NHS
Bedfordshire
Clinical Commissioning Group

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BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE (JPC)

November 2016

Review: November 2019

Bulletin 248: PCSK9 inhibitors Evolocumab and Alirocumab for the treatment of primary hyypercholesterlaemia and mixed dyslidiaemia

JPC Recommendations:

To support the East of England Priorities Advisory Committee (PAC) policy statement and recommendations (See attachment – PAC doc updated Nov 2016)

The East of England
Priorities Advisory Committee
A function of PrescQIPP

GUIDANCE STATEMENT

PCSK9 inhibitors evolocumab and alirocumab for the treatment of primary hypercholesterolaemia and mixed dyslipidaemia

East of England PAC recommendation

1. Evolocumab and alirocumab are recommended for prescribing in line with NICE TA393 and NICE TA394 for patients with low density lipoprotein concentrations that are persistently* above the thresholds specified in table 1 despite maximal tolerated lipid lowering therapy as specified in locally agreed pathways e.g. after a trial of second or third statin, dose reduction, combination treatment with ezetimibe, and where adherence to treatment has been assessed and confirmed.
2. Prescribing should be initiated by a consultant lipidologist/chemical pathologist in a lipid clinic where these exist, or by a Hospital consultant, with a special interest such as a Diabetologist or Cardiologist, as agreed locally.
3. Prescribing should be retained in secondary care and supplied via the homecare model.
4. Patients should be monitored by the initiating clinic for efficacy, adherence to treatment, and adverse effects:
   - 6 weeks after starting treatment:
     If an adequate response (30% reduction in LDL-C from baseline**) has not been achieved after 6 weeks treatment, steps should be taken to address any issues around injection technique and adherence to treatment. NB this may be undertaken via a telephone consultation rather than a face to face clinic visit as agreed locally.
   - 3 months after starting treatment
   - 6 months after starting treatment
   - Annually thereafter.
5. Treatment should continue if:
   - A minimum reduction of 30% in LDL-C from baseline** is achieved after 3 months, and is sustained at ongoing reviews.
6. Prescribers must inform the patients GP that treatment has been initiated and request that the information is added to the patients Summary Care Record.
7. The use of evolocumab for the treatment of homozygous familial hypercholesterolaemia is an NHSE commissioning responsibility.
8. These recommendations will be reviewed in the light of further published evidence on the outcomes and long term safety of each agent.

*Persistently is defined as at least two consecutive LDL-C readings taken over a minimum period of 3 months.

**Baseline LDL-C is defined as the LDL-C level on optimised oral treatments prior to initiating PCSK9 inhibitor treatment.

Key points

1. In June 2016, NICE published TAs on the use of the PCSK9 inhibitors alirocumab and evolocumab for the treatment of primary hypercholesterolaemia and mixed dyslipidaemia.[1,2] NICE recommends alirocumab and evolocumab as options for treating primary hypercholesterolaemia or mixed dyslipidaemia, only if:
   - Lowdensity lipoprotein concentrations are persistently above the thresholds specified in table 1 despite maximal tolerated lipidlowering 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, CG71), or for whom a statin is contraindicated (as defined in section 4.3 of the SPC for each drug).

The company provides alirocumab and evolocumab with the discount agreed in the patient access scheme (PAS).

The dosage of evolocumab is 140mg every 2 weeks.

The dosage of alirocumab may be 75mg or 150mg every 2 weeks.

Table 1: Lowdensity lipoprotein cholesterol concentrations above which alirocumab and evolocumab are recommended.

	Without CVD	With CVD	
		High risk of CVD[1]	Very high risk of CVD[2]
Primary nonfamilial hypercholesterolaemia or mixed dyslipidaemia	Not recommended at any LDLC concentration	Recommended only if LDLC concentration is persistently above 4.0 mmol/l	Recommended only if LDLC concentration is persistently above 3.5 mmol/l
Primary heterozygousfamilial hypercholesterolaemia	Recommended only if LDLC concentration is persistently above 5.0 mmol/l	Recommended only if LDLC 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; LDLC, lowdensity lipoprotein cholesterol.

2. Currently there are no outcome data or long term safety data for either medicine.
3. Currently there is no evidence to demonstrate the superiority of one agent over the other.
4. The PAS price currently offered for both agents is similar and there are no additional charges e.g. delivery charges for either agent when supplied via the homecare route.
5. Clinical trials have demonstrated significant reductions in LDL-C within one month of starting treatment. Patients not showing a reduction in LDL-C after 3 months treatment would be considered to be non-responders or non-adherent and treatment should be stopped.
6. In the UK, the target LDL-C for people at high risk of cardiovascular disease is usually 'no more than 2.0 millimoles per litre (mmol/L)'. A fall of 30% from the pre-treatment level is also used as an alternative target as any reduction from baseline is considered to be beneficial in patients.[3] A target of 30% reduction in LDL-C from baseline is supported by clinicians in the East of England.

7. There is currently no information to either support or advise against the sequential use of these agents should the first agent used be ineffective. Requests for sequential use should be assessed on a case by case basis.
8. Evolocumab is also licensed for the treatment of homozygous familial hypercholesterolaemia, a rare disorder for which commissioning responsibility lies with NHSE; this indication is outside the scope of NICE TA394.[4]

Document history

PAC approval date	12 September 2016	Version	2
Consultation process	PAC members East of England clinicians		
QA process	Katie Smith, Regional Medicines Information Director, East Anglia Medicines Information Service, 24 October 2016.		

References

1. Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. NICE technology appraisal guidance [TA394]. Published 22 June 2016 https://www.nice.org.uk/guidance/ta394
2. Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia. NICE technology appraisal guidance [TA393]. Published 22 June 2016 https://www.nice.org.uk/guidance/ta393
3. Labtestsonline. Accessed 11/11/2015 via http://labtestsonline.org.uk/understanding/analytes/ldl/tab/test Last updated 29th May 2015.
4. Medicines not reimbursed through national prices and directly commissioned by NHS England. Version 10.0, published April 2016. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2014/06/nhse-drugs-list-v10.pdf