# PRIMARY PREVENTION OF CHD AND STROKE IN HIGH RISK PATIENTS

Random non-fasting test for total cholesterol, HDL cholesterol (TC: HDL ratio) and LFTs. Test appropriately to allow for exclusion of secondary causes.

→ If cholesterol > 7.5 mmol/l or LDL –C ≥ 5mmol/l exclude secondary causes and consider familial hyperlipidaemia. Consider referral to lipid clinic. *

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Calculate ASSIGN score.

***http://assign-score.com/ – if already treated for HBP, use most recent pre-treatment BP for risk estimation***

QRISK®3 may give a more accurate score for those patients with mental health illness

https://qrisk.org/three/index.php

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Treat patient if 10-year cardiovascular event risk **≥ 20% using atorvastatin 20mg** daily ***(SIGN 149)***

NICE adopts a ≥10% risk threshold. SIGN guidance (≥20% risk) retains primacy in NHS Scotland.

For patients with a 10 yr. risk ≥10% and <20%, clinicians may wish to discuss the risks and benefits of statin treatment, taking into account the benefits from lifestyle modification, co-morbidities, polypharmacy, frailty, life expectancy and informed patient preferences.

NB. There is no target for cholesterol in primary prevention therefore there is no need for routine cholesterol testing once treatment is commenced unless clinically indicated. There is no evidence to support up-titration from atorvastatin 20mg or the use of additional drugs

# SECONDARY PREVENTION OF CORONARY HEART DISEASE AND ISCHAEMIC STROKE/TIA

**Patients with established vascular disease are at high risk and should be treated with a statin regardless of total blood cholesterol**

i.e. *Established cardiovascular disease/ CKD ≥stage 3 /micro- or macro- albuminuria/ Diabetic patients aged ≥ 40 years/ Diabetic patients <40yrs with additional factors SIGN 149*

Random non- fasting test for total cholesterol, HDL cholesterol and LFTs. Test appropriately to allow for exclusion of secondary causes

→ If cholesterol > 7.5 mmol/l or LDL –C ≥ 5mmol/l exclude secondary causes and consider familial hyperlipidaemia. Consider referral to lipid clinic. *

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**Treat all patients with statin regardless of baseline cholesterol concentration**

Recommended drug & daily dose:

Established cardiovascular disease: **Atorvastatin 80mg daily**

CKD ≥ stage 3 / micro- or macro- albuminuria / diabetic patients**: Atorvastatin 20mg daily initially**

**See BNF for cautions, contra-indications and clinically important interactions. Some statins potentially interact with other drugs.**

For true statin intolerance (see below re rechallenge of statins) consider the prescribing of **ezetimibe** in high risk patients. This is off label prescribing. **Bempedoic acid** may also be considered in this patient group when a PCSK9 inhibitor is deemed inappropriate (subject to SMC restrictions)

