concomitant combination of sofosbuvir/velpatasvir/voxilaprevir
- In patients receiving concomitant ciclosporin.
- During pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures.
- Moderate renal impairment (creatinine clearance < 60 ml/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 may occur
- Concomitant use of fibrates.

4.4. Special warnings and precautions for use

Bempedoic Acid

<u>Hyperuricemia</u>

Bempedoic Acid inhibits renal tubular OAT2 and may increase blood uric acid levels. In clinical studies, 26% of Bempedoic Acid L-treated patients with normal baseline uric acid values (versus 9.5% placebo) experienced hyperuricemia one or more times, and 3.5% of patients experienced clinically significant hyperuricemia reported as an adverse reaction (versus 1.1% placebo). Increases in uric acid levels usually occurred within the first 4 weeks of treatment initiation and persisted throughout treatment. After 12 weeks of treatment, the mean placebo-adjusted increase in uric acid compared to baseline was 0.8 mg/dL for patients treated with Bempedoic Acid.

Elevated blood uric acid may lead to the development of gout. Gout was reported in 1.5% of patients treated with Bempedoic Acid and 0.4% of patients treated with placebo. The risk for gout events was higher in patients with a prior history of gout (11.2% Bempedoic Acid versus

1.7% placebo), although gout also occurred more frequently than placebo in patients treated with Bempedoic Acid who had no prior gout history (1.0% Bempedoic Acid versus 0.3% placebo).

Advise patients to contact their healthcare provider if symptoms of hyperuricemia occur. Assess serum uric acid when clinically indicated. Monitor patients for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.

Tendon Rupture

Bempedoic Acid is associated with an increased risk of tendon rupture or injury. In clinical studies, tendon rupture occurred in 0.5% of patients treated with Bempedoic Acid versus 0% of placebo-treated patients and involved the rotator cuff (the shoulder), biceps tendon, or Achilles tendon. Tendon rupture occurred within weeks to months of starting Bempedoic Acid. Tendon rupture may occur more frequently in patients over 60 years of age, in those taking corticosteroid or fluoroquinolone drugs, in patients with renal failure, and in patients with previous tendon disorders.

Discontinue Bempedoic Acid immediately if the patient experiences rupture of a tendon. Consider discontinuing Bempedoic Acid if the patient experiences joint pain, swelling, or inflammation. Advise patients to rest at the first sign of tendinitis or tendon rupture and to contact their healthcare provider if tendinitis or tendon rupture symptoms occur. Consider alternative therapy in patients with a history of tendon disorders or tendon rupture.

Rosuvastatin

Skeletal muscle effects (e.g., myopathy and rhabdomyolysis):

Risks increase with use of 40 mg dose, advanced age (≥65), hypothyroidism, renal impairment, and combination use with cyclosporine, darolutamide, regorafenib, certain anti-viral medicines or their combinations. Cases of myopathy and rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported. Advise patients to promptly report to their physician unexplained and/or persistent muscle pain, tenderness, or weakness and discontinue rosuvastatin if signs or symptoms appear.

Liver enzyme abnormalities: Persistent elevations in hepatic transaminases can occur. Perform liver enzyme tests before initiating therapy and as clinically indicated thereafter.

Concomitant Coumarin Anticoagulants

Caution should be exercised when anticoagulants are given in conjunction with rosuvastatin because of its potentiation of the effect of coumarin-type anticoagulants in prolonging the prothrombin time/INR. In patients taking coumarin anticoagulants and rosuvastatin concomitantly, INR should be determined before starting rosuvastatin and frequently enough during early therapy to ensure that no significant alteration of INR occurs.

