SHARED CARE AGREEMENT

Name of medicine	Bempedoic acid (Nilemdo), Bempedoic acid / Ezetimibe (Nustendi)
Indication	Primary hypercholesterolaemia or mixed dyslipidaemia, where maximally-tolerated lipid-lowering therapy has failed to achieve target LDL cholesterol

Version: **1.0** Approval date: **March 2023** Review date: **March 2026**

The Shared Care Agreement (SCA) is intended to facilitate the accessibility and safe prescribing of complex treatments across the secondary/primary care interface. It does not contain all of the relevant product information, which should be sought using the current British National Formulary and manufacturer's Summary of Product Characteristics. The SCA must be used in conjunction with the NHS Lothian Procedure for the Shared Care of Medicines, available here.

Roles and responsibilities

Listed below are specific responsibilities that are additional to those included in the NHS Lothian Policy and Procedures for Shared Care. Please refer to the policy for core roles and responsibilities that apply to all Shared Care Agreements.

Consultant (Lipid Clinic, RIE)

Initial shared care – initiation of drug, up to 12 weeks

- Assess patient eligibility – see SMC criteria under *Key Information on the Medicine*
- Patient counselling, to include:
  - patient to contact lipid clinic to report adverse effects
  - for women of child-bearing potential - effective contraception to be used. Bempedoic acid to be stopped ideally 8 weeks before trying for pregnancy. Not to be taken during pregnancy or breast-feeding.
- Initial prescription for 12 weeks to establish tolerability and lipid-lowering efficacy
- Blood tests at baseline, 8 weeks: FBC, Cr&Es, LFTs, full lipid profile
- Management of adverse effects, or inadequate lipid-lowering efficacy
- Where long-term therapy is appropriate, write to GP to request long-term prescription. The latter should include reference to this shared-care agreement.

Longer-term shared care – beyond 12 weeks

- Provide email or telephone advice, or accept re-referral for discharged patients who develop adverse effects, or where there is concern over lipid-lowering efficacy

General Practitioner

Initial shared care – initiation of drug, up to 12 weeks

- For women - to advise on a suitable form of contraception and ongoing provision where relevant

Longer-term shared care – beyond 12 weeks

- Consider Lipid Clinic recommendation for long-term prescribing from primary care
- For women of child-bearing potential - to advise on effective contraception, and ongoing provision where relevant. Bempedoic acid to be stopped ideally 8 weeks before trying for pregnancy. Not to be taken during pregnancy or breast-feeding. If unplanned pregnancy occurs, stop bempedoic acid immediately and re-refer to lipid clinic.
- Review annual (non-fasting) lipid profile (only applicable where patients no longer under Lipid Clinic follow-up)
- Consider seeking email or telephone advice (or re-refer to lipid clinic) where patients develop adverse effects, or there is concern over lipid-lowering efficacy

Patient, relatives, carers

- Contact lipid clinic directly regarding suspected adverse effects, or other matters related to initial hospital prescription
- Otherwise, responsibilities as per: NHS Lothian Policy and Procedures for the Shared Care of Medicines

Support and Advice for the GP

- RIE.BioLipidsAdvice@nhslothian.scot.nhs.uk
- Lipid Clinic, RIE: 0131 242 6870, 0131 242 6853
- Advice can also be sought through SCI-gateway referral to Lipid Clinic, RIE

Key Information on the Medicine

Please refer to the current edition of the British National Formulary (BNF), available at www.bnf.org, and Summary of Product Characteristics (SPC), available at www.medicines.org.uk for detailed product and prescribing information and specific guidance.

Background to disease and use of drug for the given indication

Bempedoic acid▼(Nilemdo®) is an adenosine triphosphate citrate lyase (ACL) inhibitor which inhibits cholesterol synthesis in the liver, thereby lowering LDL-cholesterol. It is indicated in adults at high risk of atherosclerotic cardiovascular disease (with or without established CVD) with primary hypercholesterolaemia or mixed dyslipidaemia, where maximally-tolerated lipid-lowering therapy has failed to achieve target LDL cholesterol.