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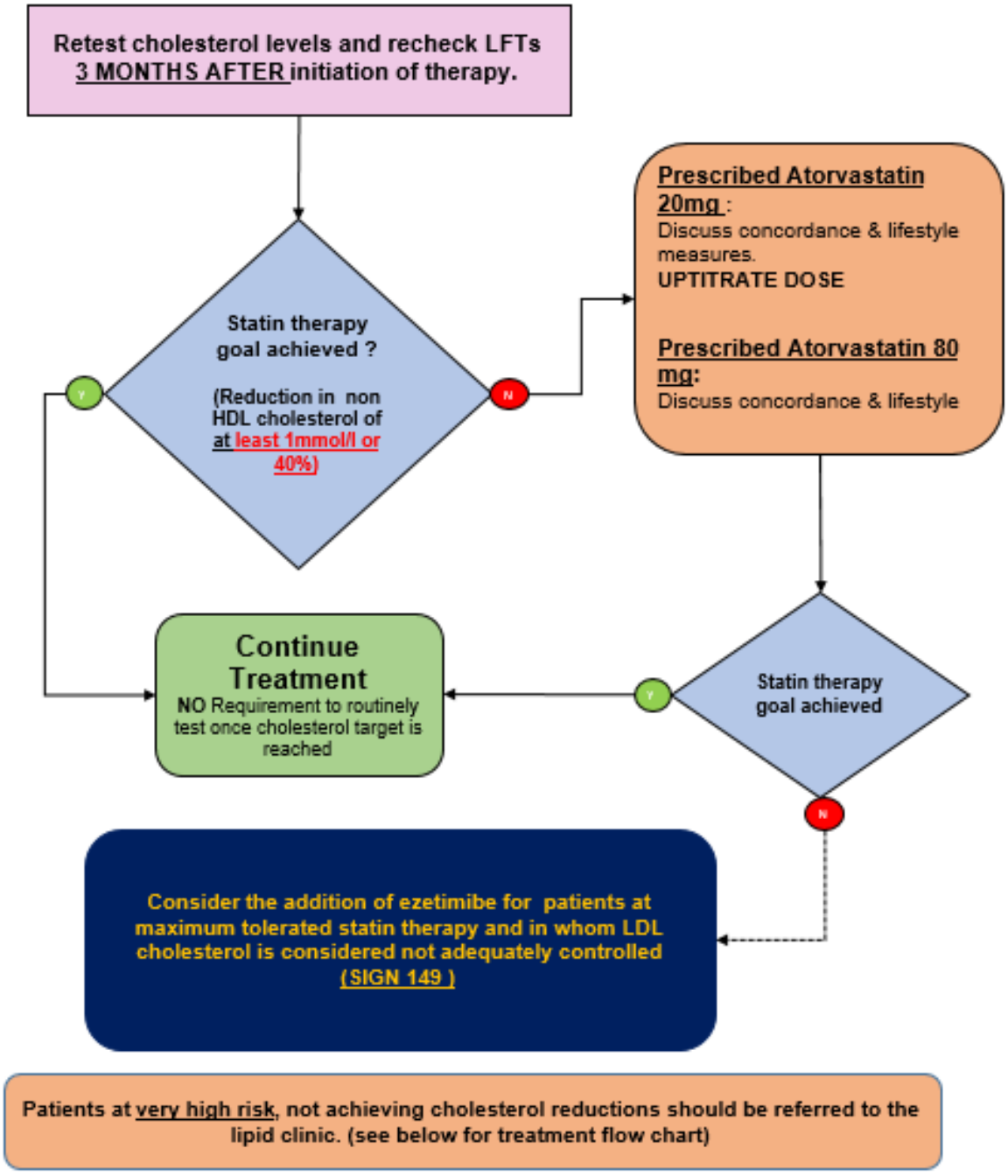
Approved by ADTC April 2022 Review by end April 2025 (V2)

# SECONDARY PREVENTION




*Referral to the lipid clinic is through a cardiology referral.

**Sign 149 Link HERE**

**Note on LDL-C and Non-HDL-C**: Both are similar in terms of correlation to C.V. disease but strictly speaking they are **not** identical or interchangeable terms.[1,2] **ASSIGN uses Non-HDL-C**.

- **Non-HDL-C is calculated directly: Non HDL-C** = TC - HDL-C**.** *This will include LDL-C as well as other lipoproteins (e.g. VLDL-C) identified as playing a causal role in C.V. disease.*
- **LDL-C:** is usually calculated indirectly from TC, HDL and an approximation of VLDL-C*. i.e. **LDL=TC–HDL–(TG/2.2)***

