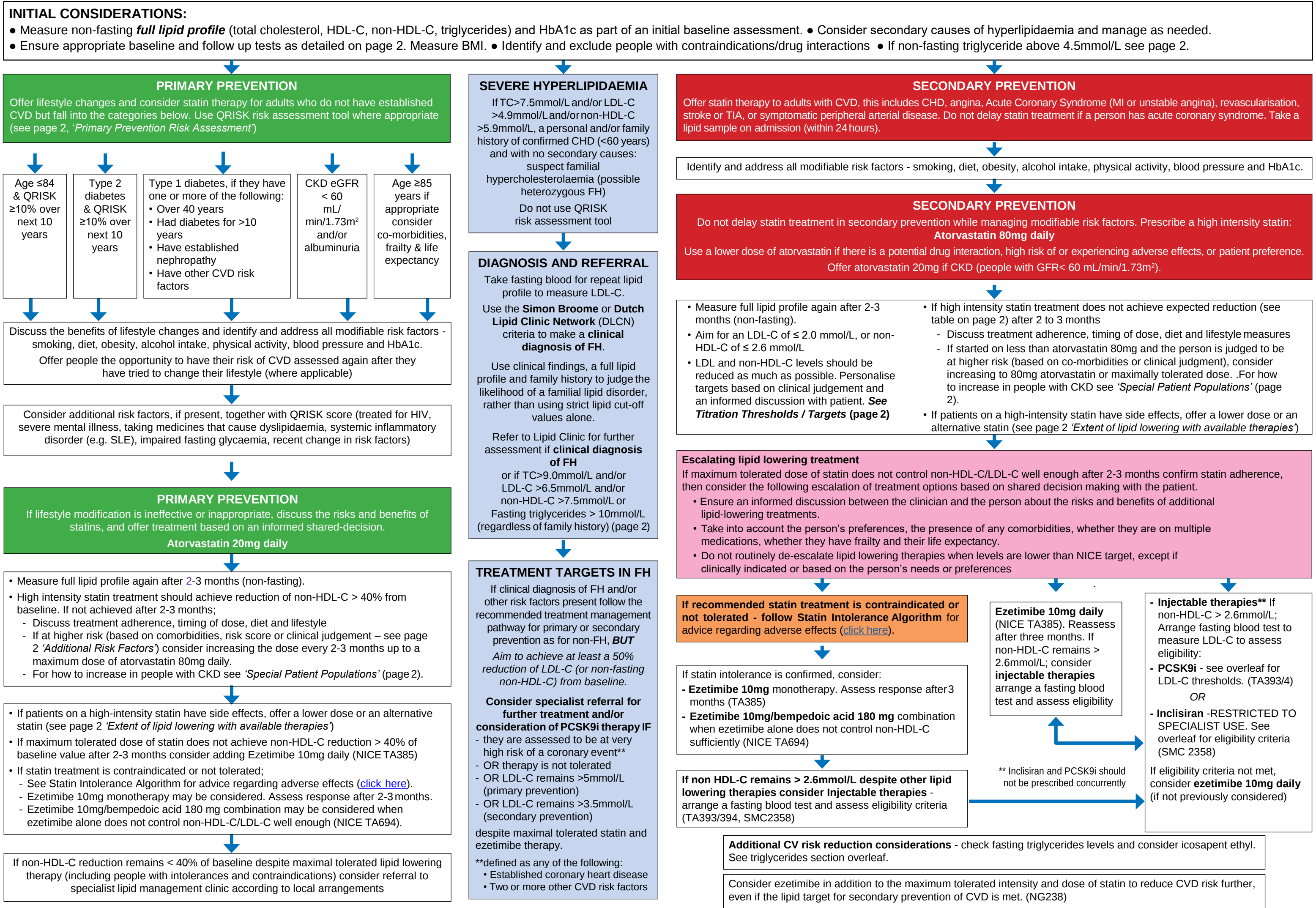


# Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD



MANAGEMENT

This guidance applies to new patients and may also be taken into consideration for those already on statins at their annual review. If 40% reduction of non-HDL-C, or target levels are not achieved, offer high intensity statins. Discuss with people who are stable on a low- or medium-intensity statin the likely benefits and potential risk of side effects if changed to a high-intensity statin when they have a medication review and agree with the person whether a change is needed.

Ezetimibe, alirocumab, evolocumab or inclisiran can be added when patients' LDL-C levels are not lowered enough with the maximally tolerated dose of statins. If statins are contraindicated or not tolerated and ezetimibe alone does not control LDL-C well enough, bempedoic acid with ezetimibe is an option. Do not offer a fibrate, nicotinic acid, bile acid binder or omega-3 fatty acids alone or in combination with statin, for the prevention of CVD (check NICE NG238 and TA805 for exceptions).

