PCSK9 inhibitor treatment in clinical practice – three case vignettes

The record form

The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

LIPID and METABOLIC CLINIC

Treatment with PCSK9 inhibitor Record Form

Completion of this form is required for patients commencing Alirocumab (Praluent) or Evolocumab (Repatha)

Patient Surname: Forename: Patient postcode: Date of birth dd/mm/yyyy: ...../...../..... Male/ Female	GP name and practice address
NHS Number: MRN	Treatment Start Date:...../...../..... dd/mm/yyyy

Indication for PCSK9 inhibitor therapy

A. Primary non-familial hypercholesterolaemia or mixed dyslipidaemia WITH CVD ☐

High CVD risk* with LDL-C >4.0 mmol/L ☐ Very high CVD† risk LDL-C >3.5mmol/L ☐

I. Has the patient achieved a 40% reduction of non-HDL-C from baseline? Y / N
II. Is non-HDL-C ≤4.0 mmol/L on maximum tolerated lipid lowering therapy? Y / N

* High CVD risk defined as history of ACS, arterial revascularisation, ischaemic stroke or PAD
† Very high CVD defined as recurrent CVD events or CVD events in more than one vascular bed

B. Primary Heterozygous familial hypercholesterolaemia ☐

Without CVD and LDL-C >5.0 mmol/L ☐ With CVD and LDL-C >3.5mmol/L ☐

☐ Definite FH (genetically confirmed) ☐ Definite FH (NMD) ☐ Probable FH ☐ Possible FH

C. Current Lipid lowering drug therapy	**Dose/Frequency**	Tick if on no therapy ☐
		Continued Y / N
		Continued Y / N
		Continued Y / N

D. Enter fasting lipid profile results used for eligibility assessment Date:...../...../.....

Total cholesterol (mmol/L)		HDL-cholesterol (mmol/L)	
Triglycerides (fasting) (mmol/L)		Non-HDL-cholesterol (mmol/L)	
Lipoprotein(a) (mg/L ☐ nmol/L ☐)		LDL-C (mmol/L) Betaquant ☐	

E. Eligibility Checklist A or B + C + D +E completed ☐ Patient eligible ☐ Not eligible ☐

I. Has patient received maximum tolerated statin and ezetimibe therapy? Y / N
II. Has the patient been concordant with drug therapy and lifestyle measures? Y / N
III. Have secondary causes of hyperlipidemia been excluded (if not recently)? Y / N
IV. If the patient has diabetes mellitus has glycaemia control been optimised? NA / Y / N
V. Is further titration of lipid lowering therapy limited by intolerance? Y / N

If Yes to V, provide details:

Details of prescribed PCSK9 inhibitor treatment

Alirocumab 75 mg ☐ Alirocumab 150 mg ☐ Evolocumab 140 mg ☐	Q2W ☐ Q4W ☐
PCSK9 inhibitor education and injection training	Date:...../...../.....
Date of PCSK9 Inhibitor prescription (7 days before required for 1st dose)	Date:...../...../.....
Date of first dose administration Tick if self-administered in clinic ☐	Date:...../...../.....
Date of on-treatment lipid profile to assess response (usually pre-5th dose)	Date:...../...../.....

Enter non-fasting lipid profile results used to assess response Date:...../...../.....

Total cholesterol (mmol/L)		HDL-cholesterol (mmol/L)	
Triglycerides (fasting) (mmol/L)		Non-HDL-cholesterol (mmol/L)	
Non-HDL-C reduction of >20% achieved? Y / N		Treatment continued?	Y / N

Name:	Designation:
Signature:	Date:

All patient details have been changed to maintain confidentiality

Case 1 – WP

WP is a 60 year old retail manager with a history of coronary artery bypass and clinically diagnosed FH at 38 years, later genetically confirmed as heterozygous FH. Despite excellent concordance with diet and lifestyle measures and careful adherence to maximal combination lipid lowering therapy (rosuvastatin 40mg, ezetimibe 10mg and colsevelam 1250mg daily) she remained short of the ideal target range and well above the eligibility threshold for PCSK9 inhibitor therapy for very high risk secondary prevention (LDL-C greater than 3.5 mmol/l).