Notes

| Statin Intolerance |
|---|
| Patients who report statin intolerance may be rechallenged, initially with the same dose/same statin unless there is significant creatinine kinase elevation. If reported intolerance persists then an alternative statin should be offered. SIGN 149 reports that 70%-90% of patients who report statin intolerance are able to take some form of statin when rechallenged.<br>**NB** The evidence for the use of statins is much stronger than for other lipid-lowering agents for both primary and secondary prevention of cardiovascular disease. It is important to emphasise this to patients, and to ensure that there is genuine intolerance before considering an alternative. |
| **Primary Prevention (those with no diagnosis of CHD, stroke/TIA or diabetes)**<br>Ensure patient is truly intolerant of statin before any change to therapy (see above). Reinforce dietary and lifestyle measures. If familial hyperlipidaemia is suspected the patient should be screened for such. Ezetimibe can be considered for primary prevention in patients at elevated CVD risk in whom statin therapy is contraindicated. |
| **Secondary Prevention (those with a diagnosis of CHD, stroke/TIA or diabetes)**<br>Ensure patient is truly intolerant of statin (see above) before any change to therapy. Reinforce dietary and lifestyle measures. Consider alternative agents - for example ezetimibe, if necessary. (The use of ezetimibe as monotherapy in secondary prevention is off label use.) PCSK9 Inhibitors and bempedoic acid can be considered within SMC restrictions. |
| **Patients with symptoms of muscle pain and CK>10 times the upper limit of normal should stop statin therapy.** |