PRIMARY PREVENTION RISK ASSESSMENT

Use [QRISK3](#) version of the calculator (or QRISK2 if not available).

- Do not use this risk assessment tool for people with established CVD or those who are already at high risk of developing CVD because of FH or other inherited disorders of lipid metabolism.
- Do not use a risk assessment tool to assess CVD risk in people with type 1 diabetes, or eGFR < 60 mL/min/1.73 m² and/or albuminuria (as already at high risk of developing CVD).
- Consider people aged ≥ 85 at increased risk of CVD because of age alone particularly people who smoke or have raised BP.
- If QRISK <10% over next 10 years, do not rule out treatment if there is an informed preference for taking a statin or a concern that risk may be underestimated.

- Consider a lifetime risk tool (e.g. [QRISK3-lifetime](#)) to inform discussions on CVD risk and to motivate lifestyle changes, particularly for people with a 10-year score < 10%, and people < 40 who have CVD risk factors.

Additional Risk Factors

- Note, standard CVD risk scores including QRISK may underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These include, but not limited to the following group of people;
- obesity increases CVD risk (NICE CG189)
  - treated for HIV
  - severe mental illness
  - taking medicines that can cause dyslipidaemia such as antipsychotic medication, corticosteroids or immunosuppressant drugs
  - already taking medicines to treat CVD risk factors
  - autoimmune disorders such as SLE, and other systemic inflammatory disorders
  - non-diabetic hyperglycaemia
  - significant hypertriglyceridaemia (fasting triglycerides 4.5-9.9mmol/L)
  - recent risk factor changes e.g. quit smoking, BP or lipid treatment

Consider socio-economic status as an additional factor contributing to CVD risk (if not already in the risk calculator).

SPECIAL PATIENT POPULATIONS

Type 1 Diabetes

While NICE recommends offering statins to patients with Type 1 diabetes as detailed in the algorithm, it also states to consider statins in those aged 18 to 40 with type 1 diabetes, including those who have had diabetes for ≤ 10 years

Chronic Kidney Disease

Offer atorvastatin 20mg for the primary or secondary prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73m² and/or albuminuria)

Increase the dose if target is not achieved and eGFR is 30 mL/min/1.73m² or more. Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m²

Statins in Pregnancy and Lactation

Statins should be stopped 3 months before attempting to conceive and not be restarted until breastfeeding is finished. Stop statins if pregnancy is a possibility.

ABBREVIATIONS

- |                                                   |                                                                                       |
|---------------------------------------------------|---------------------------------------------------------------------------------------|
| <b>ALT:</b> alanine aminotransferase              | <b>non-HDL-C:</b> non-high density lipoprotein cholesterol                            |
| <b>AST:</b> aspartate aminotransferase            | <b>PCSK9i:</b> proprotein convertase subtilisin kexin 9 monoclonal antibody inhibitor |
| <b>CHD:</b> coronary heart disease                | <b>QOF:</b> Quality and Outcomes Framework                                            |
| <b>CKD:</b> chronic kidney disease                | <b>SLE:</b> systemic lupus erythematosus                                              |
| <b>CVD:</b> cardiovascular disease                | <b>SPC:</b> summary of product characteristics                                        |
| <b>FH:</b> familial hypercholesterolaemia         | <b>TC:</b> total cholesterol                                                          |
| <b>JBS:</b> Joint British Societies               |                                                                                       |
| <b>LDL-C:</b> low density lipoprotein cholesterol |                                                                                       |

STATIN INTOLERANCE

Statin intolerance is defined as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or that may result in adherence to therapy being compromised. For people who are intolerant of the recommended statin treatment see the Statin Intolerance Algorithm [here](#).

EXTENT OF LIPID LOWERING WITH AVAILABLE THERAPIES

| Approximate reduction in LDL-C |     |     |     |     |     |
|--------------------------------|-----|-----|-----|-----|-----|
| Statin dose mg/day             | 5   | 10  | 20  | 40  | 80  |
| Fluvastatin                    |     |     | 21% | 27% | 33% |
| Pravastatin                    |     | 20% | 24% | 29% |     |
| Simvastatin                    |     | 27% | 32% | 37% | 42% |
| Atorvastatin                   |     | 37% | 43% | 49% | 55% |
| Rosuvastatin                   | 38% | 43% | 48% | 53% |     |
| Atorvastatin + Ezetimibe 10mg  |     | 52% | 54% | 57% | 61% |