Proteinuria and Hematuria

In the rosuvastatin clinical studies, dipstick-positive proteinuria and microscopic hematuria were observed among rosuvastatin treated patients. These findings were more frequent in patients taking rosuvastatin 40 mg, when compared to lower doses of rosuvastatin or comparator HMG-CoA reductase inhibitors, though it was generally transient and was not

associated with worsening renal function. Although the clinical significance of this finding is unknown, a dose reduction should be considered for patients on rosuvastatin therapy with unexplained persistent proteinuria and/or hematuria during routine urinalysis testing.

Endocrine Effects

Increases in HbA1c and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including rosuvastatin. Based on clinical trial data with rosuvastatin, in some instances these increases may exceed the threshold for the diagnosis of diabetes mellitus.

Although clinical studies have shown that rosuvastatin alone does not reduce basal plasma cortisol concentration or impair adrenal reserve, caution should be exercised if rosuvastatin is administered concomitantly with drugs that may decrease the levels or activity of endogenous steroid hormones such as ketoconazole, spironolactone, and cimetidine.

4.5. Drugs interactions

No interaction studies have been performed for Bempedoic Acid and Rosuvastatin tablets. The following statements reflect the information available on the individual active substances.

Bempedoic Acid

Pharmacokinetic interactions

Simvastatin	
Clinical Impact:	Concomitant use of Bempedoic Acid with simvastatin causes an increase in simvastatin concentration and may increase the risk of simvastatin-related myopathy.
Intervention:	Avoid concomitant use of Bempedoic Acid with simvastatin greater than 20 mg.
Pravastatin	
Clinical Impact:	Concomitant use of Bempedoic Acid with pravastatin causes an increase in pravastatin concentration and may increase the risk of pravastatin-related myopathy.
Intervention:	Avoid concomitant use of Bempedoic Acid with pravastatin greater than 40 mg.

Rosuvastatin

- Combination of sofosbuvir/velpatasvir/voxilaprevir or ledipasvir/sofosbuvir: Combination increases rosuvastatin exposure. Use with rosuvastatin is not recommended.
- Cyclosporine and darolutamide: Combination increases rosuvastatin exposure. Limit rosuvastatin dose to 5 mg once daily.
- Gemfibrozil: Combination should be avoided. If used together, limit rosuvastatin dose to 10 mg once daily.
- Atazanavir/ritonavir, lopinavir/ritonavir, simeprevir or combination of dasabuvir/ombitasvir/paritaprevir/ritonavir, elbasvir/grazoprevir, sofosbuvir/velpatasvir and glecaprevir/pibrentasvir: Combination increases rosuvastatin exposure. Limit rosuvastatin dose to 10 mg once daily.

- Regorafenib: Combination increases rosuvastatin exposure. Limit rosuvastatin dose to 10 mg once daily.
- Coumarin anticoagulants: Combination prolongs INR. Achieve stable INR prior to starting rosuvastatin. Monitor INR frequently until stable upon initiation or alteration of rosuvastatin therapy.

  Concomitant lipid-lowering therapies: Use with fibrates or lipid-modifying doses (≥1 g/day) of niacin increases the risk of adverse skeletal muscle effects. Caution should be used when prescribing with rosuvastatin

4.6. Use in special populations (such as pregnant women, lactating women, fertility etc.)

Pregnancy

There are no available data on drug use in pregnant women to evaluate for a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.

Due to lack of human data, Bempedoic Acid and Rosuvastatin Tablets should not be used during pregnancy.

Breast-feeding

There is no information regarding the presence of Bempedoic Acid and Rosuvastatin in human or animal milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production.

Fertility

The effect of this medicinal product or Bempedoic Acid and Rosuvastatin on fertility in humans has not been studied.

4.7. Effects on ability to drive and use machines

Bempedoic Acid and Rosuvastatin have no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

Bempedoic Acid and Rosuvastatin have been demonstrated to be bioequivalent with co administered Bempedoic Acid and Rosuvastatin. There have been no therapeutic clinical studies conducted with Bempedoic Acid and Rosuvastatin tablets.

Tabulated list of adverse reactions of Bempedoic Acid

Adverse reactions reported with bempedoic acid are displayed by system organ class and frequency in below table .

Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); and not known (cannot be estimated from the available data).

TableAdverse reactions of Bempedoic Acid

System Organ Class (SOC)	Adverse reactions	Frequency Categories
	Anaemia	Common

Blood and lymphatic system disorders	Haemoglobin decreased	Uncommon
Metabolism and nutrition disorder	Gout	Common
	Hyperuricaemia[a]	Common
Hepatobiliary disorders	Aspartate aminotransferase increased	Common
	Alanine aminotransferase increased	Uncommon
	Liver function test increased	Uncommon
Musculoskeletal and connective tissue disorders	Pain in extremity	Common
Renal and urinary disorders	Blood creatinine increased	Uncommon
	Blood urea increased	Uncommon
	Glomerular filtration rate decreased	Uncommon

a. Hyperuricaemia includes hyperuricaemia and blood uric acid increased

The safety profile of bempedoic acid has been studied in clinical studies. The most commonly reported adverse reactions with bempedoic acid during pivotal studies were hyperuricaemia (3.8%), pain in extremity (3.1%), and anaemia (2.5%). More patients on bempedoic acid compared to placebo discontinued treatment due to muscle spasms (0.7% versus 0.3%), diarrhoea (0.5% versus <0.1%). pain in extremity (0.4% versus 0), and nausea (0.3% versus 0.2%), although differences between bempedoic acid and placebo were not significant.

Tabulated list of adverse reactions of Rosuvastatin

Adverse reactions reported with rosuvastatin are displayed by system organ class and frequency in below table.

Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); and not known (cannot be estimated from the available data).

Table Adverse reactions of Rosuvastatin

System Organ Class (SOC)	Adverse reactions	Frequency Categories
Blood and lymphatic system disorders	Thrombocytopenia	Rare
Immune system disorders	Hypersensitivity reactions including angioedema	Rare
Endocrine disorders	Diabetes mellitus	Common
Psychiatric disorders	Depression	Not known

Nervous system disorders	Headache Dizziness	Common
	Polyneuropathy Memory loss	Very rare
	Peripheral neuropathy Sleep disturbances (including insomnia and nightmares)	Not known
Respiratory, thoracic and mediastinal disorders	Cough Dyspnoea	Not known
Gastrointestinal disorders	Constipation Nausea Abdominal pain	Common
	Pancreatitis	Rare
	Diarrhoea	Not known
Hepatobiliary disorders	Increased hepatic transaminases	Rare
	Jaundice Hepatitis	Very Rare
Skin and subcutaneous tissue disorders	Pruritus Rash Urticaria	Uncommon
	Stevens-Johnson syndrome	Not known
Musculoskeletal and connective tissue disorders	Myalgia	Common
	Myopathy (including myositis) Rhabdomyolysis Lupus-like syndrome Muscle rupture	Rare
	Arthralgia	Very Rare

	Immune-mediated necrotising myopathy Tendon disorders, sometimes complicated by rupture	Not known
Renal and urinary disorders	Haematuria	Very Rare
Reproductive system and breast disorders	Gynaecomastia	Very Rare
General disorders and administration site conditions	Asthenia	Common
	Oedema	Not Known

Reporting of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting By reporting side effects, you can help provide more information on the safety of this medicine.

4.9. Overdose

Bempedoic Acid

There is no clinical experience with Bempedoic Acid overdose.

Rosuvastatin

There is no specific treatment in the event of overdose. In the event of overdose, the patient should be treated symptomatically and supportive measures instituted as required. Liver function and CK levels should be monitored. Haemodialysis is unlikely to be of benefit.

5. Pharmacological properties

Pharmacotherapeutic group: Drugs used in adenosine triphosphate-citrate lyase (ACL) inhibitors and HMG-CoA reductase inhibitors (statins).

