Summary of Product Characteristics
BEMPETOL – R40
(Bempedoic Acid 180 mg / Rosuvastatin 40 mg Film-coated Tablets)

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1. Name of the medicinal product

BEMPETOL – R40

Bempedoic Acid 180 mg and Rosuvastatin 40 mg Film-coated Tablets

2. Qualitative and quantitative composition

Each film-coated tablet contains:

Bempedoic Acid … 180 mg

Rosuvastatin Calcium BP equivalent to Rosuvastatin … 40 mg

Excipient with known effect
Each film-coated tablet contains 85.4 mg of lactose (as Lactose BP).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Light pink, round, biconvex film-coated tablets with a break-line on one side and plain on the other. The break-line is not intended for dividing the tablet into equal doses.

4. Clinical particulars

4.1 Therapeutic indications

BEMPETOL – R40 is indicated as an adjunct to diet in adults with established atherosclerotic cardiovascular disease (ASCVD) and/or heterozygous familial hypercholesterolaemia who require additional low-density lipoprotein cholesterol (LDL-C) lowering.

The fixed-dose combination is intended for use in patients for whom treatment with both bempedoic acid 180 mg and rosuvastatin 40 mg is appropriate, as a replacement for the two active substances given concurrently at the same dose levels. It is not indicated for the initiation of statin therapy (see section 4.2).

4.2 Posology and method of administration

Posology
The recommended dose is one film-coated tablet (bempedoic acid 180 mg / rosuvastatin 40 mg) taken once daily.

As a fixed-dose combination containing the maximum rosuvastatin dose of 40 mg, BEMPETOL – R40 is only appropriate for patients in whom both the 180 mg bempedoic acid and the 40 mg rosuvastatin components are individually

indicated and tolerated. Patients should first be titrated on, and shown to require, the individual active substances at these dose levels before being switched to the fixed-dose combination. The 40 mg rosuvastatin dose should only be used in patients with severe hypercholesterolaemia at high cardiovascular risk (in particular those with familial hypercholesterolaemia) who have not achieved their treatment goal on rosuvastatin 20 mg and in whom routine follow-up will be performed; specialist supervision is recommended when the 40 mg rosuvastatin dose is used (see section 4.4).

Special populations

Elderly

A rosuvastatin start dose of 5 mg is recommended in patients over 70 years of age; the fixed 40 mg rosuvastatin content of this combination is generally not appropriate for the initiation of therapy in this population. No dose adjustment of the bempedoic acid component is required in elderly patients.

Renal impairment

No dose adjustment is required in mild renal impairment. The 40 mg rosuvastatin dose is contraindicated in patients with moderate renal impairment (creatinine clearance < 60 mL/min); BEMPETOL – R40 must therefore not be used in these patients. Use in severe renal impairment (creatinine clearance < 30 mL/min) is contraindicated for all rosuvastatin doses (see section 4.3). Experience with bempedoic acid in severe renal impairment is limited and additional monitoring for adverse reactions is warranted.

Hepatic impairment

BEMPETOL – R40 is contraindicated in active liver disease (see section 4.3). No dose adjustment of the bempedoic acid component is required in mild or moderate hepatic impairment (Child-Pugh A or B); it has not been studied in severe hepatic impairment (Child-Pugh C). Increased systemic exposure to rosuvastatin has been observed at Child-Pugh scores of 8 and 9.

Race

Increased systemic exposure to rosuvastatin has been observed in Asian subjects, in whom the 40 mg rosuvastatin dose is contraindicated. BEMPETOL – R40 must therefore not be used in patients of Asian ancestry (see section 4.3).

Paediatric population

The safety and efficacy of this fixed-dose combination in children and adolescents below 18 years of age have not been established. No data are available.

Method of administration

For oral use. The tablet should be swallowed whole with water and may be taken with or without food.

4.3 Contraindications

BEMPETOL – R40 is contraindicated in the following situations:

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Pregnancy and breast-feeding, and in women of childbearing potential not using appropriate contraceptive measures (see section 4.6).
- Active liver disease, including unexplained persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3 times the upper limit of normal (ULN).
- Severe renal impairment (creatinine clearance < 30 mL/min).
- Myopathy.
- Concomitant use of ciclosporin.
- Concomitant use of the combination sofosbuvir/velpatasvir/voxilaprevir.
- Concomitant use with simvastatin > 40 mg daily.