 **Low intensity statins** will produce an LDL-C reduction of 20-30%

 **Medium intensity statins** will produce an LDL-C reduction of 31-40%

 **High intensity statins** will produce an LDL-C reduction above 40%

 **Simvastatin** 80mg is not recommended due to risk of muscle toxicity

- **Rosuvastatin** may be used as an alternative to atorvastatin if compatible with other drug therapy. Some people may need a lower starting dose (see BNF).
- Low/medium intensity statins should only be used if intolerance or drug interactions.
- **Ezetimibe** when combined with any statin is likely to give greater reduction in non-HDL-C or LDL-C than doubling the dose of the statin.
- **PCSK9i** (NICE TA393, TA394) alone or in combination with statins or ezetimibe produce an additional LDL-C reduction of approximately 50% (range 25-70%).
- **Bempedoic acid** when combined with ezetimibe (TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%).
- **Inclisiran** (SMC 2358) alone or in combination with statins or ezetimibe produces an additional LDL-C reduction of approximately 50% (range 48-52%) but no clinical outcome evidence is currently available.

MONITORING

Baseline Measurements

In addition to full lipid profile, measure renal, thyroid and liver profiles (including albumin) and HbA1c to exclude secondary causes and co-morbidities. Measure baseline liver transaminase (ALT or AST) before starting a statin. Measure CK if unexplained muscle pain before starting a statin. CK should not be measured routinely especially if a patient is asymptomatic.

|            | Primary Prevention                                                                                                                                                                      |            | Secondary prevention |            |
|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|----------------------|------------|
|            | Lipid Profile                                                                                                                                                                           | ALT or AST | Lipid Profile        | ALT or AST |
| Baseline   | ✓                                                                                                                                                                                       | ✓          | ✓                    | ✓          |
| 2-3 months | ✓                                                                                                                                                                                       | ✓          | ✓                    | ✓          |
| 6-9 months | If targets are not met, and up-titration is agreed, repeat full lipid profile and ALT or AST within 2-3 months of each up-titration of statin dose or addition of ezetimibe as required |            |                      |            |
| 12 months  | ✓                                                                                                                                                                                       | ✓          | ✓                    | ✓          |
| Yearly     | ✓*                                                                                                                                                                                      |            | ✓*                   |            |

*Provide annual medication reviews for people taking statins to discuss effectiveness of therapy, medicines adherence, lifestyle modification and address CVD risk factors.*

***\*Offer in secondary prevention, and consider in primary prevention an annual non-fasting full lipid profile to inform the discussion around effectiveness of lipid lowering therapy and any medicines non-adherence.***

Monitoring

Repeat full lipid profile is non-fasting.

Do not stop statins because of an increase in blood glucose level or HbA1c.

Advise that the risk of muscle pain, tenderness or weakness associated with statins is small and the rate of severe muscle adverse effects (rhabdomyolysis) is extremely low.

Liver Transaminases

Measure liver transaminase within 3 months of starting treatment and then within 2-3 months of every additional up titration and then again at 12 months, but not again unless clinically indicated.

If ALT or AST are greater than 3 times the upper limit of normal then do not initiate a statin or discontinue statin therapy already prescribed and repeat the LFTs in a month.

- If ALT or AST are elevated but are less than 3 times the upper limit of normal then:
- Do not routinely exclude from statin treatment
  - Continue the statin and repeat in a month.
  - If they remain elevated but are less than 3 times the upper limit of normal then continue statin and repeat again in 6 months.

REFERENCES

|                                                                                |                                  |                                                                                   |
|--------------------------------------------------------------------------------|----------------------------------|-----------------------------------------------------------------------------------|
| <a href="#">JBS3, 2014.</a>                                                    | <a href="#">NICE 2016, TA385</a> | <a href="#">NICE 2022, TA805</a>                                                  |
| <a href="#">Kirsten et al. 2005. Hospital Pharmacy 40(8):687-692</a>           | <a href="#">NICE 2016, TA393</a> | <a href="#">NICE 2023, NG238</a>                                                  |
| <a href="#">Navarese et al. 2015. Annals of internal medicine 163(1):40-51</a> | <a href="#">NICE 2016, TA394</a> | <a href="#">NICE 2023, CG189</a>                                                  |
|                                                                                | <a href="#">NICE 2008, CG71</a>  | <a href="#">SMC 2021, SMC2358</a>                                                 |
|                                                                                | <a href="#">NICE 2021, TA694</a> | <a href="#">Soon Jun Hong et al. 2018. Clinical therapeutics 40(2):226-241.e4</a> |