| **Failure to reach Cholesterol Targets** |
| **Primary Prevention (those with no diagnosis of CHD, stroke/TIA or diabetes)**<br>There is no primary prevention target in SIGN 149, in NICE guidance, nor in this guideline. Further cholesterol checking once treatment has started, or up titration from atorvastatin 20mg is not recommended. |
| **Secondary Prevention (those with a diagnosis of CHD, stroke/TIA or diabetes)**<br>Patients who fail to achieve a reduction of 1mmol/l or 40% from baseline of non HDL cholesterol should be considered for the addition of ezetimibe once the maximum tolerated statin dose is reached. |
| **Lipid-lowering Drugs - Formulary Options** |
| Statins listed in the NHSL formulary: **atorvastatin (preferred)**, simvastatin and rosuvastatin. |
| Other Agents: ezetimibe; bempedoic acid (within SMC restrictions). Bempedoic acid / ezetimibe provides a single tablet alternative to bempedoic acid plus ezetimibe. |

**Prevention of atherosclerotic arterial disease requires control of all risk factors.**

**No single risk factor, including cholesterol concentration, should be viewed in isolation.**

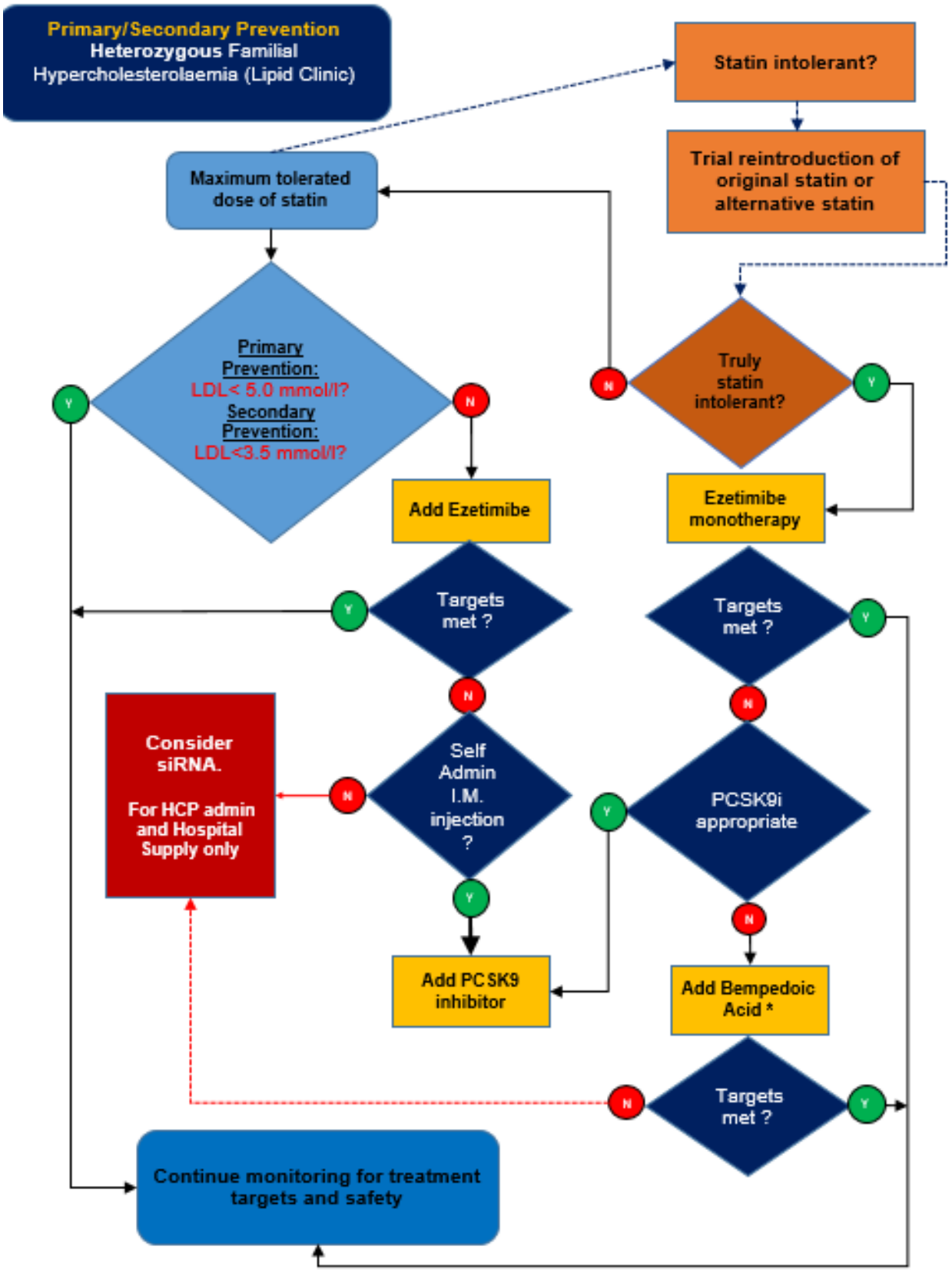
- All other risk factors (e.g. smoking, blood pressure, diabetic control) should be addressed.
- Dietary and other lifestyle advice (e.g. alcohol, obesity, physical activity, diet) should be given.
- Addition of other medication should be considered in the secondary prevention of vascular disease (anti- platelet therapy, beta blockers, ACE inhibitors etc.)
- **Ensure secondary causes of dyslipidaemia (hypothyroidism, renal impairment, liver disease, alcohol excess and diabetes) have been excluded.**