Because BEMPETOL – R40 contains the 40 mg rosuvastatin dose, it is additionally contraindicated in patients with pre-disposing factors for myopathy/rhabdomyolysis, namely:

- 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.
- Patients of Asian ancestry.
- Concomitant use of fibrates.

4.4 Special warnings and precautions for use

Musculoskeletal effects and risk of myopathy

Effects on skeletal muscle, e.g. myalgia, myopathy and, rarely, rhabdomyolysis, have been reported in rosuvastatin-treated patients at all doses and in particular at doses above 20 mg. Bempedoic acid increases plasma concentrations of statins, including a 1.4- to 1.5-fold increase in rosuvastatin exposure (see section 4.5); the reporting rates for rhabdomyolysis, serious renal events and serious hepatic events are higher at the 40 mg rosuvastatin dose contained in this product. All patients should be advised to report promptly any unexplained muscle pain, tenderness, weakness or cramps, particularly if associated with malaise or fever.

Creatine kinase (CK) should not be measured following strenuous exercise or in the presence of another plausible cause of CK increase. If CK is markedly elevated at baseline (> 5× ULN), a confirmatory test should be performed within 5–7 days and treatment should not be started if the elevation is confirmed. Therapy should

be discontinued if CK levels are markedly elevated (> 5× ULN) or if muscular symptoms are severe and cause daily discomfort (even where CK is ≤ 5× ULN). If myopathy is confirmed by a CK level > 10× ULN, treatment must be discontinued immediately.

There have been very rare reports of immune-mediated necrotising myopathy (IMNM) during or after treatment with statins, characterised by proximal muscle weakness and elevated serum creatine kinase that persist despite discontinuation. Statins may also induce de novo or aggravate pre-existing myasthenia gravis or ocular myasthenia; treatment should be discontinued if symptoms worsen.

BEMPETOL – R40 should not be used in any patient with an acute, serious condition suggestive of myopathy or predisposing to renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, or severe metabolic, endocrine or electrolyte disorders; or uncontrolled seizures). It must not be co-administered with systemic fusidic acid, or within 7 days of stopping fusidic acid (see section 4.5).

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS), which may be life-threatening or fatal, have been reported with rosuvastatin. Patients should be advised of the signs and symptoms and closely monitored. If signs or symptoms suggestive of these reactions appear, treatment should be discontinued immediately. If a patient has developed SJS or DRESS with the use of this product, treatment must not be restarted at any time.

Hepatic effects

Elevations of > 3× ULN in ALT and AST have been reported with bempedoic acid; these have generally been asymptomatic and reversible. Liver function tests should be performed prior to initiation and are recommended at 3 months after initiation. Treatment should be discontinued or the dose reduced if serum transaminases exceed 3× ULN. The product should be used with caution in patients who consume excessive quantities of alcohol or have a history of liver disease.

Renal effects

Proteinuria, mostly tubular in origin, has been observed with higher rosuvastatin doses, in particular 40 mg, and is usually transient. An assessment of renal function should be considered during routine follow-up. Bempedoic acid may cause minor, reversible increases in serum creatinine and blood urea nitrogen through inhibition of OAT2-dependent tubular secretion of creatinine; this does not appear to reflect worsening renal function but should be considered when interpreting estimated creatinine clearance.

Increased serum uric acid and gout

Bempedoic acid may raise serum uric acid through inhibition of renal tubular OAT2 and may precipitate or exacerbate gout in predisposed patients. Treatment should be discontinued if hyperuricaemia accompanied by symptoms of gout occurs.

Endocrine effects – diabetes mellitus

Statins as a class may raise blood glucose and, in some patients at high risk of diabetes, produce hyperglycaemia warranting formal diabetes care. This risk is outweighed by the vascular risk reduction and is not a reason to stop treatment. At-risk patients should be monitored clinically and biochemically.