5.1. Mechanism of Action

Bempedoic acid

Bempedoic acid is an adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers low-density lipoprotein cholesterol (LDL-C) by inhibition of cholesterol synthesis in the liver. ACL is an enzyme upstream of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway. Bempedoic acid and its active metabolite, ESP15228, require coenzyme A (CoA) activation by very long-chain acyl-CoA synthetase 1 (ACSVL1) to ETC-1002-CoA and ESP15228-CoA, respectively. ACSVL1 is expressed primarily in the liver. Inhibition of ACL by ETC-1002-CoA results in decreased cholesterol synthesis in the liver and lowers LDL-C in blood via upregulation of low-density lipoprotein receptors.

Rosuvastatin

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol. In vivo studies in animals, and in vitro studies in cultured animal and human cells have shown rosuvastatin to have a high uptake into, and selectivity for, action in the liver, the target organ for cholesterol lowering. In in vivo and in vitro studies, rosuvastatin produces its lipid-modifying effects in two ways. First, it increases the number of hepatic LDL receptors on the cell-surface to enhance uptake and catabolism of LDL. Second, rosuvastatin inhibits hepatic synthesis of VLDL, which reduces the total number of VLDL and LDL particles.

5.2. Pharmacodynamic properties

Bempedoic acid

Administration of bempedoic acid in combination with maximally tolerated statins, with or without other lipid modifying agents, decreases LDL-C, non-high density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (apo B), and total cholesterol (TC) in patients with hyperlipidemia.

Cardiac Electrophysiology at a dose of 240 mg (1.3 times the approved recommended dose), bempedoic acid does not prolong the QT interval to any clinically relevant extent.

Rosuvastatin

Rosuvastatin dose dependently reduces elevated LDL-cholesterol and reduces total cholesterol and triglycerides and increases HDL-cholesterol. A therapeutic response to Rosuvastatin is evident within 1 week of commencing therapy and 90% of maximum response is usually achieved in 2 weeks. The maximum response is usually achieved by 4 weeks and is maintained after that. Individualization of drug dosage should be based on the therapeutic response.

5.3. Pharmacokinetic properties

Bempedoic acid

Absorption

Pharmacokinetic data indicate that bempedoic acid is absorbed with a median time to maximum concentration of 3.5 hours when administered as bempedoic acid 180 mg tablets.

Effect of Food

Concomitant food administration had no effect on the oral bioavailability of bempedoic acid.

Distribution

The bempedoic acid apparent volume of distribution (V/F) was 18 L. Plasma protein binding of bempedoic acid, its glucuronide and its active metabolite, ESP15228, were 99.3%, 98.8% and 99.2%, respectively. Bempedoic acid does not partition into blood cells.

Metabolism

The primary route of elimination for bempedoic acid is through metabolism of the acyl glucuronide. Bempedoic acid is also reversibly converted to an active metabolite (ESP15228) based on aldo- keto reductase activity observed in vitro from human liver. Mean plasma AUC metabolite/parent drug ratio for ESP15228 following repeat-dose administration was 18% and remained constant over time. Both compounds are converted to inactive glucuronide

conjugates in vitro by UGT2B7. Bempedoic acid, ESP15228 and their respective conjugated forms were detected in plasma with bempedoic acid accounting for the majority (46%) of the AUC_{0-48h} and its glucuronide being the next most prevalent (30%). ESP15228 and its glucuronide represented 10% and 11% of the plasma AUC_{0-48h}, respectively.

Excretion

Following single oral administration of 240 mg of bempedoic acid (1.3 times the approved recommended dose), approximately 70% of the total dose (bempedoic acid and its metabolites) was recovered in urine, primarily as the acyl glucuronide conjugate of bempedoic acid, and approximately 30% was recovered in feces. Less than 5% of the administered dose was excreted as unchanged bempedoic acid in feces and urine combined.