**NHSL Guideline for the Management of Cholesterol in adults**

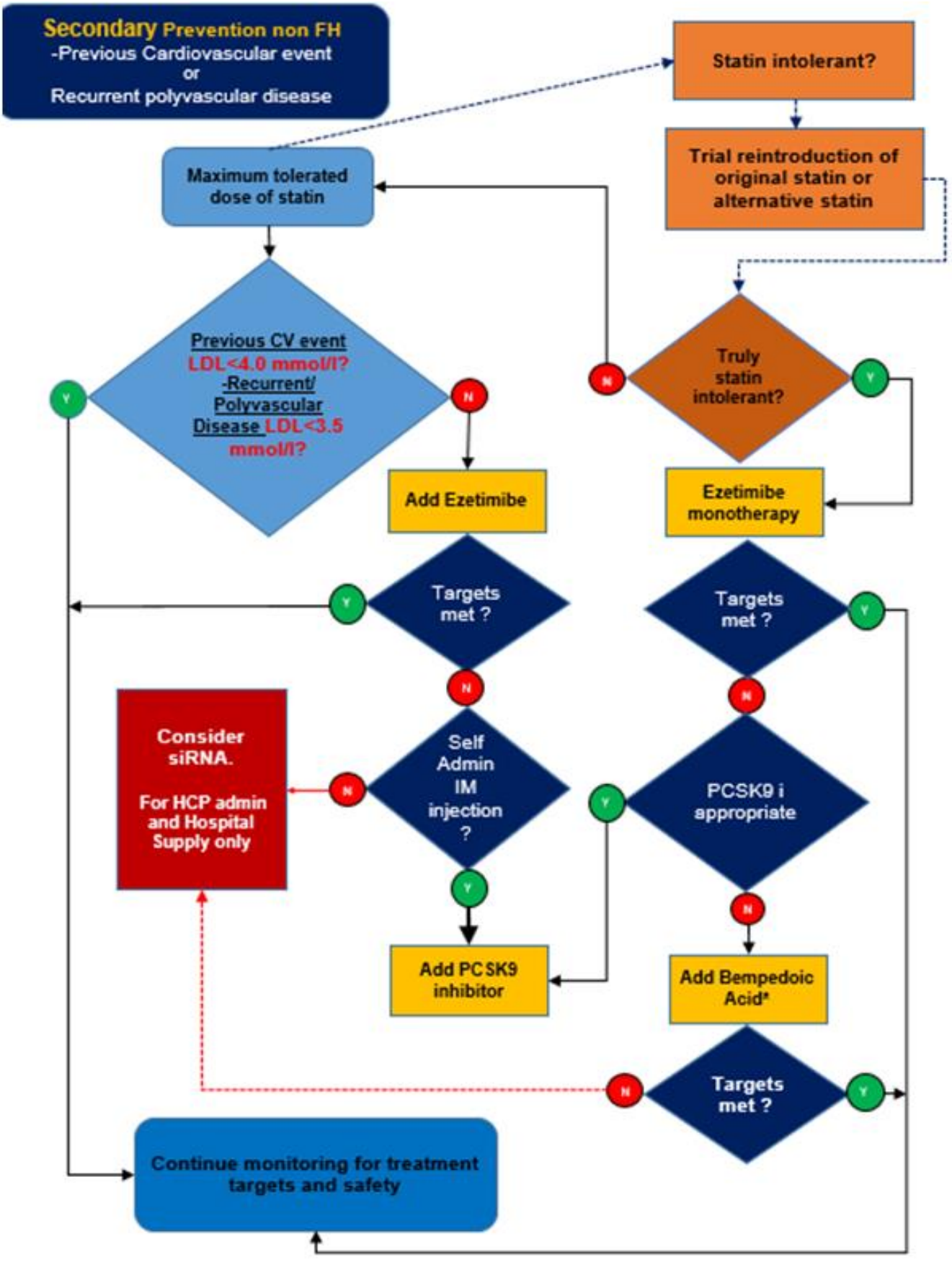
## Treatment Flow charts for patients at very high risk referred to lipid clinic.

[These patients will be monitored and managed by the lipid clinic staff.]

While SIGN 149 has no defined cholesterol level targets but aims for a percentage reduction from baseline, acceptance for treatment with a **PCSK9 inhibitor is subject to SMC restrictions,** which defines LDL cholesterol levels. **See Appendix 1**
The siRNA is accepted with restrictions, **see appendix 1C**, but remains Hospital Supply and requires HCP administration.
Bempedoic acid is not accepted for use alongside a Statin. **See Appendix 1B** for details.




*bempedoic acid **Plus** ezetimibe **or** also available as a single tablet alternative (bempedoic acid / ezetimibe)




*bempedoic acid **Plus** ezetimibe **or** also available as a single tablet alternative (bempedoic acid / ezetimibe)

## Appendix 1 - PCSK-9 inhibitors

Patient identification

Treatment initiation decisions will be made by clinicians at the lipid clinic taking into consideration the eligibility of the patient within the SMC restrictions and precautions/contraindications and adverse effects of the treatment.

Prescribing

Prescribing will be on hospital prescriptions ('blue pads') from clinicians in the lipid clinic. This may be reviewed in future as confidence is gained in the use of these drugs. PCSK-9 inhibitors are also available via Homecare.

Administration

Treatment will be administered by the patient in their own home. Patient education and training will be delivered by the lipid clinic.

Monitoring

Dose titration will be undertaken at the lipid clinic. Routine follow up of patients will be arranged by the lipid clinic and reviewed by the cardiologist who initiated treatment. This may be reviewed in future as confidence is gained in the use of these drugs.

## Medication

### ALIROCUMAB

**Medicine Name:**

Alirocumab (Praluent®) 75mg/1ml solution for injection prefilled pen
150mg/1ml solution for injection prefilled pen
300mg/2ml solution for injection prefilled pen

**Licensed indication:**

- 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.