Interstitial lung disease

Exceptional cases of interstitial lung disease have been reported with statins, especially with long-term therapy. If a patient develops signs such as dyspnoea, non-productive cough and deterioration in general health, statin therapy should be discontinued.

Concomitant use of fibrates and protease inhibitors

Concomitant administration of fibrates increases the risk of myopathy and, with bempedoic acid, may increase triglycerides and decrease HDL-cholesterol; the 40 mg rosuvastatin dose is contraindicated with fibrates. Increased systemic exposure to rosuvastatin has been observed with certain protease inhibitors; concomitant use requires careful consideration of the benefit-risk balance (see sections 4.3 and 4.5).

Fertility, contraception and pregnancy

Women of childbearing potential should be advised on effective contraception before initiating treatment and should stop treatment immediately if they plan to become, or become, pregnant (see section 4.6).

Excipients

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. This medicinal product contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction between the active substances

Co-administration of bempedoic acid 180 mg with rosuvastatin resulted in a 1.4- to 1.5-fold increase in rosuvastatin AUC through weak inhibition of OATP1B1/OATP1B3. This interaction is intrinsic to the fixed-dose combination and reinforces the need for the muscle-related monitoring described in section 4.4.

Effects of other medicinal products

- Ciclosporin: rosuvastatin AUC increased approximately 7-fold; concomitant use is contraindicated.
- Protease inhibitors: combinations such as atazanavir/ritonavir increased rosuvastatin AUC and Cmax approximately 3-fold and 7-fold, respectively; concomitant use is not recommended unless the dose is adjusted.
- Gemfibrozil and other fibrates: gemfibrozil increased rosuvastatin Cmax and AUC approximately 2-fold; the 40 mg rosuvastatin dose is contraindicated with fibrates.
- Sofosbuvir/velpatasvir/voxilaprevir: increased rosuvastatin AUC approximately 7.4-fold; concomitant use is contraindicated.
- Fusidic acid: risk of myopathy, including rhabdomyolysis (with some fatalities); must not be co-administered with systemic fusidic acid or within 7 days of stopping it.
- Erythromycin: rosuvastatin AUC decreased by 20% and Cmax by 30%.
- Antacids (aluminium/magnesium hydroxide): rosuvastatin plasma concentration decreased by approximately 50%; the effect is mitigated when the antacid is taken 2 hours after the dose.
- Ticagrelor: may reduce renal excretion of rosuvastatin, with reports of decreased renal function, increased CPK and rhabdomyolysis; renal function and CPK monitoring is recommended.
- Probenecid: increased bempedoic acid AUC 1.7-fold and its active metabolite (ESP15228) AUC 1.9-fold; not considered clinically meaningful.

Effects of the active substances on other medicinal products

- Vitamin K antagonists (e.g. warfarin): initiation or up-titration may increase the INR; appropriate INR monitoring is advised.
- Oral contraceptives: rosuvastatin increased ethinylestradiol and norgestrel AUC by 26% and 34%, respectively.
- OATP1B1/OATP1B3 substrates: bempedoic acid may increase plasma concentrations of substrates such as certain statins, bosentan and selected antivirals.

4.6 Fertility, pregnancy and lactation

Pregnancy

BEMPETOL – R40 is contraindicated during pregnancy. Because cholesterol and other products of cholesterol biosynthesis are essential for foetal development, the potential risk from inhibition of HMG-CoA reductase and of ATP-citrate lyase outweighs any advantage of treatment during pregnancy. Animal studies with both active substances have shown reproductive toxicity. If a patient becomes pregnant during treatment, the product should be discontinued immediately.

Breast-feeding

BEMPETOL – R40 is contraindicated during breast-feeding. Rosuvastatin is present in human milk and there is a potential risk of serious adverse reactions in the breast-fed infant.

Fertility

There are no data on the effect of the combination on human fertility. Based on animal studies, no effect on fertility is expected with bempedoic acid, and no effects on fertility have been observed with rosuvastatin.