TITRATION THRESHOLD / TARGETS

|                      | NICE titration threshold / QOF                                                             | JBS3**                                  |
|----------------------|--------------------------------------------------------------------------------------------|-----------------------------------------|
| Primary prevention   | Escalate lipid lowering therapy if non-HDL-C reduction from baseline ≤ 40%                 | non-HDL-C <2.5mmol/L (LDL-C <1.8mmol/L) |
| Secondary Prevention | Aim for an LDL-C of ≤ 2.0 mmol/L, or non-HDL-C of ≤ 2.6 mmol/L at least*                   |                                         |
| FH                   | Optimise lipid lowering therapy to achieve at least 50% reduction in LDL-C (or non-HDL-C.) |                                         |

\*Consider ezetimibe to reduce CVD risk further, even if the NICE lipid target for secondary prevention of CVD is met.

\*\*LDL-C and non-HDL-C levels should be reduced as much as possible in people with CVD. Consider a personalised target, as clinically indicated, e.g. JBS3 consensus recommendation

**Non-HDL-C** = TC minus HDL-C     **LDL-C** = non-HDL-C minus (Fasting triglycerides<sup>a</sup>/2.2)

<sup>a</sup> valid only when fasting triglycerides are less than 4.5 mmol/L

SPECIALIST SERVICES

Scope of specialist service available locally may include; lipid clinic, FH genetic diagnosis and cascade testing, lipoprotein apheresis service, PCSK9i and inclisiran clinic. The decision to prescribe any injectable is taken in secondary care. PCSK9i are amber list drugs and are initiated in secondary care and can then be prescribed in primary care— see [GP info sheet](#). Inclisiran is currently restricted to specialist use and must be initiated and prescribed in secondary care only. Eligibility criteria and fasting LDL-C thresholds for PCSK9i and inclisiran are summarised below.

| NICE TA393 Alirocumab<br>NICE TA394 Evolocumab | Without CVD        | With CVD               |                             |
|------------------------------------------------|--------------------|------------------------|-----------------------------|
|                                                |                    | High risk <sup>1</sup> | Very high risk <sup>2</sup> |
| Primary non-FH or mixed dyslipidaemia          | Not recommended    | LDL C > 4.0 mmol/L     | LDL C > 3.5 mmol/L          |
| Primary heterozygous-FH                        | LDL C > 5.0 mmol/L | LDL C > 3.5 mmol/L     |                             |

<sup>1</sup> History of any of the following: ACS; coronary or other arterial revascularisation procedures; CHD, ischaemic stroke; PAD. <sup>2</sup> Recurrent CV events or CV events in more than 1 vascular bed (that is, polyvascular disease).

**Inclisiran is RESTRICTED TO SPECIALIST USE** and only in patients at high cardiovascular risk as follows (SMC 2358):

- 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

Bempedoic acid/ezetimibe are available in primary care and do not require initiation by specialist services.

TRIGLYCERIDES

| Triglyceride concentration | Action                                                                                                                                                                                                                                                                                                        |
|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Greater than 20mmol/L      | <b>Refer to lipid clinic for urgent specialist review</b> if not a result of excess alcohol or poor glycaemic control. At risk of acute pancreatitis.                                                                                                                                                         |
| 10 - 20mmol/L              | Repeat the TG measurement with a fasting test (after an interval of 5 days, but within 2 weeks) and review for potential secondary causes of hyperlipidaemia. Seek specialist advice if the TG concentration remains > 10mmol/litre. At risk of acute pancreatitis                                            |
| 4.5 - 9.9mmol/L            | If non-fasting triglycerides are greater than 4.5mmol/L, repeat with a fasting TG measurement Be aware that the CVD risk may be underestimated by risk assessment tools, optimise the management of other CVD risk factors present and seek specialist advice if non-HDL-C concentration is > 7.5 mmol/litre. |

**Icosapent ethyl (TA805)**

- Check fasting triglycerides levels.
- Manage secondary causes of hypertriglyceridaemia.
- Consider icosapent ethyl (TA805) if patient has established cardiovascular disease (secondary prevention) **and**
  - on statins and fasting TG ≥ 1.7mmol/L and LDL-C\* between 1.04<sup>‡</sup> and ≤2.6mmol/L
- See table above and refer as appropriate.

\* LDL-C cannot be calculated using Friedewald’s formula if TG >4.5. Discuss with your lab. Consider using an alternative equation (eg Sampson, doi: 10.1001/jamacardio.2020.0013) or beta-quantification.

‡ Labs don’t report calculated LDL-C beyond one decimal point