Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Bempetol 180mg Tablets
(Bempedoic Acid 180mg)

2. Qualitative and quantitative composition

Each film-coated tablet contains 180mg of Bempedoic Acid.

This product contains lactose
For a full list of excipients, see section 6.1

3. Pharmaceutical form

White coloured, round shaped, biconvex, film-coated tablet, plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

Bempedoic acid is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin (see sections 4.2, 4.3, and 4.4)
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

4.2 Posology and method of administration

Posology

The recommended dose of Bempedoic acid is one film-coated tablet of 180 mg taken once daily.

Concomitant simvastatin therapy
When Bempedoic acid is coadministered with simvastatin, simvastatin dose should be limited to 20 mg daily (or 40 mg daily for patients with severe hypercholesterolaemia and high risk for cardiovascular complications, who have not achieved their treatment goals on lower doses and when the benefits are
expected to outweigh the potential risks) (see sections 4.4 and 4.5).

Special populations

Elderly patients

No dose adjustment is necessary in elderly patients (see section 5.2).

Patients with renal impairment

No dose 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 m^2), 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 (see section 4.4).

Patients with hepatic impairment
No dose adjustment is necessary in patients with mild or moderate hepatic impairment (Child-Pugh A or B). 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 (see section 4.4).

Paediatric population

The safety and efficacy of Bempedoic acid in children aged less than 18 years have not yet been established. No data are available.

Method of administration

Each film-coated tablet should be taken orally with or without food. Tablet should be swallowed whole.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Pregnancy (see section 4.6)
- Breast Feeding (see section 4.6)
- Concomitant use with simvastatin >40mg daily (see section 4.2, 4.4, and 4.5)

4.4 Special warnings and precautions for use

Potential risk of myopathy with concomitant use of statins

Bempedoic acid increases plasma concentrations of statins (see section 4.5). Patients receiving Bempedoic acid 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 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 and a statin, a lower maximum dose of the same statin or an alternative statin, or discontinuation of Bempedoic acid 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 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 (see sections 4.2 and 4.3).

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 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 should be discontinued if an increase in transaminases of > 3× ULN persists (see section 4.8).

Renal impairment

There is limited experience with bempedoic acid in patients with severe renal impairment (defined as eGFR < 30 mL/min/1.73 m^2), and patients with ESRD on dialysis have not been studied (see section 5.2). Additional monitoring for adverse reactions may be warranted in these patients when Bempedoic acid is administered.

Hepatic impairment

Patients with severe hepatic impairment (Child-Pugh C) have not been studied (see section 5.2). 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 before stopping contraceptive measures if they plan to become pregnant.

Excipients

Bempedoic acid contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other medicinal products on bempedoic acid

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

Probenecid, an inhibitor of glucuronide conjugation, was studied to evaluate the potential effect of these inhibitors on the pharmacokinetics of bempedoic acid. 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 (see section 4.4).

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 (i.e., bosentan, fimasartan, asunaprevir, glecaprevir, grazoprevir, voxilaprevir, and statins such as atorvastatin, pravastatin, fluvastatin, pitavastatin, rosuvastatin, and simvastatin [see section 4.4]) 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 (see section 4.8). 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.

Ezetimibe

Total ezetimibe (ezetimibe and its glucuronide form) and ezetimibe glucuronide AUC and C_{max} 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. Increases in AUC and C_{max} for ezetimibe were less than 20%. These elevations are not clinically meaningful and do not impact dosing recommendations.

Other interactions studied

Bempedoic acid had no effect on the pharmacokinetics or pharmacodynamics of metformin or the pharmacokinetics of oral contraceptive norethindrone/ethinyl estradiol.

4.6 Pregnancy and Lactation

Pregnancy

Bempedoic acid is contraindicated during pregnancy (see section 4.3).

There are no or limited amount of data from the use of bempedoic acid in pregnant women. Studies in animals with bempedoic acid have shown reproductive toxicity (see section 5.3).

Because bempedoic acid decreases cholesterol synthesis and possibly the synthesis of other cholesterol derivatives needed for normal foetal development, Bempedoic acid may cause foetal harm when administered

to pregnant women. Bempedoic acid should be discontinued prior to conception or as soon as pregnancy is recognized (see section 4.3).

