Bempedoic acid and Bempedoic acid with Ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia
Prescribing Support Information for Primary Care.

This information is provided to support primary care clinicians prescribing Bempedoic acid and Bempedoic acid with ezetimibe (Nilemdo® and Nustendi®) for treating primary hypercholesterolaemia or mixed dyslipidaemia as an adjunct to diet in adults.

Category	Bempedoic acid is an adenosine triphosphate citrate lyase (ACL) inhibitor that inhibits cholesterol synthesis in the liver, thereby lowering LDL cholesterol. Bempedoic acid is activated in the liver and not in most peripheral tissues, including skeletal muscle, reducing the potential for adverse effects on muscle (and so is of benefit for patients experiencing statin intolerance).
Therapeutic indications	Bempedoic acid is recommended by NICE TA694 https://www.nice.org.uk/guidance/TA694 (April 2021) in combination with ezetimibe as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults. It is recommended only if: • statins are contraindicated or not tolerated. • ezetimibe alone does not control low-density lipoprotein cholesterol well enough. • Bempedoic acid alone may be appropriate in those patients' intolerant of ezetimibe following consideration of other pharmacological options (Nilemdo®)
Pharmaceutical Form	Bempedoic acid is available currently as monotherapy or in a fixed combination with ezetimibe 10mg. Bempedoic acid (Nilemdo®) (180 mg film-coated tablets) Bempedoic acid in combination with ezetimibe (Nustendi ®) (180 mg/10 mg film-coated tablets)
NICE Guidance and place in therapy	Bempedoic acid with ezetimibe is recommended as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults. It is recommended only if: • statins are contraindicated or not tolerated. • ezetimibe alone does not control low-density lipoprotein cholesterol well enough. **Place in BLMK Lipid Management Pathway** Primary prevention • For patients who are contraindicated or intolerant of statins and have not reached lipid targets (40% non-HDL reduction for primary prevention)

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	consider Bempedoic acid 180mg OD in combination with ezetimibe 10mg to be taken once daily (Nustendi®). • Bempedoic acid alone may be appropriate in those patients' intolerant of ezetimibe following consideration of other pharmacological options (Nilemdo®) • For use in accordance with the NICE TA694. Secondary prevention • For patients who are contraindicated or intolerant of statins and have not reached lipid targets (HDL < 2.6mmol/L and/or LDL-C < 1.8mmol/L for secondary prevention) consider Bempedoic acid 180mg OD in combination with ezetimibe 10mg to be taken once daily (Nustendi®). • Bempedoic acid alone may be appropriate in those patients' intolerant of ezetimibe following consideration of other pharmacological options (Nilemdo®) • For use in accordance with the NICE TA 694.
Initiation and dosing advice	Initiation should be in accordance with NICE recommendations and licensed indication. Refer to SPC. Nustendi® (Bempedoic acid/Ezetimibe) 180mg/10mg tablet: One tablet daily Nilemdo® (Bempedoic acid) 180 mg tablet: One tablet daily Nustendi® and Nilemdo® are green medicines on the BLMK Formulary Note: It is more cost-effective to prescribe Bempedoic acid 180mg/ Ezetimibe 10mg tablets combination product than Bempedoic acid and Ezetimibe as two separate products.
Method of administration	Each Nilemdo® OR Nustendi® tablet should be taken orally with or without food. The tablet should be swallowed whole.
Missed Doses	**If a dose is missed:** • If later the same day the missed dose can be taken and the next can be taken at the regular time the next day. • If the previous days dose has been missed the tablet can be taken at the regular time. The forgotten dose does not need to be taken.
Monitoring and Continuation Criteria	**At baseline** • Full blood count – particularly haemoglobin level (Hb level). Do not start if existing anaemia and discuss risk/ benefit in a patient with history of anaemia. • Serum uric acid – do not start in active gout • Liver function- refer to caution below • Renal function - do not start if eGFR <30ml/min - refer to cautions below

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	• Non-fasting full lipid profile - total cholesterol, HDL-C, non-HDL-C, triglycerides and LDL • If patient develops adverse effects discontinue the medication and seek alternative. **12 weeks post initiation** Full blood count, serum uric acid, liver function, renal function and non-fasting full lipid profile. **Non fasting full Lipid profile** Aim for >40% reduction in non-HDL-C from baseline. Once expected reduction in non-HDL-C is achieved, lipids can be checked every 12 months. Please see BLMK lipid pathway for next steps if >40% reduction in non-HDL-C from baseline is not achieved. **Elevated Urate Levels** Patients with signs or symptoms of hyperuricemia should contact their healthcare provider if symptoms occur (see caution below). **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 in 0.7% compared to 0.2% in placebo. Treatment with Bempedoic acid should be discontinued if an increase in transaminases of >3 × ULN persists. **Haemoglobin** Decrease in haemoglobin was 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. Stop if Hb decrease by ≥20g/L from baseline or < LLN, investigate other possible causes/refer to appropriate specialist The decreases in haemoglobin usually occurred within the first 4 weeks of treatment and returned to baseline following discontinuation of treatment.
Co-prescribing with other medication (see SPC for full details)	• Dosing of Bempedoic acid or Bempedoic acid in combination with ezetimibe should occur either at least 2 hours before or at least 4 hours after administration of a bile acid sequestrant. • When Bempedoic acid or Bempedoic acid in combination with ezetimibe, is co-administered 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). The BNF also states that Bempedoic acid increases the exposure to pravastatin - moderate severity interaction

