**BEMPESTA**

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

abbreviated prescribing information for BEMPESTA (Bempedoic Acid Film coated Tablets 180 mg) [Please refer the complete prescribing information available at www.torrentpharma.com ]

**PHARMACOLOGICAL PROPERTIES** 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-glutarylcoenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway. Bempedoic acid requires coenzyme A (CoA) activation by very long-chain acyl-CoA synthetase 1 (ACSVL1) to ETC-1002-CoA. ACSVL1 is expressed primarily in the liver and not in skeletal muscle. 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. Additionally, inhibition of ACL by ETC-1002-CoA results in concomitant suppression of hepatic fatty acid biosynthesis.

**INDICATION:** It is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic Cardiovascular disease who require additional lowering of LDL-C.

**DOSAGE AND ADMINISTRATION:** The recommended dose of Bempedoic Acid Tablets 180 mg is one film-coated tablet of 180 mg taken once daily.

**CONTRAINDICATION:** Hypersensitivity to the active substance or to any of the excipients. Pregnancy, Breast-feeding,Concomitant use with simvastatin > 40 mg daily

**WARNINGS & PRECAUTIONS**: *Potential risk of myopathy with concomitant use of statins:* Bempedoic acid increases plasma concentrations of statins. Patients receiving Bempedoic Acid Tablets 180 mg as adjunctive therapy to a statin should be monitored for adverse reactions that are associated with the use of high doses of statins. Statins occasionally cause myopathy. In rare cases, myopathy may take the form of rhabdomyolysis with or without acute renal failure secondary to myoglobinuria, and can lead to fatality. All patients receiving Bempedoic Acid Tablets 180 mg in addition to a statin should be advised of the potential increased risk of myopathy and told to report promptly any unexplained muscle pain, tenderness, or weakness. If such symptoms occur while a patient is receiving treatment with Bempedoic Acid Tablets 180 mg and a statin, a lower maximum dose of the same statin or an alternative statin, or discontinuation of Bempedoic Acid Tablets 180 mg and initiation of an alternative lipid-lowering therapy should be considered under close monitoring of lipid levels and adverse reactions. If myopathy is confirmed by a creatine phosphokinase (CPK) level > 10× upper limit of normal (ULN), Bempedoic Acid Tablets 180 mg and any statin that the patient is taking concomitantly should be immediately discontinued. Myositis with a CPK level > 10× ULN was rarely reported with bempedoic acid and background simvastatin 40 mg therapy. Doses of simvastatin > 40 mg should not be used with Bempedoic Acid Tablets 180 mg. *Increased serum uric acid:* Bempedoic acid may raise the serum uric acid level due to inhibition of renal tubular OAT2 and may cause or exacerbate hyperuricaemia and precipitate gout in patients with a medical history of gout or predisposed to gout (see section 4.8). Treatment with Bempedoic Acid Tablets 180 mg should be discontinued if hyperuricaemia accompanied with symptoms of gout appear. *Elevated liver enzymes:* In clinical trials, elevations of > 3× ULN in the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been reported with bempedoic acid. These elevations have been asymptomatic and not associated with elevations ≥ 2× ULN in bilirubin or with cholestasis and have returned to baseline with continued treatment or after discontinuation of therapy. Liver function tests should be performed at initiation of therapy. Treatment with Bempedoic Acid Tablets 180 mg should be discontinued if an increase in transaminases of > 3× ULN persists.

*Renal impairment:* There is limited experience with bempedoic acid in patients with severe renal impairment (defined as eGFR < 30 mL/min/1.73 m2), and patients with ESRD on dialysis have not been studied. Additional monitoring for adverse reactions may be warranted in these patients when Bempedoic Acid Tablets 180 mg is administered. *Hepatic impairment:* Patients with severe hepatic impairment (Child-Pugh C) have not been studied. Periodic liver function tests should be considered for patients with severe hepatic impairment. *Contraception:* Women of childbearing potential must use effective contraception during treatment. Patients should be advised to stop taking Bempedoic Acid Tablets 180 mg before stopping contraceptive measures if they plan to become pregnant.

**DRUG INTERACTIONS:** Transporter-mediated drug interactions in vitro drug interaction studies suggest bempedoic acid, as well as its active metabolite and glucuronide form, are not substrates of commonly characterised drug transporters with the exception of bempedoic acid glucuronide, which is an OAT3 substrate. *Probenecid:* an inhibitor of glucuronide conjugation, Administration of bempedoic acid 180 mg with steady-state probenecid resulted in a 1.7-fold increase in bempedoic acid area under the curve (AUC) and a 1.9-fold increase in bempedoic acid active metabolite (ESP15228) AUC. These elevations are not clinically meaningful and do not impact dosing recommendations. *Effects of bempedoic acid on other medicinal products:* Statins: The pharmacokinetic interactions between bempedoic acid 180 mg and simvastatin 40 mg, atorvastatin 80 mg, pravastatin 80 mg, and rosuvastatin 40 mg were evaluated in clinical trials. Administration of a single dose of simvastatin 40 mg with steady-state bempedoic acid 180 mg resulted in a 2-fold increase in simvastatin acid exposure. Elevations of 1.4-fold to 1.5-fold in AUC of atorvastatin, pravastatin, and rosuvastatin (administered as single doses) and/or their major metabolites were observed when coadministered with bempedoic acid 180 mg. Higher elevations have been observed when these statins were coadministered with a supratherapeutic 240 mg dose of bempedoic acid. *Transporter-mediated drug interactions:* Bempedoic acid and its glucuronide weakly inhibit OATP1B1 and OATP1B3 at clinically relevant concentrations. Coadministration of bempedoic acid with medicinal products that are substrates of OATP1B1 or OATP1B3 may result in increased plasma concentrations of these medicinal products. Bempedoic acid inhibits OAT2 in vitro, which may be the mechanism responsible for minor elevations in serum creatinine and uric acid. Inhibition of OAT2 by bempedoic acid may also potentially increase plasma concentrations of medicinal products that are substrates of OAT2. Bempedoic acid may also weakly inhibit OAT3 at clinically relevant concentrations. Total ezetimibe (ezetimibe and its glucuronide form) and ezetimibe glucuronide AUC and Cmax increased approximately 1.6- and 1.8-fold, respectively, when a single dose of ezetimibe was taken with steady-state bempedoic acid. This increase is likely due to inhibition of OATP1B1 by bempedoic acid, which results in decreased hepatic uptake and subsequently decreased elimination of ezetimibe-glucuronide.

**ADVERSE REACTIONS:** Blood and lymphatic system disorders: Anaemia (Common), Haemoglobin decreased (Uncommon ). Metabolism and nutrition disorders: Gout (Common), Hyperuricaemia (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)

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

**IN/ BEMPESTA/MAY-2022/01/ABPI**

(Additional information is available on request)