Rosuvastatin

Absorption

In clinical pharmacology studies in man, peak plasma concentrations of rosuvastatin were reached 3 to 5 hours following oral dosing. Both C_{max} and AUC increased in approximate proportion to rosuvastatin dose. The absolute bioavailability of rosuvastatin is approximately 20%.

Administration of rosuvastatin with food did not affect the AUC of rosuvastatin.

The AUC of rosuvastatin does not differ following evening or morning drug administration.

Distribution

Mean volume of distribution at steady-state of rosuvastatin is approximately 134 liters. Rosuvastatin is 88% bound to plasma proteins, mostly albumin. This binding is reversible and independent of plasma concentrations.

Metabolism

Rosuvastatin is not extensively metabolized; approximately 10% of a radiolabeled dose is recovered as metabolite. The major metabolite is N-desmethyl rosuvastatin, which is formed principally by cytochrome P450 \ 2C9, and in vitro studies have demonstrated that N-desmethyl rosuvastatin has approximately one-sixth to one-half the HMG-CoA reductase inhibitory activity of the parent compound. Overall, greater than 90% of active plasma HMG-CoA reductase inhibitory activity is accounted for by the parent compound.

Elimination

Following oral administration, rosuvastatin and its metabolites are primarily excreted in the feces (90%). After an intravenous dose, approximately 28% of total body clearance was via the renal route, and 72% by the hepatic route.

6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

Bempedoic acid was not teratogenic when given orally at doses of 60 and 80 mg/kg/day, resulting in 11 and 12 times the systemic exposure in humans at the maximum recommended human dose (MRHD) of 180 mg to pregnant rats and rabbits, respectively. In an embryofetal development study in rats, bempedoic acid was given orally to pregnant rats at 10, 30, and 60

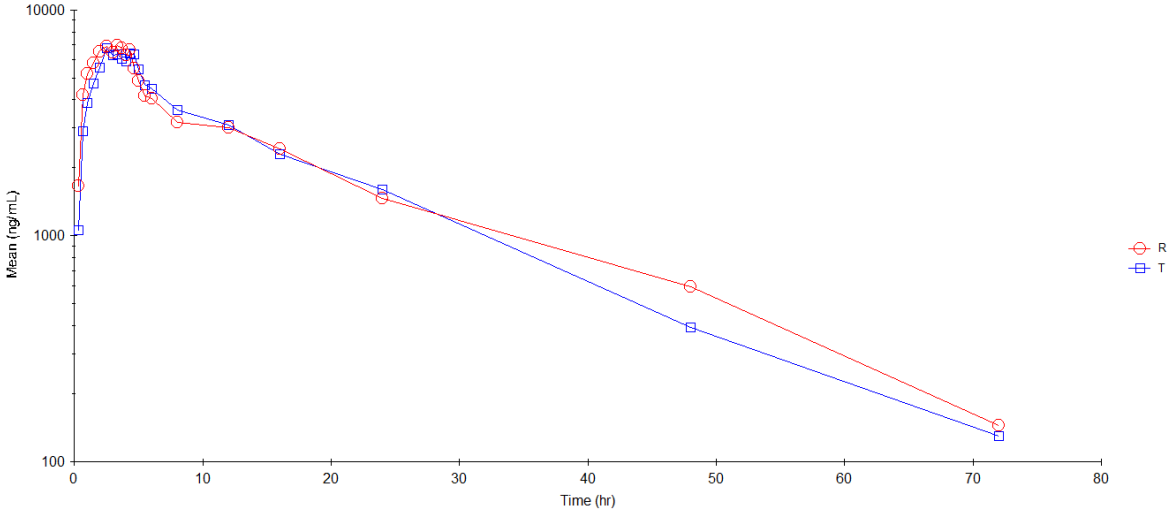
mg/kg/day during the period of organogenesis from gestation day 6 to 17. There were increases in the incidence of non-adverse fetal skeletal variations (bent long bones and bent scapula and incomplete ossification) at doses ≥ 10 mg/kg/day (less than the clinical exposure) in the absence of maternal toxicity. At maternally toxic doses, bempedoic acid caused decreases in the numbers of viable fetuses, increases in post-implantation loss, and increased total resorptions at 60 mg/kg/day (11 times MRHD) and reduced fetal body weight at ≥ 30 mg/kg/day (4 times the MRHD). No adverse development effects were observed when bempedoic acid was given to pregnant rabbits during the period of organogenesis (gestation day 6 to 18) at doses up to 80 mg/kg/day (12 times MRHD). In a pre- and post-natal development study in pregnant rats given oral doses of bempedoic acid at 5, 10, 20, 30 and 60 mg/kg/day throughout pregnancy and lactation (gestation day 6 to lactation day 20), there were adverse effects on delivery in the presence of maternal toxicity, including: increases in stillborn pups, reductions in numbers of live pups, pup survival, pup growth and slight delays in learning and memory at ≥ 10 mg/kg/day (at exposures equivalent to the MRHD).