Women of childbearing potential

Women of childbearing potential should use effective contraception during treatment (see section 4.4). Breast-feeding

It is unknown whether bempedoic acid/metabolites are excreted in human milk. Because of the potential for serious adverse reactions, women taking Bempedoic acid should not breast-feed their infants. Bempedoic acid is contraindicated during breast-feeding (see section 4.3).

Fertility

No data on the effect of Bempedoic acid on human fertility are available. Based on animal studies, no effect on reproduction or fertility is expected with Bempedoic acid (see section 5.3).

4.7 Effects on ability to drive and use machines

Bempedoic acid has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

Summary of the safety profile

The safety profile of bempedoic acid has been studied in 4 controlled phase 3 clinical studies (N=3,621) including patients with hypercholesterolemia on maximum tolerated statin dose (2 studies; n=3008) and patients on no or low dose statins (2 studies; n=613). The most commonly reported adverse reactions with bempedoic acid during pivotal trials 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

Adverse reactions reported with bempedoic acid are displayed by system organ class and frequency in table 1.

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 1: Adverse reactions

System organ class (SOC)	Adverse reactions	Frequency categories
Blood and lymphatic system disorders	Anaemia	Common
	Haemoglobin decreased	Uncommon
Metabolism and nutrition disorders	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

Description of selected adverse reactions

Hepatic enzyme elevations
Increases in serum transaminases (AST and/or ALT) have been reported with bempedoic acid. In controlled clinical studies, the incidence of elevations (≥ 3× ULN) in hepatic transaminase levels was 0.7% for patients treated with bempedoic acid and 0.3% for placebo. These elevations in transaminases were not associated with other evidence of liver dysfunction (see section 4.4).

Increased serum uric acid
Increases in serum uric acid were observed in clinical trials with bempedoic acid possibly related to inhibition of renal tubular OAT2 (see section 4.5). In the pooled placebo-controlled trials, a mean increase of 0.8 mg/dL (47.6 micromole/L) in uric acid compared to baseline was observed with bempedoic acid at week 12. The elevations in serum uric acid usually occurred within the first 4 weeks of treatment and returned to baseline following discontinuation of treatment. Gout was reported in 1.4% of patients treated with bempedoic acid and 0.4% of patients treated with placebo (see section 4.4). In both treatment groups, patients who reported gout were more likely to have a medical history of gout and/or baseline levels of uric acid above the ULN.

Effects on serum creatinine and blood urea nitrogen

Bempedoic acid has been shown to increase serum creatinine and blood urea nitrogen (BUN). In the pooled placebo-controlled trials, a mean increase of 0.05 mg/dL (4.4 micromole/L) in serum creatinine and a mean increase of 1.7 mg/dL (0.61 mmol/L) in BUN compared to baseline was observed with bempedoic acid at week 12. The elevations in serum creatinine and BUN usually occurred within the first 4 weeks of treatment, remained stable, and returned to baseline following discontinuation of treatment.

The observed elevations in serum creatinine may be associated with bempedoic acid inhibition of OAT2-dependent renal tubular secretion of creatinine (see section 4.5), representing a drug- endogenous substrate interaction and does not appear to indicate worsening renal function. This effect should be considered when interpreting changes in estimated creatinine clearance in patients on Bempedoic acid therapy, particularly in patients with medical conditions or receiving medicinal products that require monitoring of estimated creatinine clearance.

Decreased haemoglobin
Decreases in haemoglobin were observed in clinical trials with bempedoic acid. In the pooled placebo-controlled trials, a decrease in haemoglobin from baseline of ≥ 20 g/L and < lower limit of normal (LLN) was observed in 4.6% of patients in the bempedoic acid group compared with 1.9% of patients on placebo. Greater than 50 g/L and < LLN decreases in haemoglobin were reported at similar rates in bempedoic acid and placebo groups (0.2% versus 0.2%, respectively). The decreases in haemoglobin usually occurred within the first 4 weeks of treatment and returned to baseline following discontinuation of treatment. Among patients who had normal haemoglobin values at baseline, 1.4% in the bempedoic acid group and 0.4% in the placebo group experienced haemoglobin values below LLN while on treatment. Anaemia was reported in 2.5% of patients treated with bempedoic acid and 1.6% of patients treated with placebo.