4.7 Effects on ability to drive and use machines

BEMPETOL – R40 has no or negligible influence on the ability to drive and use machines. When driving or operating machines it should be taken into account that dizziness may occur during treatment.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions with bempedoic acid are hyperuricaemia, pain in extremity, anaemia and gout. Adverse reactions with rosuvastatin are generally mild and transient, the most frequent being headache, myalgia, gastrointestinal disturbances, diabetes mellitus and asthenia; the reporting rates for rhabdomyolysis and serious renal and hepatic events are higher at the 40 mg dose.

Tabulated list of adverse reactions

Adverse reactions are listed by MedDRA system organ class and frequency category, 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 1. Adverse reactions reported with bempedoic acid

System Organ Class	Adverse reaction	Frequency
Blood and lymphatic system disorders	Anaemia	Common
	Haemoglobin decreased	Uncommon
Metabolism and nutrition disorders	Gout	Common
	Hyperuricaemia	Common
	Weight decreased	Uncommon
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	Glomerular filtration rate decreased	Common
	Blood creatinine increased	Uncommon
	Blood urea increased	Uncommon

Table 2. Adverse reactions reported with rosuvastatin

System Organ Class	Adverse reaction	Frequency
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	Common
	Dizziness	Common
	Polyneuropathy	Very rare
	Memory loss	Very rare
	Peripheral neuropathy	Not known
	Sleep disturbances (including insomnia and nightmares)	Not known
	Myasthenia gravis	Not known
Eye disorders	Ocular myasthenia	Not known
Respiratory, thoracic and mediastinal disorders	Cough	Not known
	Dyspnoea	Not known
Gastrointestinal disorders	Constipation	Common
	Nausea	Common
	Abdominal pain	Common
	Pancreatitis	Rare
	Diarrhoea	Not known
Hepatobiliary disorders	Increased hepatic transaminases	Rare
	Jaundice	Very rare
	Hepatitis	Very rare
Skin and subcutaneous tissue disorders	Pruritus	Uncommon
	Rash	Uncommon
	Urticaria	Uncommon
	Stevens-Johnson syndrome	Not known
	Drug reaction with eosinophilia and systemic symptoms (DRESS)	Not known
Musculoskeletal and connective tissue disorders	Myalgia	Common
	Myopathy (including myositis)	Rare
	Rhabdomyolysis	Rare
	Lupus-like syndrome	Rare
	Muscle rupture	Rare
	Arthralgia	Very rare
	Tendon disorders, sometimes complicated by rupture	Not known
	Immune-mediated necrotising myopathy	Not known
Renal and urinary disorders	Haematuria	Very rare
Reproductive system and breast disorders	Gynaecomastia	Very rare

System Organ Class	Adverse reaction	Frequency
General disorders and administration site conditions	Asthenia	Common
	Oedema	Not known

The following adverse reactions have been reported with some statins: sexual dysfunction and, exceptionally, interstitial lung disease.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

There is no specific antidote for BEMPETOL – R40; in the event of overdose the patient should be treated symptomatically and supportive measures instituted as required.

Bempedoic acid: doses up to 240 mg/day (1.3 times the recommended dose) have been administered in clinical trials with no evidence of dose-limiting toxicity.

Rosuvastatin: there is no specific treatment in the event of overdose. Liver function and CK levels should be monitored. Haemodialysis is unlikely to be of benefit.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: bempedoic acid – lipid modifying agents, other lipid modifying agents, ATC code: C10AX15; rosuvastatin – HMG-CoA reductase inhibitors, ATC code: C10AA07.

Mechanism of action

Bempedoic acid is an adenosine triphosphate citrate lyase (ACL) inhibitor that lowers LDL-C by inhibiting cholesterol synthesis in the liver. ACL is an enzyme upstream of HMG-CoA reductase in the cholesterol biosynthesis pathway. Bempedoic acid is a prodrug requiring coenzyme A activation by very long-chain acyl-CoA synthetase 1 (ACSVL1), an enzyme expressed primarily in the liver and not in skeletal muscle; inhibition of ACL results in decreased hepatic cholesterol synthesis and up-regulation of LDL receptors, increasing LDL-C clearance from the blood.

Rosuvastatin is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts HMG-CoA to mevalonate, a precursor of cholesterol. It acts primarily in the liver, increasing the number of hepatic LDL receptors on the cell surface, thereby enhancing uptake and catabolism of LDL and inhibiting hepatic synthesis of very-low-density lipoprotein (VLDL).

