East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Briefing Paper for Prescribing Clinical Network on NICE Technology Appraisal TA393: June 2016

NICE TA Guidance	Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia
Date of issue	22 June 2016
Available at	https://www.nice.org.uk/guidance/ta393

Medicine details	
Name, brand name and manufacturer	Alirocumab, Praluent®, Sanofi
Licensed indication, formulation and usual dosage	Alirocumab 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 or, - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated. Alirocumab is a solution for injection, administered using a pre-filled pen and comes as a 75mg and 150mg strength. The usual starting dose for Alirocumab is 75 mg administered subcutaneously once every 2 weeks. Patients requiring larger LDL-C reduction (>60%) may be started on 150 mg administered subcutaneously once every 2 weeks. The dose of alirocumab can be individualised based on patient characteristics such as baseline LDL-C level, goal of therapy, and response. Lipid levels can be assessed 4 weeks after treatment initiation or titration, when steady-state LDL-C is usually achieved, and dose adjusted accordingly (up-titration or down-titration). Patients should be treated with the lowest dose necessary to achieve the desired LDL-C reduction.

Disease and potential patient group	
Brief description of disease	Primary hypercholesterolaemia and mixed dyslipidaemia are a medical terms implying that a person's cholesterol levels are too high. High cholesterol can increase the risk of heart disease. There are several types of cholesterol-lowering drugs that work in different ways. They include statins and ezetimibe.

	Alirocumab is a type of drug called a monoclonal antibody. Over time, certain receptors in the liver stop working as well and take less cholesterol from the blood. Alirocumab helps to keep these receptors working, and so lowers levels of cholesterol.
Potential patient numbers per 100,000	1. % Patients with non-familiar hypercholesterolaemia with an LDL-C of 4mmol/litre or over and high risk of CVD is 0.19% or 190 patients per 100,000 2. % Patients with non-familiar hypercholesterolaemia with an LDL-C of 3.5mmol/litre or over and very high risk of CVD is 0.17% or 170 patients per 100,000 3. % patients with familial hypercholesterolaemia with a LDL-C of 5mmol/litre or over and no history of CVD – 0.01% or 10 patients per 100,000 4. % patients with familial hypercholesterolaemia with a LDL-C of 3.5mmol/litre or over and history of CVD – 0.02% or 20 patients per 100,000 Number of patients expected to receive either Alirocumab or evolocumab for :

CCG	Non-familial hypercholesterolaemia	Familial hypercholesterolaemia
Guildford & Waverley	46	6
East Surrey	40	6
North West Surrey	76	10
Surrey Heath	22	4
Surrey Downs	64	10
Crawley	24	4
Horsham & Mid-Sussex	50	8

SUMMARY

Guidance

Recommendations

1.1 Alirocumab is recommended as an option for treating primary hypercholesterolaemia or mixed dyslipidaemia, only if:

- Low-density lipoprotein concentrations are persistently above the thresholds specified in table 1 despite maximal tolerated lipid-lowering therapy. That is, either the maximum dose has been reached or further titration is limited by intolerance (as defined in NICE's guideline on familial hypercholesterolaemia: identification and management.
- The company provides alirocumab with the discount agreed in the patient access scheme.

Table 1 Low-density lipoprotein cholesterol concentrations above which alirocumab is recommended

	Without CVD	With CVD	
		High risk of CVD [1]	**Very high risk of CVD [2]**
Primary non-familial hypercholesterolaemia or mixed dyslipidaemia	Not recommended at any LDL-C concentration	Recommended only if LDL-C concentration is persistently above 4.0 mmol/l	Recommended only if LDL-C concentration is persistently above 3.5 mmol/l
Primary heterozygous-familial hypercholesterolaemia	Recommended only if LDL-C concentration is persistently above 5.0 mmol/l	Recommended only if LDL-C concentration is persistently above 3.5 mmol/l	

[1]High risk of cardiovascular disease is defined as a 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.

[2]Very high risk of cardiovascular disease is defined as recurrent cardiovascular events or cardiovascular events in more than 1 vascular bed (that is, polyvascular disease).

Abbreviations: CVD, cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.

1.2 This guidance is not intended to affect the position of patients whose treatment with alirocumab was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

Cost implications

Cost: alirocumab costs £168 for a 75 mg or 150 mg single-use prefilled pen (excluding VAT; MIMS, January 2016).

Annual cost per patient: The annual cost of treatment per patient is £4,383 for 75 mg or 150 mg every 2 weeks. The company has agreed a patient access scheme with the Department of Health that will provide a simple discount to the list price of alirocumab with

the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme would not constitute an excessive administrative burden on the NHS.