Indication

Bempedoic acid has been accepted for restricted use within NHS Scotland by the SMC (SMC2363) in combination with ezetimibe for patients who are:

- statin intolerant, or for whom a statin is contra-indicated

AND

- where ezetimibe alone does not appropriately control LDL-C

AND

- where proprotein convertase subtilisin/ kexin type 9 (PCSK9) inhibitors are not appropriate.

Bempedoic acid and ezetimibe may be prescribed as separate tablets, or in a fixed-dosed combination tablet (Nustendi®).

Dosage and administration

• Nilemdo – one film-coated tablet of bempedoic acid 180 mg taken once daily

• Nustendi – one film-coated tablet of bempedoic acid 180 mg / ezetimibe 10 mg taken once daily

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

Monitoring

Test	Frequency	Abnormal Result	Action if Abnormal Result
Initial shared care (until week 12) **Lipid Clinic, RIE** FBC, Cr&Es, LFTs, full lipid profile	baseline, 8 weeks	- Significant reduction in haemoglobin - Significant increase in creatinine - ALT, ALP, GGT newly above reference range, or significantly increased from baseline - <20% reduction in LDL-C, or non-HDL-C	Deranged bloods - Stop bempedoic acid - Repeat bloods after further 4 to 8 weeks Inadequate LDL-C lowering Review compliance
Beyond week 12 **GP***	every 12 months	Significant rise in LDL-C, or non-HDL-C (to pre-treatment levels)	Review compliance, consider new-onset secondary causes of hyperlipidaemia

Full lipid profile Consider serum urate (uric acid) if symptoms of gout, or serum CK if symptoms of myopathy *only where no longer under lipid clinic		Urate > ULN CK > ULN (or accepted previous baseline)	- Stop bempedoic acid if urate >ULN, or CK >3xULN - Repeat bloods after further 4 to 8 weeks Consider seeking lipid clinic advice, and/or re-referral

Cautions, contraindications - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

Cautions

Increased risk of gout. And increased risk of elevated liver enzymes:

- Avoid in patients with gout, or history of elevated urate. Discontinue Nilemdo/Nustendi where symptoms of gout and hyperuricaemia.
- Discontinue Nilemdo/Nustendi if ALT persistently > 3xULN.

Limited (or no) experience in renal impairment, or moderate to severe hepatic impairment. Avoid or consider extra monitoring of renal function or liver function tests:

- Renal impairment (eGFR <30 mL/min/1.73m2)
- Moderate to severe hepatic impairment (Child-Pugh B or C)

Do not routinely prescribe alongside the following medications. See **Interactions** section below (or SPC), and consider seeking Lipid Clinic (RIE) advice:

- statins, fibrates
- warfarin, fluindione - monitor INR
- ciclosporin - monitor levels
- bosentan, fimasartan (anti-hypertensives)
- asunaprevir, glecaprevir, grazoprevir, voxilaprevir (anti-viral hepatitis therapies)

Contraindications

- Concomitant prescription with simvastatin at dose >40 mg once-daily (risk of myopathy)
- Concomitant prescription with any statin AND active liver disease, or unexplained persistent elevations in serum liver enzymes (ALT, AST, GGT)
- Hypersensitivity to the active substances, or to any of the excipients
- Nilemdo/Nustendi contain lactose. Contraindicated in rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption.
- Women of childbearing potential must use effective contraception during treatment. Nilemdo/Nustendi should be stopped before trying for pregnancy.

Not licensed for use in:

- Children (no information)
- Pregnancy (toxicity in animal studies), breast-feeding (no information)

Adverse effects - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

Common (≥1/100 to <1/10):

Anaemia, gout, hyperuricaemia, dizziness, headache, diarrhoea, constipation, flatulence, nausea, back pain, myalgia, arthralgia, pain in extremity.

Uncommon (≥1/1,000 to <1/100):

Increased liver enzymes, increased creatinine, lowered eGFR, increased urea.