A recent Cochrane review update found alirocumab decreased the risk of CVD when **added** to other LDL-C-lowering medicines (e.g. statins or ezetimibe). Alirocumab additionally showed a decrease in death from any cause. There was only limited low quality evidence when compared **against** other LDL-C-lowering drugs.[1]

**SMC Restriction:** for specialist use only in patients at high cardiovascular risk as follows:

- Patients with heterozygous familial hypercholesterolaemia (HeFH) and LDL-C ≥5.0mmol/L, for primary prevention of cardiovascular events or,
- patients with HeFH and LDL-C ≥3.5mmol/L, for secondary prevention of cardiovascular events or,
- patients at high risk due to previous cardiovascular events and LDL-C ≥4.0mmol/L or,
- patients with recurrent/polyvascular disease and LDL-C ≥3.5mmol/L.

## EVOLOCUMAB

**Medicine Name:**

Evolocumab (Repatha Sureclick®)
140mg/1ml solution for injection prefilled disposable device

**Licensed Indication:**

Hypercholesterolaemia and mixed dyslipidaemia - 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.
-Homozygous familial hypercholesterolaemia - adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.

A recent Cochrane review update found Evolocumab decreased the risk of CVD when **added** to other LDL-C-lowering medicines (e.g. statins or ezetimibe). There was insufficient evidence to demonstrate a reduction in all-cause mortality. There was only limited low quality evidence when compared **against** other LDL-C-lowering drugs[3].

**SMC restriction**: for specialist use only, when administered at a dose of 140mg every two weeks, in patients at high cardiovascular risk as follows:
-patients with heterozygous familial hypercholesterolaemia (HeFH) and LDL-C ≥5.0mmol/L for primary prevention of cardiovascular events or,
-patients with HeFH and LDL-C ≥3.5mmol/L for secondary prevention of cardiovascular events or,
-patients at high risk due to previous cardiovascular events and LDL-C ≥4.0mmol/L or
-patients with recurrent/polyvascular disease and LDL-C ≥3.5mmol/L

## Appendix 1B Adenosine triphosphate citrate lyase (ACL) inhibitor

## BEMPEDOIC ACID

**Medicine Name:**

Bempedoic Acid (Nilemdo®) 180mg tablets ▼
Bempedoic acid 180mg/ezetimibe 10mg (Nustendi ®) ▼

**Licensed Indication:**

Primary hypercholesterolaemia or mixed dyslipidaemia in patients who have not responded adequately to other appropriate measures [in combination with a statin, or with a statin and other lipid-lowering therapies, or with other lipid-lowering therapies or alone if a statin contra-indicated or not tolerated
The trial data has not assessed the effect of Bempedoic Acid on CV outcomes. An ongoing trial is due to report on this in 2023[4].

**SMC restriction:** For use in combination with ezetimibe in patients who are:

-statin intolerant or for whom a statin is contra-indicated

**and**

-where ezetimibe alone does not appropriately control LDL-C

**and**

-where proprotein convertase subtilisin/ kexin type 9 (PCSK9) inhibitors are not appropriate

## Appendix 1C - small interfering ribonucleic acid (siRNA) (RNA interference mediated reduction of PCSK9 production)

### INCLISIRAN

**Medicine Name**:

Inclisiran (Leqvio® )284mg/1.5ml solution for injection pre-filled syringes) ▼

**Administration:**

For specialist use only. Hospital supply. Administration to be carried out by a Health Care Professional.

**Licensed Indication:**

Indication under review: for 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 who are 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.
The effect of Inclisiran on Cardiovascular outcomes is not yet known (trial data only demonstrates surrogate indicator of LDL-C reductions). Data on the direct comparison of inclisiran with other therapies is lacking at present also.[5]

**SMC restriction**: for specialist use only in patients at high cardiovascular risk as follows:

-patients with heterozygous familial hypercholesterolaemia (HeFH) and LDL-C ≥5.0mmol/L, for primary prevention of cardiovascular events or,
-patients with HeFH and LDL-C≥3.5mmol/L, for secondary prevention of cardiovascular events or,
-patients with high risk due to previous cardiovascular events and LDL-C≥4.0mmol/L or,
-patients with recurrent/polyvascular disease and LDL-C≥3.5mmol/L.

## References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