This guideline is currently under review. Please continue to use this version until the review has been completed

Information Summary: Specialist prescribing of PCSK9 inhibitors for the management of primary hypercholesterolemia (heterozygous familial and non-familial) and mixed dyslipidaemia

Alirocumab (Praluent®▼) and evolocumab (Repatha®▼) are proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. They are potent lipid lowering agents recommended by the National Institute for Health and Care Excellence (NICE) as an option in the treatment of primary hypercholesterolaemia (heterozygous and non-familial) and mixed dyslipidaemia.

In South London, these agents can be considered in line with the NICE guidance, as summarised in the algorithm overleaf.

Commissioning Arrangements

- Funding for these drugs is through Payment by Results (PbR) exclusion. Prescribers should follow their host commissioning process for managing PbR funding arrangements.
- Reimbursement will be at the rate specified in the relevant patient access scheme agreed by NICE.
- Use of these agents outside of the agreed pathway will not be reimbursed[1]. Individual funding requests can be made for patients where there is a clinical need for PCSK9 inhibitor treatment outside the agreed pathway, where a case for exceptionality can be made.

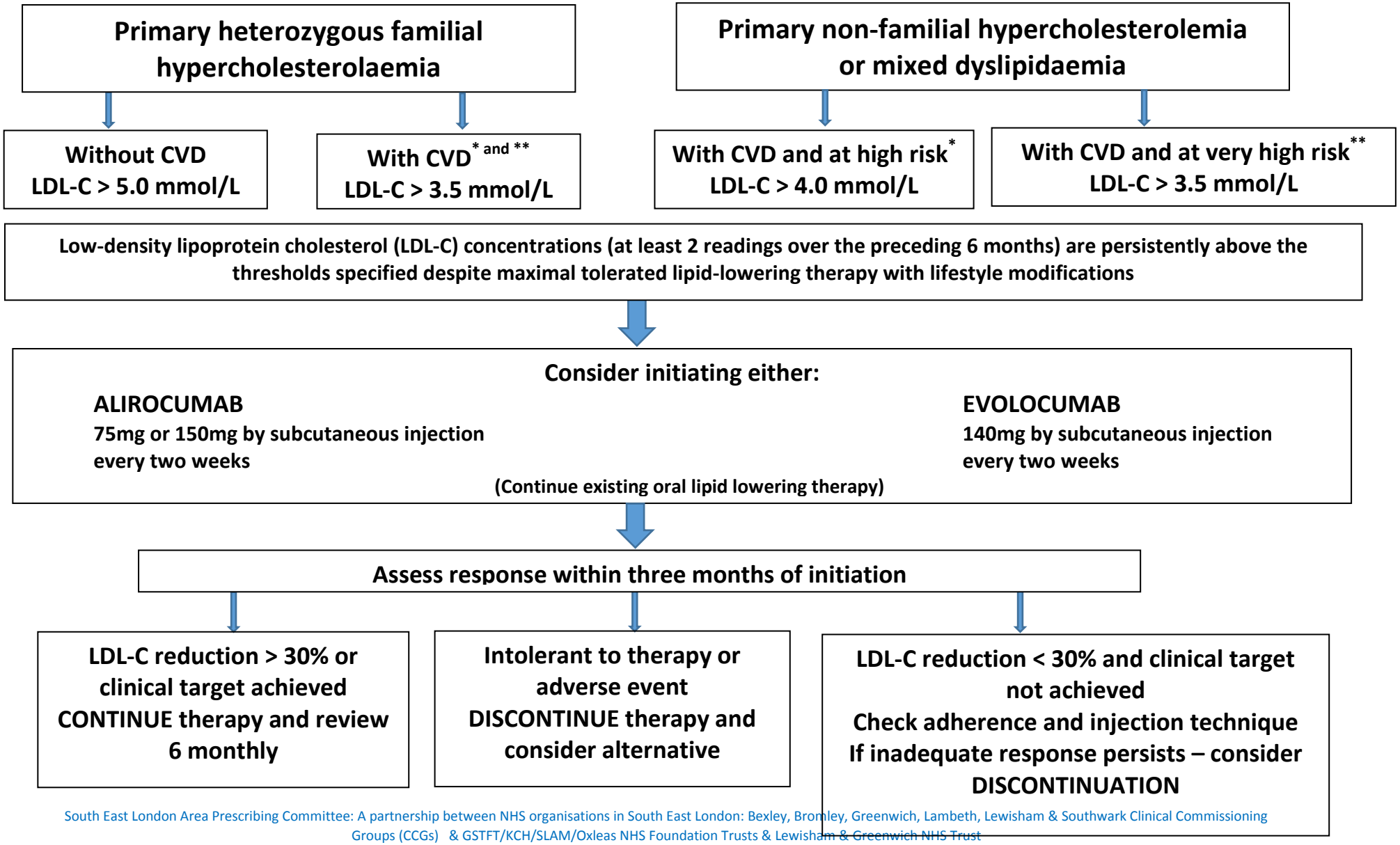
Prescribing and Supply

- These drugs should only be initiated and managed by secondary care clinicians with appropriate experience in the management of lipid disorders. Prescribing will be retained in secondary care and General Practitioners (GPs) should not be asked to take over prescribing responsibility at anytime. Other lipid lowering treatments (such as statins, ezetimibe, fibrates) should be continued by GPs unless a specialist advises otherwise.
- Homecare is included as part of the cost of the drugs and may be used, where appropriate, to facilitate supply of the drug to the patients' home.
- Both manufactures have developed patient support programmes which may be considered, where appropriate, to support patient education and adherence.

Alirocumab (Praluent®▼) and evolocumab (Repatha®▼) are subject to additional monitoring under the black triangle scheme – Healthcare professionals are asked to report any suspected adverse reactions to the MHRA using the yellow card system and via the local incident reporting system.

[1] Evolocumab is also licenced for homozygous familial hypercholesterolaemia, which falls under NHS England specialist commissioning within specified criteria and designated apheresis centres only.

Pathway for the use of PCSK9 Inhibitors for the management of primary hypercholesterolaemia (heterozygous-familial and non-familial) and mixed dyslipidaemia



Additional Information

Diagnosis:

- **Primary Familial hypercholesterolemia:**
  - The diagnosis of primary FH should be made in line with the recommendations in CG71: Familial Hypercholesterolemia Identification and Management
