Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia Prescribing Support Information for Primary Care.

This information is provided to support primary care clinicians prescribing Inclisiran (Leqvio®) for treating primary hypercholesterolaemia or mixed dyslipidaemia in adults.

Category	Inclisiran is a small interfering RNA (siRNA) that works by inhibiting the production of PCSK9 in the liver. This increases the number of LDL-C receptors able to clear LDL-C from the bloodstream and reduces the level of LDL-C in the blood.
Therapeutic indications	Inclisiran is recommended under the NICE TA 733 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 there is a history of cardiovascular events and low-density lipoprotein cholesterol (LDL-C) concentrations are persistently 2.6 mmol/L or more, despite maximum tolerated lipid-lowering therapy.
Pharmaceutical Form	Leqvio® 284 mg solution for injection in prefilled syringe Leqvio® 284 mg solution for injection in prefilled syringe with needle guard Solution for injection (injection). The solution is clear, colourless to pale yellow, and essentially free of particulates.
NICE Guidance and place in therapy	Inclisiran 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: There is a history of any of the following cardiovascular events: • acute coronary syndrome (such as myocardial infarction or unstable angina needing hospitalisation) • coronary or other arterial revascularisation procedures • coronary heart disease • ischaemic stroke or • peripheral arterial disease, and Low-density lipoprotein cholesterol (LDL-C) concentrations are persistently 2.6 mmol/l or more, despite maximum tolerated lipid-lowering therapy, that is: • maximum tolerated statins with or without other lipid-lowering therapies or, • other lipid-lowering therapies when statins are not tolerated or are contraindicated, and • the company provides Inclisiran according to the commercial arrangement. Inclisiran is recommended only in research for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed

This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

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	dyslipidaemia in adults who have no history of cardiovascular events. This research is in the form of a clinical trial currently in development. **Place in BLMK Lipid Management Pathway** Guidelines recommend that Inclisiran initiation is intended to be carried out within the primary care setting in patients with cardiovascular disease (CVD). Secondary prevention • For patients who have not reached lipid targets for secondary prevention (LDL-C ≥ 2.6 mmol/L) and have exhausted current pathway including Statins, Ezetimibe and Bempedoic acid. • For use in accordance with the following NICE TA(s) 694.
Initiation and dosing advice	Each pre-filled syringe contains Inclisiran sodium equivalent to 284 mg Inclisiran in 1.5 ml Solution. 284 mg Inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months. Initiation should be in accordance with NICE recommendations and licensed indication. Refer to SPC.
Method of administration	Inclisiran is for subcutaneous injection into the abdomen; alternative injection sites include the upper arm or thigh. Injections should not be given into areas of active skin disease or injury such as sunburns, skin rashes, inflammation, or skin infections. Each 284 mg dose is administered using a single pre-filled syringe. Each pre-filled syringe is for single use only. Inclisiran is intended for administration by a healthcare professional. Novartis "How do I administer Inclisiran?" information available on the link in the Novartis UK HCP Portal
Missed Doses	If a dose is missed, • If a planned dose is missed by ≤ 3 months: administer Inclisiran and continue dosing according to the original schedule. • If a planned dose is missed by > 3 months: start a new dosing schedule (i.e. administer initial dose, second dose at 3 months, followed by a dose every 6 months).
Monitoring and Continuation Criteria	At baseline and 12 weeks post initiation: • Liver function, renal function, non-fasting full lipid profile including LDL, thyroid, Hba1c • If patient develops adverse effects discontinue the medication and seek alternative. • Following initiation, cholesterol monitoring and adherence to medication should be in line with lipid guidelines.

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Co-prescribing with other medication. (see SPC for full details)	Inclisiran is not a substrate for common drug transporters and, although in vitro studies were not conducted, it is not anticipated to be a substrate for cytochrome P450. Inclisiran is not an inhibitor or inducer of cytochrome P450 enzymes or common drug transporters. Therefore, Inclisiran is not expected to have clinically significant interactions with other medicinal products. Based on the limited data available, clinically meaningful interactions with atorvastatin, rosuvastatin or other statins are not expected.
Special Patient Population	**Elderly age ≥ 65 years** No dose adjustment is necessary in elderly patients. **Renal impairment** No dose adjustments are necessary for patients with mild, moderate, or severe renal impairment or patients with end-stage renal disease. There is limited experience with Inclisiran in patients with severe renal impairment. Inclisiran should be used with caution in these patients. Haemodialysis The effect of haemodialysis on Inclisiran pharmacokinetics has not been studied. Considering that Inclisiran is eliminated renally, haemodialysis should not be performed for at least 72 hours after Inclisiran dosing. **Hepatic impairment** No dose adjustments are necessary for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment. No data are available in patients with severe hepatic impairment (Child-Pugh class C). Inclisiran should be used with caution in patients with severe hepatic impairment. **Paediatric population** The safety and efficacy of Inclisiran in children aged less than 18 years have not yet been established. No data are available.
Contraindications	• Hypersensitivity to the active substance or to any of the excipients • Pregnancy / breastfeeding due to no or limited clinical experience
Cautions (see SPC for full details)	• Severe renal impairment (CrCl <30 ml/min) or requiring haemodialysis due to limited clinical experience. Haemodialysis should not be performed for at least 72 hours after Inclisiran dosing. • Severe liver impairment (Child-Pugh class C) due to limited clinical experience. • Each Inclisiran injection contains <1 mmol (23mg) sodium.
Adverse Effects (see SPC for full details)	The only adverse reactions associated with Inclisiran were adverse reactions at the injection site (8.2%).

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▼ drug – report suspected adverse effects to the MHRA	Mild to moderate injection site reaction are transient and resolve: pain, erythema, rash
Pregnancy, lactation and fertility	**Pregnancy** There are no or limited amount of data from the use of Inclisiran in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Inclisiran during pregnancy. **Breast-feeding** It is unknown whether Inclisiran is excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of Inclisiran in milk. A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Inclisiran therapy, considering the benefit of breast-feeding for the child and the benefit of therapy for the woman. **Fertility** No data on the effect of Inclisiran on human fertility are available. Animal studies did not show any effects on fertility.
References	1. Summary of product characteristics https://www.medicines.org.uk/emc/product/12039/smpc Accessed 28/11/2024. 2. Summary of product characteristics https://www.medicines.org.uk/emc/product/13927/smpc Accessed 28/11/2024. 3. BNF https://bnf.nice.org.uk/drugs/inclisiran/ Accessed 28/11/2024. 4. NICE Technology appraisal guidance [TA733]. Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia https://www.nice.org.uk/guidance/TA733 Published: 06 October 2021 Accessed 28/11/2024.