Indication for PCSK9 Inhibitor therapy

A. Primary non-familial hypercholesterolaemia or mixed dyslipidaemia WITH CVD ☐

High CVD risk* with LDL-C >4.0 mmol/L ☐ Very high CVD† risk LDL-C >3.5mmol/L ☐

I. Has the patient achieved a 40% reduction of non-HDL-C from baseline? Y / N
II. Is non-HDL-C ≤4.0 mmol/L on maximum tolerated lipid lowering therapy? Y / N

* High CVD risk defined as history of ACS, arterial revascularisation, ischaemic stroke or PAD
† Very high CVD defined as recurrent CVD events or CVD events in more than one vascular bed

B. Primary Heterozygous familial hypercholesterolaemia ☑

Without CVD and LDL-C >5.0 mmol/L ☐ With CVD and LDL-C >3.5mmol/L ☑

☑ Definite FH (genetically confirmed) ☐ Definite FH (NMD) ☐ Probable FH ☐ Possible FH

C. Eligibility Checklist ☑

I. Has patient received maximum tolerated statin and ezetimibe therapy? (Y) / N
II. Has the patient been concordant with drug therapy and lifestyle measures? (Y) / N
III. Have secondary causes of hyperlipidemia been excluded (if not recently)? (Y) / N
IV. If the patient has diabetes mellitus has glycaemia control been optimised? ~~Y / N~~
V. Is further titration of lipid lowering therapy limited by intolerance? Y (N)

If Yes to V, provide details:

D. Current Lipid lowering drug therapy	Dose/Frequency	Tick if on no therapy ☐
ROSUVASTATIN	40mg O.D.	Continued (Y) N
EZETIMIBE	10 mg O.D	Continued (Y) N
COLESEVELAM	625mg x 2 b.d	Continued Y (N)

Enter fasting lipid profile results used for eligibility assessment Date:

Total cholesterol (mmol/L)	7.0	HDL-cholesterol (mmol/L)	1.4
Triglycerides (fasting) (mmol/L)	1.6	Non-HDL-cholesterol (mmol/L)	5.6
Lipoprotein(a) (mg/L ☐ nmol/L ☑)	<20	LDL-C (mmol/L) Betaquant ☐	4.9

This new PCSK9 inhibitor treatment option was explained at her annual lipid clinic follow-up appointment but initially she was apprehensive about having to give herself injections. However, when the self- injection procedure was demonstrated using a training device she was reassured and wished to proceed with treatment. Alirocumab was then ordered and she was invited to return a week later for her first dose, which she self-injected successfully under supervision.

Details of PCSK9 inhibitor treatment	
Alirocumab 75 mg ☐ Alirocumab 150 mg ☑ Evolocumab 140 mg ☐	Q2W ☑ Q4W ☐
PCSK9 inhibitor education and injection training	Date:
Date of PCSK9 Inhibitor prescription (7 days before required for 1st dose)	Date:
Date of first dose administration Tick if self-administered in clinic ☑	Date:
Date of on-treatment lipid profile to assess response (usually pre-5th dose)	Date:

A repeat non-fasting lipid profile was arranged just before her 5th injection was due, 8 weeks later, to assess her treatment response. The results showed that her non-HDL-cholesterol had fallen by 73% and was now well inside the ideal target range (non-HDL-C less than 2.5 mmol/L).

Enter non-fasting lipid profile results used to assess response Date:

Total cholesterol (mmol/L)	3.0	HDL-cholesterol (mmol/L)	1.5
Triglycerides (fasting) (mmol/L)	1.3	Non-HDL-cholesterol (mmol/L)	1.5
Non-HDL-C reduction of >20% achieved? (Y) / N		Treatment continued?	(Y) / N

She was therefore happy to continue and so was re-prescribed a further 3 month supply of Alirocumab. This would be re-prescribed six-monthly thereafter once the repeat blood test confirmed that the initial response was maintained.

All patient details have been changed to maintain confidentiality

Case 2 – CH

CH is a 39 year old biology teacher with a paternal family history of hypercholesterolaemia and premature heart disease. She was given a clinically diagnosis of FH at 18 years, later confirmed on genetic tests as heterozygous FH in both her and her sister. A keen runner, she suffered from muscle fatigue and pain after exercise when treated with the high intensity statins required to bring her cholesterol under control, a problem she shared with her sister. She was also unable to tolerate ezetimibe or colesevelam, both of which caused gastrointestinal upsets. When she was told to avoid all statins during long term treatment for a fungal infection, she was alarmed to see her cholesterol increase to the highest ever levels, so she contacted the lipid clinic.