Elderly population
Of the 3,621 patients treated with bempedoic acid in the placebo-controlled studies, 2,098 (58%) were
> 65 years old. No overall difference in safety was observed between elderly and the younger population.

4.9 Overdose

Doses up to 240 mg/day (1.3 times the approved recommended dose) have been administered in clinical trials with no evidence of dose limiting toxicity.

No adverse events were observed in animal studies at exposures up to 14-fold higher than those in patients treated with bempedoic acid at 180 mg once daily.

There is no specific treatment for a Bempedoic acid overdose. In the event

of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Lipid modifying agents, other lipid modifying agents, ATC code: C10AX15

Mechanism of action

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 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.

Pharmacodynamic effects

Administration of bempedoic acid alone and in combination with other lipid modifying medicinal products decreases LDL-C, non-high density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (apo B), and total cholesterol (TC) in patients with hypercholesterolaemia or mixed dyslipidaemia.

Because patients with diabetes are at elevated risk for atherosclerotic cardiovascular disease, the clinical trials of bempedoic acid included patients with diabetes mellitus. Among the subset of patients with diabetes, lower levels of HbA1c were observed as compared to placebo (on average 0.2%). In patients without diabetes, no difference in HbA1c was observed between bempedoic acid and placebo and there were no differences in the rates of hypoglycaemia.

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.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with bempedoic acid in paediatric population from 4 to

less than 18 years of age in the treatment of elevated cholesterol. See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

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. Bempedoic acid pharmacokinetic parameters are presented as the mean [standard deviation (SD)] unless otherwise specified. Bempedoic acid can be considered a prodrug that is activated intracellularly by ACSVL1 to ETC-1002-CoA. The steady-state C_{max} and AUC following multiple dose administration in patients with hypercholesterolaemia were 24.8 (6.9) microgram/mL and 348 (120) microgram·h/mL, respectively. Bempedoic acid steady-state pharmacokinetics were generally linear over a range of 120 mg to 220 mg. There were no time-dependent changes in bempedoic acid pharmacokinetics following repeat administration at the recommended dose, and bempedoic acid steady-state was achieved after 7 days. The mean accumulation ratio of bempedoic acid was approximately 2.3-fold.

Concomitant food administration had no effect on the oral bioavailability of bempedoic acid when administered as Bempedoic acid 180 mg tablets. Food slows the absorption rate of bempedoic acid; the absorption rate constant with food is 0.32/h.

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 red blood cells.

Biotransformation

In vitro metabolic interaction studies suggest that bempedoic acid, as well as its active metabolite and glucuronide forms are not metabolised by and do not inhibit or induce cytochrome P450 enzymes.

The primary route of elimination for bempedoic acid is through metabolism to 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 $AUC_{0\text{-}48h}$, respectively.

The steady-state C_{max} and AUC of the equipotent active metabolite (ESP15228) of bempedoic acid in patients with hypercholesterolaemia were 3.0 (1.4) microgram/mL and 54.1 (26.4) microgram·h/mL, respectively. ESP15228 likely made a minor contribution to the overall clinical activity of bempedoic acid based on systemic exposure and pharmacokinetic properties.

Elimination

The steady-state clearance (CL/F) of bempedoic acid determined from a population PK analysis in patients with hypercholesterolaemia was 12.1 mL/min after once-daily dosing; renal clearance of unchanged bempedoic acid represented less than 2% of total clearance. The mean (SD) half-life for bempedoic acid in humans was 19 (10) hours at steady-state.

Following single oral administration of 240 mg of bempedoic acid (1.3 times the approved recommended dose), 62.1% of the total dose (bempedoic acid and its metabolites) was recovered in urine, primarily as the acyl glucuronide conjugate of bempedoic acid, and 25.4% was recovered in faeces. Less than 5% of the administered dose was excreted as unchanged bempedoic acid in faeces and urine combined.

Special populations

Renal impairment
Pharmacokinetics of bempedoic acid was evaluated in a population PK analysis performed on pooled data from all clinical trials (n=2,261) to assess renal function on the steady-state AUC of bempedoic acid and in a single-dose pharmacokinetic study in subjects with varying degrees of renal function.
Compared to patients with normal renal function, the mean bempedoic acid exposures were higher in patients with mild or moderate renal impairment by 1.4-fold (90% PI: 1.3, 1.4) and 1.9-fold
(90% PI: 1.7, 2.0), respectively (see section 4.4).