Rosuvastatin Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenicity potential. Specific tests for effects on hERG have not been evaluated. Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels were as follows: In repeated-dose toxicity studies histopathologic liver changes likely due to the pharmacologic action of rosuvastatin were observed in mouse, rat, and to a lesser extent with effects in the gall bladder in dogs, but not in monkeys. In addition, testicular toxicity was observed in monkeys and dogs at higher dosages. Reproductive toxicity was evident in rats, with reduced litter sizes, litter weight and pup survival observed at maternally toxic doses, where systemic exposures were several times above the therapeutic exposure level.

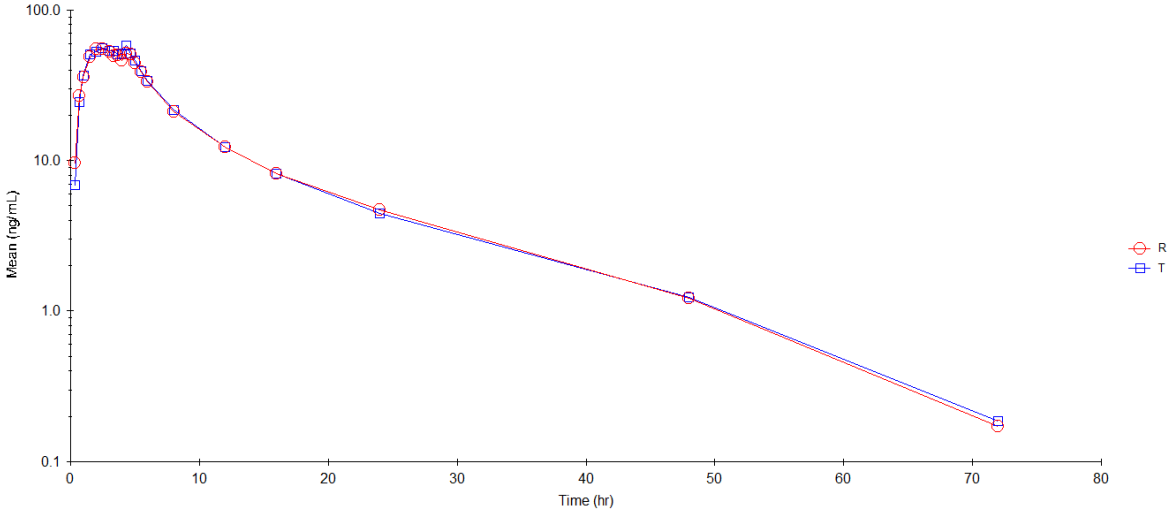
Clinical studies

- An open label, randomized, balanced, two treatment, two sequence, two period, cross-over, single oral dose bioequivalence study in 24 healthy, adult, human subjects under fasting conditions were completed. Upon completion of the clinical phase of the study, assessment of the vital signs measurements, post-study laboratory test results and the overall state of health of all the participated subjects were concluded to be clinically fit. Both products were found to be safe and well tolerated in participated subjects. There were no adverse events or serious adverse events or deaths reported in the study.
- The descriptive statistics (mean, median, minimum, maximum, standard deviation and coefficient of variation) for the pharmacokinetic parameters (primary parameters: C_{max}, AUC_{0-t}, and AUC_{0-inf} and secondary parameters: t_{max}, $t_{1/2}$, Kel and AUC_%Extrap_obs) were estimated for both test and reference products.
- The 90% confidence intervals for Ln-transformed pharmacokinetic parameters AUC_{0-t} and AUC_{0-inf} are within the bioequivalence limits of 80.00 to 125.00%. Based on the results, it is concluded that the test formulation i.e., Bempedoic Acid and Rosuvastatin Tablets (180 mg + 40 mg) is bioequivalent to reference formulation as shown in below graphs.

Mean plot Bempedoic Acid