Indication for PCSK9 Inhibitor therapy

A. Primary non-familial hypercholesterolaemia or mixed dyslipidaemia WITH CVD ☐

High CVD risk* with LDL-C >4.0 mmol/L ☐ Very high CVD† risk LDL-C >3.5mmol/L ☐

I. Has the patient achieved a 40% reduction of non-HDL-C from baseline? Y / N
II. Is non-HDL-C ≤4.0 mmol/L on maximum tolerated lipid lowering therapy? Y / N

* High CVD risk defined as history of ACS, arterial revascularisation, ischaemic stroke or PAD
† Very high CVD defined as recurrent CVD events or CVD events in more than one vascular bed

B. Primary Heterozygous familial hypercholesterolaemia ☑

Without CVD and LDL-C >5.0 mmol/L ☑ With CVD and LDL-C >3.5mmol/L ☐

☑ Definite FH (genetically confirmed) ☐ Definite FH (NMD) ☐ Probable FH ☐ Possible FH

C. Eligibility Checklist ☑

I. Has patient received maximum tolerated statin and ezetimibe therapy? (Y) N
II. Has the patient been concordant with drug therapy and lifestyle measures? (Y) N
III. Have secondary causes of hyperlipidemia been excluded (if not recently)? (Y) N
IV. If the patient has diabetes mellitus has glycaemia control been optimised? Y / NA
V. Is further titration of lipid lowering therapy limited by intolerance? (Y) N

If Yes to V, provide details: myalgia on atorva + rosuva GI upset on ezetimibe, funcinazole Rx

D. Current Lipid lowering drug therapy	Dose/Frequency	Tick if on no therapy ☑
		Continued Y / N
		Continued Y / N
		Continued Y / N

Enter fasting lipid profile results used for eligibility assessment Date:

Total cholesterol (mmol/L)	12.2	HDL-cholesterol (mmol/L)	2.1
Triglycerides (fasting) (mmol/L)	1.6	Non-HDL-cholesterol (mmol/L)	10.1
Lipoprotein(a) (mg/L ☐ nmol/L ☑)	87	LDL-C (mmol/L) Betaquant ☐	9.4

At her clinic appointment the new treatment option of injectable PCSK9 inhibitor was therefore offered and after explanation and demonstration of the self-injection device she wished to commence treatment.

Details of PCSK9 inhibitor treatment

Alirocumab 75 mg ☐ Alirocumab 150 mg ☐ Evolocumab 140 mg ☑	Q2W ☑ Q4W ☐
PCSK9 inhibitor education and injection training	Date
Date of PCSK9 Inhibitor prescription (7 days before required for 1st dose)	Date
Date of first dose administration Tick if self-administered in clinic ☑	Date
Date of on-treatment lipid profile to assess response (usually pre-5th dose)	Date

She found the self-injection procedure easy to manage and reported no recurrence of muscle symptoms after exercise. A non-fasting blood test just before her 5th injection, after 8 weeks of treatment, showed a 33% reduction of her non-HDL-C.

Enter non-fasting lipid profile results used to assess response Date:

Total cholesterol (mmol/L)	8.8	HDL-cholesterol (mmol/L)	2.1
Triglycerides (fasting) (mmol/L)	0.9	Non-HDL-cholesterol (mmol/L)	6.7
Non-HDL-C reduction of >20% achieved? (Y) N		Treatment continued?	(Y) / N

Although this was sufficient to warrant continuation the results remained well short of the best results seen on high dose statins before discontinuation. A repeat test after a further six weeks treatment showed no further improvement and treatment options were reviewed. As only higher statin doses had caused problems in the past she agreed to add a small dose of rosuvastatin 10mg daily, and arranged to have a repeat blood test after 6 weeks of combination therapy. She remained free of post-exercise symptoms and the non-fasting blood test results showed that her non-HDL-C had fallen by 70% to 2.0 mmol/L, an overall reduction of 80% from her untreated profile and now in the ideal range (non-HDL-C less than 2.5 mmol/L).