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	(Note: included for information. Use of Bempedoic acid in combination with a statin is outside the scope of this guidance). • The safety and efficacy of ezetimibe administered with fibrates has not been established. If cholelithiasis is suspected in a patient receiving Bempedoic acid in combination with ezetimibe, and fenofibrate, gallbladder investigations are indicated, and this therapy should be discontinued. • Caution should be exercised when initiating Bempedoic acid or Bempedoic acid in combination with ezetimibe, in combination with ciclosporin and ciclosporin concentrations should be monitored. • If Bempedoic acid or Bempedoic acid in combination with ezetimibe is added to warfarin or other coumarin anticoagulants, the International Normalised Ratio (INR) should be appropriately monitored.
Special Patient Population	**Elderly, gender, race, ethnicity, or body weight** No dose adjustment is needed based on age, gender, race, ethnicity, or body weight. **Renal impairment** No dose adjustment is necessary in patients with mild or moderate 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 end stage renal disease on dialysis have not been studied with Bempedoic acid. Additional monitoring for adverse reactions may be warranted in these patients when Nustendi® or Nilemdo® 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 when considering Nustendi® or Nilemdo®. Due to the unknown effects of the increased exposure to ezetimibe in patients with moderate to severe hepatic impairment (Child-Pugh B and C), Nustendi® is not recommended in these patients. **Paediatric population** The safety and efficacy of Nilemdo® and Nustendi® in children aged less than 18 years have not yet been established. No data are available. **Excipients** Nustendi® and Nilemdo® both contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take these medications.

Contraindications	**Bempedoic acid (Nilemdo®) (180 mg film-coated tablets)** • Hypersensitivity to the active substance or to any of the excipients • Pregnancy • Breast-feeding • Concomitant use with simvastatin 40 mg OD or higher dose. **Bempedoic acid / ezetimibe (Nustendi ®) (180 mg/10 mg film-coated tablets)** • Hypersensitivity to the active substance or to any of the excipients • Pregnancy • Breast-feeding • Concomitant use with simvastatin 40 mg OD or higher dose. • Coadministration with a statin is contraindicated in patients with active liver disease or unexplained persistent elevations in serum transaminases (included for information)
Cautions (see SPC for full details)	• Age ≤ 18 yrs. • Patients with hyperuricemia or history of gout • CKD stage 4 and 5 • Patients with severe hepatic impairment • Allergy or hypersensitivity to any excipients/ active substance • Pregnant and lactating women.
Adverse Effects (see SPC for full details) **▼ drug – report suspected adverse effects to the MHRA**	**Common or very common** Anaemia, reduced Haemoglobin, gout, hyperuricaemia, decreased Appetite, Dizziness, headache, hypertension, cough, constipation, diarrhoea, abdominal pain, nausea, dry mouth, flatulence, gastritis, back pain, muscle spasms, myalgia, pain in extremity, arthralgia, fatigue, asthenia.
Pregnancy, lactation and fertility	**Pregnancy** Contraindicated and manufacturer advises avoid—toxicity in animal studies. Women of childbearing potential must use effective contraception during treatment. Patients should be advised to stop taking Bempedoic acid or Bempedoic acid in combination with ezetimibe before stopping contraceptive measures if they plan to become pregnant. **Breast-feeding** Contraindicated and manufacturer advises avoid—no information available.
Counselling Points	**Elevated Urate Levels** • Advise patients of the risk of elevated serum uric acid levels, including development of gout. • Inform patients that serum uric acid levels may be monitored during treatment with Bempedoic acid. • Patients with signs or symptoms of hyperuricemia should contact their clinician if symptoms occur.

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	Pregnancy • Women of childbearing potential must use effective contraception during treatment. Patients should be advised to stop taking Nustendi® and Nilemdo® before stopping contraceptive measures if they plan to become pregnant.
References	1. Summary of product characteristics https://www.medicines.org.uk/emc/product/11743/smpc Accessed 25/11/2024. 2. Summary of product characteristics https://www.medicines.org.uk/emc/product/11744/smpc . Accessed 25/11/2024. 3. BNF https://bnf.nice.org.uk/drugs/bempedoic-acid-with-ezetimibe/ Accessed 25/11/2024. 4. BNF https://bnf.nice.org.uk/drugs/bempedoic-acid/ Accessed 25/11/2024. 5. BNF https://bnf.nice.org.uk/interactions/ezetimibe/ Accessed 25/11/2024. 6. NICE Technology appraisal guidance [TA694]. Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia. Published: 28 April 2021 https://www.nice.org.uk/guidance/TA694 Accessed 25/11/2024.