Availability of PAS and details (if appropriate): There is a Patient Access Scheme in place which can only be accessed through hospital supply routes.

Availability of homecare service (if appropriate): Alirocumab is available via Homecare

Alternative treatments and cost per patient per year

Annual cost per patient for evolocumab: The annual cost of treatment per patient is about £4,422.60 for 140 mg every 2 weeks, and £6,123.60 for 420 mg monthly. The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of evolocumab, with the discount applied at the point of purchase or invoice.

Lipoprotein apheresis
The lipid clinic at RSCH they refer patients to the Royal Brompton for LDL apheresis. The lipidology outpatient clinic, at the Royal Surrey, mainly treats patients with statins and diet guidance. The Royal Brompton is listed as a specialist centre, for this procedure, which is commissioned by NHS England.

Atorvastatin / ezetimibe
Annual cost of atorvastain 80 mg daily - £27.43
Annual cost ezetimibe 10mg daily - £342.03
Drug tariff (July 2016)

Impact to patients

- The committee concluded that alirocumab is clinically effective in reducing LDL-C levels when compared with placebo, ezetimibe or statins in people with hypercholesterolaemia.
- There was no evidence of additional gains in health-related quality of life over those already included in the quality-of-life (QALY) calculations.
- Alirocumab was shown to have a similar safety profile to control groups.
- Injection only treatment which will exclude people who will not accept injection based therapies, including many from ethnic minority groups.
- Requires cold chain however; it can be out of fridge for up to 30 days.
- Access to alirocumab will negate the inequality of access to LDL-apheresis due to high set up costs for treatment and few established centres with appropriate expertise.

Impact to primary care

- Prior to initiation with a PCSK9 inhibitor, all patients should be optimised for statin treatment and consider a trial with high intensity statin therapy if appropriate.
- In almost all of the trials, PCSK9 inhibitors were used in addition to maximally

tolerated doses of statins. In addition, statin intolerance for licensing purposes is defined as patients who experience clinically significant adverse effects which put the patient at unacceptable risk after taking two separate trials of statins. This does not include patients who refuse to take a statin.

- Interfacing and communication required between secondary and primary care for patient receiving alirocumab.
- Alirocumab is not available via Primary care supply routes (information supplied via Sanofi).

Impact to secondary care

- The initiation, administration and on-going treatment needs to be managed by secondary care, (RED drug PbRe).
- Organising homecare.
- Clearly defined stop criteria should be developed to aid review if the treatment proves ineffective (i.e. no response within three months of starting treatment).
- Cohort currently not routinely treated in secondary care so additional resource required to manage extra appointments.

Impact to CCGs

- The NICE committee concluded that the current treatment options for hypercholesterolaemia may not be sufficient in all cases, and that alternative treatment options are desirable.
- The NICE committee considered specific groups of people for whom the technology is particularly cost effective and concluded that alirocumab would be beneficial for people with a lifelong risk of cardiovascular events in the heterozygous-familial hypercholesterolaemia (secondary prevention) population.
- The trials mainly reported surrogate end points (especially LDL-C) and were not powered to measure cardiovascular outcomes, which the NICE committee considered to be an important limitation of the evidence base.
- There is limited data available regarding cardiovascular events, particular in relation to hospitalisation rates and mortality and morbidity rates.
- It's a PbRe drug so all drug costs would impact on CCG budgets, creating a significant cost pressure.

Implementation

Developing pathways to ensure patients have optimised all other treatments before initiation.

Completion of Blueteq forms.

Recommendation to PCN

PbRe:
Yes

Traffic light status: Red – Hospital Only

Additional comments:
Alirocumab can only be supplied through a secondary care route. It is not available through wholesalers supplying primary care.

References:

1. NICE TA393; Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia https://www.nice.org.uk/guidance/ta393

2. Alirocumab SPC
http://www.medicines.org.uk/emc/medicine/30956
3. The East of England Priorities Advisory Committee (a function of the PresQIPP programme) Guidance statement on PSCK9 inhibitors: Alirocumab and evolocumab
http://www.westessexccg.nhs.uk/your-health/medicines-optimisation/prescribing-formularies/14-mopb-decisions/2459-alirocumab-evolocumab/file

4. NICE Resource impact report: Alirocumab(TA393)and evolocumab (TA394) for treating primary hypercholesterolaemia and mixed dyslipidaemia. Published: June 2016
https://www.nice.org.uk/guidance/ta394/resources/resource-impact-report-2543362381