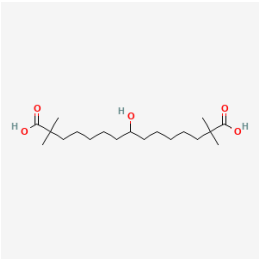
Mean plot Rosuvastatin



7. Description

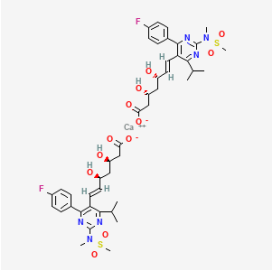
Bempedoic Acid

Bempedoic Acid is 8-hydroxy-2,2,14,14-tetramethylpentadecanedioic acid. The empirical formula is $C_{19}H_{36}O_5$ and its molecular weight is 344.5 g/mol. The chemical structural formula is:



Rosuvastatin Calcium:

Rosuvastatin Calcium are calcium;(E,3R,5S)-7-[4-(4-fluorophenyl)-2-[methyl(methylsulfonyl)amino]-6-propan-2-ylpyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate. The empirical formula is $C_{44}H_{54}CaF_2N6O_{12}S_2$ and its molecular weight is 1001.1 g/mol. The chemical structural formula is:



ROZUCOR B 10 Bempedoic Acid and Rosuvastatin are Pink colored, round, biconvex, film coated tablets, plain on both side. The Excipients used are Microcrystalline Cellulose, Pregelatinised starch, Povidone, Isopropyl alcohol, Sodium Starch Glycolate, Purified Talc, Calcium Stearate, Lactose Monohydrate, Ferric oxide yellow, Ferric oxide red, Crospovidone, Magnesium Sterate and Instacoate Aqua Pink.

ROZUCOR B 20

Bempedoic Acid and Rosuvastatin are Yellow colored, round, biconvex, film coated tablets, plain on both sides. The Excipients used are Microcrystalline Cellulose, Pregelatinised Starch, Povidone, Isopropyl alcohol, Sodium Starch Glycolate, Purified Talc, Calcium Sterate, Lactose Monohydrate, Ferric oxide yellow, Crospovidone, Magnesium Stearate, Instacoat Aqua Yellow.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than date of expiry

8.3. Packaging information

ROZUCOR B 10/ ROZUCOR B 20 is available in pack of 10 Tablets.

8.4. Storage and handing instructions

Store below 30^0 C.

Keep out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. **Details of manufacturer**

    Exemed Pharmaceuticals

    Plot No. 133/1 & 133/2,

    G.I.D.C., Selvas Road,

    Vapi-396195, Dist. Valsad, Gujarat.

11. **Details of permission or licence number with date**

    Mfg. Licence. No : G/25/2011 Issued on: 16.08.2024

12. **Date of revision**

    Sep 2024

MARKETED BY

Torrent Pharmaceuticals Limited.

IN/ ROZUCOR B 10 and 20 mg/SEP-2024/01/PI