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Case 3 – JD

JD is a 69 year old retired engineer who had been admitted to hospital a year before with an acute coronary syndrome and required emergency PCI and stents for 2 vessel coronary artery disease. While in hospital he was commenced on high intensity statin treatment (atorvastatin 80 mg daily) but a few weeks later he complained of progressive worsening of his chronic low back pain and calf muscle aches. On the advice of his GP he stopped his atorvastatin and his symptoms quickly improved, but subsequently recurred when he was changed to rosuvastatin, even when later tried on a non-daily dose of 5 mg after referral to the lipid clinic. He was then offered ezetimibe which he was able to take without difficulty but despite this his lipids remained well above the ideal target range and also above the threshold for eligibility for PCSK9 inhibitor treatment as a high risk patient (fasting LDL-C greater than 4 mmol/L).

Indication for PCSK9 Inhibitor therapy

A. Primary non-familial hypercholesterolaemia or mixed dyslipidaemia WITH CVD ☑

High CVD risk* with LDL-C >4.0 mmol/L ☑ Very high CVD† risk LDL-C >3.5mmol/L ☐

I. Has the patient achieved a 40% reduction of non-HDL-C from baseline? Y (N)
II. Is non-HDL-C ≤4.0 mmol/L on maximum tolerated lipid lowering therapy? Y (N)

* High CVD risk defined as history of ACS, arterial revascularisation, ischaemic stroke or PAD
† Very high CVD defined as recurrent CVD events or CVD events in more than one vascular bed

B. Primary Heterozygous familial hypercholesterolaemia ☐

Without CVD and LDL-C >5.0 mmol/L ☐ With CVD and LDL-C >3.5mmol/L ☐

☐ Definite FH (genetically confirmed) ☐ Definite FH (NMD) ☐ Probable FH ☐ Possible FH

C. Eligibility Checklist ☐

I. Has patient received maximum tolerated statin and ezetimibe therapy? (Y)/ N
II. Has the patient been concordant with drug therapy and lifestyle measures? (Y)/ N
III. Have secondary causes of hyperlipidemia been excluded (if not recently)? (Y)/ N
IV. If the patient has diabetes mellitus has glycaemia control been optimised? ~~Y/N~~ NA
V. Is further titration of lipid lowering therapy limited by intolerance? (Y)/ N

If Yes to V, provide details: myalgia on atorva, rosuva 5 mg

D. Current Lipid lowering drug therapy	Dose/Frequency	Tick if on no therapy ☐
EZETIMIBE	10mg OD	Continued (Y)/ N
		Continued Y / N
		Continued Y / N

Enter fasting lipid profile results used for eligibility assessment Date:

Total cholesterol (mmol/L)	6.2	HDL-cholesterol (mmol/L)	1.0
Triglycerides (fasting) (mmol/L)	2.2	Non-HDL-cholesterol (mmol/L)	5.2
Lipoprotein(a) (mg/L ☐ nmol/L ☐)		LDL-C (mmol/L) Betaquant ☐	4.2

This new treatment option was explained and after demonstration of the self-injection device he wished to proceed with fortnightly evolocumab injections as recommended.

Details of PCSK9 inhibitor treatment	
Alirocumab 75 mg ☐ Alirocumab 150 mg ☐ Evolocumab 140 mg ☑	Q2W ☑ Q4W ☐
PCSK9 inhibitor education and injection training	Date
Date of PCSK9 Inhibitor prescription (7 days before required for 1st dose)	Date
Date of first dose administration Tick if self-administered in clinic ☑	Date
Date of on-treatment lipid profile to assess response (usually pre-5th dose)	Date

After 8 weeks on the combination of ezetimibe and evolcumab, he arranged a repeat non- fasting blood lipid profile, just before his 5th injection was due. The results showed a 58% reduction of his non-HDL-cholesterol which brought it to within the ideal target range (non- HDL-C less than 2.5 mmol/L).

Enter non-fasting lipid profile results used to assess response Date:

Total cholesterol (mmol/L)	3.2	HDL-cholesterol (mmol/L)	1.0
Triglycerides (fasting) (mmol/L)	3.2	Non-HDL-cholesterol (mmol/L)	2.2
Non-HDL-C reduction of >20% achieved? (Y)/ N		Treatment continued?	(Y)/ N

He expressed surprise that the results had improved as he has assumed that if his cholesterol was lowered again his back and muscle pains would return, but happily it had not.

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