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 m^2) compared to those with normal renal function. Clinical studies of bempedoic acid did not include patients with ESRD on dialysis (see section 4.4).

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 C_{max} and AUC were decreased by 11% and 22%, respectively, in patients with mild hepatic impairment 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).

Other special populations
The pharmacokinetics of bempedoic acid were not affected by age, gender, or race. Body weight was a statistically significant covariate. The lowest quartile of body weight (< 73 kg) was associated with an approximate 30% greater exposure. The increase in exposure was not clinically significant and no dose adjustments are recommended based on weight.

5.3 Preclinical safety data

The standard battery of genotoxicity studies has not identified any mutagenic or clastogenic potential of bempedoic acid. In full lifetime carcinogenicity studies in rodents, bempedoic acid increased the incidence of hepatocellular and thyroid gland follicular tumours in male rats and hepatocellular tumours in male mice. Because these are common tumours observed in rodent lifetime bioassays and the mechanism for tumourigenesis is secondary to a rodent-specific PPAR alpha activation, these tumours are not considered to translate to human risk.

Increased liver weight and hepatocellular hypertrophy were observed in rats only and were partially reversed after the 1-month recovery at ≥ 30 mg/kg/day or 4 times the exposure in humans at 180 mg. Reversible, non-adverse changes in laboratory parameters indicative of these hepatic effects, decreases in red blood cell and coagulation parameters, and increases in urea nitrogen and creatinine were observed in both species at tolerated doses. The NOAEL for adverse response in the chronic studies was 10 mg/kg/day and 60 mg/kg/day associated with exposures below and 15 times the human exposure at 180 mg in rats and monkeys, respectively.

Bempedoic acid was not teratogenic or toxic to embryos or foetuses in pregnant rabbits at doses up to 80 mg/kg/day or 12 times the systemic exposure in humans at 180 mg. Pregnant rats given bempedoic acid at 10, 30, and 60 mg/kg/day during organogenesis had decreased numbers of viable foetuses and reduced foetal body weight at ≥ 30 mg/kg/day or 4 times the systemic exposure in humans at 180 mg. An increased incidence of foetal skeletal findings (bent scapula and ribs) were observed at all doses, at exposures below the systemic exposure in humans at 180 mg. In a pre- and post-natal development study, pregnant rats administered bempedoic acid at 5, 10, 20 and 30 mg/kg/day throughout

pregnancy and lactation had adverse maternal effects at ≥ 20 mg/kg/day and reductions in numbers of live pups and pup survival, pup growth and learning and memory at ≥ 10 mg/kg/day, with maternal exposures at 10 mg/kg/day, less than the exposure in humans at 180 mg.

No data are available on the effect of Bempedoic acid on human fertility. Administration of bempedoic acid to male and female rats prior to mating and through gestation day 7 in females resulted in changes in estrous cyclicity, decreased numbers of corpora lutea and implants at ≥ 30 mg/kg/day with no effects on male or female fertility or sperm parameters at 60 mg/kg/day (4 and 9 times the systemic exposure in humans at 180 mg, respectively).

6. Pharmaceutical Particulars

6.1 List of Excipients

Microcrystalline Cellulose
Lactose
Sodium Starch Glycolate
Colloidal Anhydrous Silica
Hydroxy Propyl Cellulose
Sodium Starch Glycolate
Purified Talc
Magnesium Stearate
Opadry II 89F580003

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life

2 years

6.4 Special Precautions for storage

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

6.5 Nature and Content of container

Alu-Alu 1x10s' blister pack, 3 blisters in one unit carton

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorization Holder

Manufacturing Authorization Holder:
Tiba HealthCare Limited
Address: Power Technics Complex, Mombasa Road
P. O. Box: 243-00623
Nairobi, Kenya
Manufacturing Site Address
Ravenbhel Healthcare Private Limited.

16-17, EPIP, SIDCO, Kartholi
Bari Brahmana- 181133, Jammu, India

8. Marketing Authorization Number
CTD10317

9. Date of first authorization/renewal of the authorization
01/04/2023

10. Date of revision of the text
13/09/2023

11. Dosimetry
Not Applicable

12. Instructions for preparation of Radiopharmaceuticals
Not Applicable