- **Primary non-familial hypercholesterolemia and mixed dyslipidaemia i.e.**
  - **Elevated cholesterol (greater than 5 mmol/L) not associated with autosomal dominant pattern of inheritance or caused by a single gene defect**
  - **Mixed dyslipidaemia is defined as total cholesterol greater than 5 mmol/L; and fasting triglycerides greater than 1.7mmol/L but less than 4mmol/L**

Definitions (as per NICE guidance)

Maximum tolerated lipid lowering therapy: the maximum dose has been reached or further dose titration is limited by intolerance. We would anticipate this to include intolerance to statins and/or ezetimibe.

Intolerance to lipid lowering therapy: defined as the presence of clinically significant adverse effects that represent an unacceptable risk to the patient or that may reduce compliance with therapy (as per NICE **CG 71**).

Additional advice on statin intolerance is given in **CG181**:

- If a person is not able to tolerate a high-intensity statin aim to treat with the maximum tolerated dose. If someone reports adverse effects when taking high-intensity statin discuss the following possible strategies with them:
  - stopping the statin and trying again when the symptoms have resolved to check if the symptoms are related to the statin
  - reducing the dose within the same intensity group
  - changing the statin to a lower intensity group.
- Seek specialist advice about options for treating people at high risk of CVD such as those with CKD, type 1 diabetes, type 2 diabetes or dyslipidaemias associated with metabolic/inherited disease, and those with CVD, who are intolerant to 3 different statins.

Cardiovascular Disease (CVD) is defined by the NICE TAs as:

- ***With CVD and are at high risk**: History of any of the following: acute coronary syndrome (such as myocardial infarction or unstable angina requiring hospitalisation); coronary or other arterial revascularisation procedures; chronic heart disease; ischaemic stroke; peripheral arterial disease.
- ****With CVD and are at very high risk:** Recurrent cardiovascular events or cardiovascular events in more than 1 vascular bed (that is, poly-vascular disease).

References

1. Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia NICE technology appraisal guidance [TA394] available at https://www.nice.org.uk/guidance/ta394
2. Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia NICE technology appraisal guidance [TA393] available at https://www.nice.org.uk/guidance/ta393
3. Familial hypercholesterolaemia: identification and management. NICE Clinical guideline [CG71] available at https://www.nice.org.uk/guidance/cg71
4. Lipid Modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE Clinical Guideline [CG181] [Online] available at: https://www.nice.org.uk/guidance/cg181
5. Roth EM, Mckenney JM, Hanotin DC, *et al.* Atorvastatin with or without an antibody to PCSK9 in primary hypercholesterolemia. *N Engl J Med* 2012; 367:1891-1900. Available at http://www.nejm.org/doi/pdf/10.1056/NEJMoa1201832