Pharmacodynamic effects

Administration of bempedoic acid, alone and in combination with other lipid-modifying agents, decreases LDL-C, non-HDL-C, apolipoprotein B, total cholesterol and C-reactive protein. Rosuvastatin reduces elevated LDL-C, total cholesterol and triglycerides and increases HDL-C. The combined use of the two complementary mechanisms provides additional LDL-C lowering in patients requiring intensified therapy.

5.2 Pharmacokinetic properties

Bempedoic acid

Absorption: bempedoic acid is absorbed with a median time to maximum concentration of approximately 3.5 hours; food has no effect on oral bioavailability. Steady state is achieved after about 7 days with a mean accumulation ratio of approximately 2.3-fold.

Distribution: the apparent volume of distribution is approximately 18 L. Plasma protein binding of bempedoic acid, its glucuronide and its active metabolite (ESP15228) is approximately 99.3%, 98.8% and 99.2%, respectively. Bempedoic acid does not partition into red blood cells.

Biotransformation: the primary route of elimination is metabolism to the acyl glucuronide; bempedoic acid is also reversibly converted to the active metabolite ESP15228 by aldo-keto reductase activity. Both compounds are converted to inactive glucuronide conjugates by UGT2B7. Bempedoic acid does not inhibit or induce cytochrome P450 enzymes.

Elimination: the steady-state clearance is approximately 12.1 mL/min and renal clearance of unchanged drug is less than 2% of total clearance. The mean half-life is approximately 19 hours at steady state. Following a 240 mg dose, approximately 62% is recovered in urine and 25% in faeces.

Rosuvastatin

Absorption: peak plasma concentrations are reached 3 to 5 hours after oral dosing; absolute bioavailability is approximately 20%. Cmax and AUC increase in approximate proportion to dose and are not affected by food or time of administration.

Distribution: rosuvastatin is taken up extensively by the liver, its primary site of action; the volume of distribution is approximately 134 L and plasma protein binding (mainly to albumin) is approximately 88%.

Biotransformation: rosuvastatin undergoes limited metabolism (approximately 10%), principally by CYP2C9 to N-desmethyl rosuvastatin, which has less activity than the parent; the parent compound accounts for more than 90% of HMG-CoA reductase inhibitory activity.

Elimination: approximately 90% of the dose is excreted unchanged in the faeces and the remainder in the urine; the elimination half-life is approximately 19 hours. Increased systemic exposure has been observed in Asian subjects and in patients with certain SLCO1B1/ABCG2 polymorphisms.

5.3 Preclinical safety data

Bempedoic acid: non-clinical data reveal no special hazard for humans based on studies of safety pharmacology and repeated-dose toxicity, other than reproductive and developmental toxicity observed in animals, which underlies the contraindication in pregnancy. Bempedoic acid was not genotoxic in a standard battery of tests.

Rosuvastatin: preclinical data, based on conventional studies of safety pharmacology, genotoxicity and carcinogenic potential, reveal no special hazard for humans other than effects consistent with the pharmacological action of the class. Animal studies provide limited evidence of reproductive toxicity, consistent with the contraindication in pregnancy and lactation.

6. Pharmaceutical particulars

6.1 List of excipients

- Microcrystalline Cellulose BP
- Lactose BP
- Croscarmellose Sodium BP
- Low Substituted Hydroxypropyl Cellulose (L-HPC LH 11) BP
- Isopropyl Alcohol BP
- Magnesium Stearate BP
- Colloidal Silicon Dioxide BP
- Easy Coat AFC Iron Oxide Red IHS
- Purified Water BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

Light pink, round, biconvex film-coated tablets with a break-line on one side and plain on the other. Ten tablets are packed in an Alu-Alu blister; three Alu-Alu blisters (30 tablets) are packed in a printed carton together with a package insert.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

TIBA HEALTHCARE LIMITED

8. Marketing Authorisation Number

CTD12673

9. Date of first authorisation / renewal of the authorisation

06.07.2026

10. Date of revision of the text

02.07.2026