Not known (cannot be estimated from available data):

Myopathy, cholelithiasis, hypersensitivity (rash, urticaria, anaphylaxis, angio-oedema).

Description of selected adverse effects

Dizziness

Advise patients to try bempedoic acid / ezetimibe combination before driving or operating machinery. They should avoid these activities if they experience dizziness.

Nustendi has minor influence on the ability to drive and use machines. When driving vehicles or using machines, it should be taken into account that dizziness has been reported with bempedoic acid and ezetimibe. Note that bempedoic acid without ezetimibe is described as having "no or little influence on the ability to drive and use machines."

Raised urate (uric acid), symptoms of gout

Recomend discontinuation of Nilemdo/Nustendi where raised urate and symptoms of gout.

In the pooled placebo-controlled trials, gout was reported in 1.4% of patients treated with bempedoic acid and 0.4% of patients treated with placebo. 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. Elevations in serum uric acid usually occurred within the first 4 weeks of treatment and returned to baseline following discontinuation of treatment.

Elevated liver enzymes

Recommend discontinuation of Nilemdo/Nustendi where ALT persistently above 3 x ULN. Seek lipid clinic advice for other significant LFT derangements.

(In controlled clinical studies, the incidence of elevations (≥ 3× ULN) in hepatic transaminase levels was increased fo patients treated with bempedoic acid (0.7% verus 0.3% for placebo). These elevations in transaminases were not associated with other evidence of liver dysfunction.)

Anaemia, decreased haemoglobin

Seek lipid clinic advice if anaemia suspected to be secondary to Nilemdo / Nustendi. Haemoglobin reductions associated with bempedoic acid in the clinical trials were mild and neither BNF/SPC recommend specific monitoring.

(Decreases in haemoglobin usually occurred within the first 4 weeks of treatment and returned to baseline following discontinuation of treatment.)

Increased creatinine (lower eGFR), increased urea

Seek lipid clinic advice if a deterioration in renal function is suspected to be secondary to Nilemdo / Nustendi. Creatinine and urea increases associated with bempedoic acid in the clinical trials were mild and neither BNF/SPC recommend specific monitoring.

(A mean increase of 1.8 micromol/L in serum creatinine and 1.0 mmol/L in urea compared to baseline was observed with bempedoic acid / ezetimibe at week 12. These elevations usually occurred within the first 4 weeks of treatment, remained stable, and returned to baseline following discontinuation of therapy.)

Drug interactions - Refer to current Summary of Product Characteristics (SPC): www.medicines.org.uk

Statins, fibrates

Patients on statins or fibrates are NOT eligible for bempedoic acid under SMC restriction. For awareness, SPC recommends avoiding prescribing alongside:

- Statins (high-doses) – increased risk of myopathy. Contraindicated for simvastatin >40 mg once-daily.
- Fibrates (limited evidence) – possible increased risk of myopathy and cholelithiasis

Bile-acid sequestrants, e.g. cholestyramine

May reduce absorption and efficacy of Nilemdo / Nustendi. Take either at least 2 hours before or at least 4 hours after administration of a bile acid sequestrant.

Other medication

Please consider seeking Lipid Clinic advice if considering prescribing bempedoic acid alongside any of the following. Levels of these medications may be altered by bempedoic acid, or ezetimibe:

- warfarin, fluindione - **monitor INR**
- ciclosporin - **monitor levels**
- bosentan, fimasartan (anti-hypertensives) – levels may be increased by bempedoic acid
- asunaprevir, glecaprevir, grazoprevir, voxilaprevir (anti-viral hepatitis therapies) – levels may be increased by bempedoic acid

The presence of this SCA does not compel a primary care prescriber to prescribe if they feel that it is out with the scope of their competencies (as per GMC guidance on safe prescribing) or resources, as ultimate responsibility lies with the prescribing, not the recommending, clinician.

For office use only:

Approved by the General Practice Prescribing Committee (GPPC) March 2023