North Central London
Joint Formulary Committee

Guidance for the management of hypertriglyceridaemia

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Document control

Date	Version	Amendments
18/02/19	1.0	New document developed
14/08/23	2.0	Additional information added to Omega-3 fatty acids advice. Inclusion of Icosapent ethyl and supporting information in line with NICE TA 805.

Document management

Groups / Individuals who have overseen the development of this guidance:	Dr Devaki Nair, Royal Free London NCL JFC Support Pharmacist
Groups which were consulted and have given approval:	NCL ICB Medicines Optimisation team NCL Formulary Pharmacists and specialists Dr Sarit Ghosh
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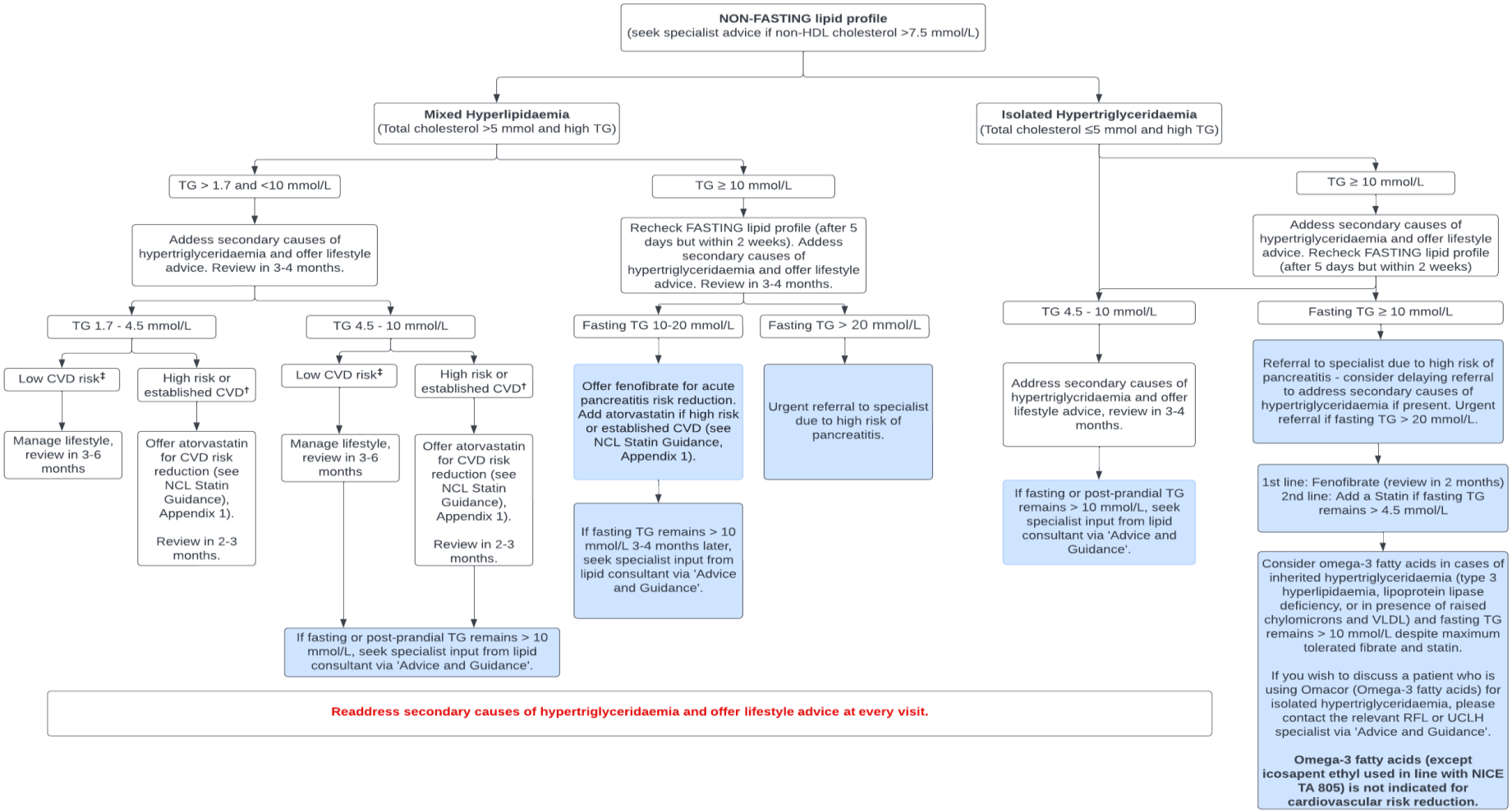
Management of raised triglyceride concentration



Key:

= Manage in primary care

= Manage in secondary care

Abbreviations:
TG = Triglycerides
CVD = Cardiovascular disease
HDL = High density lipoprotein
VLDL = Very low density lipoprotein

Definitions:
Fasting lipid profile = 10-12 hours after food
Post-prandial lipid profile = 3-4 hours after food
† **High risk of established CVD:**
- CVD risk ≥ 10% over next 10 years (QRISK assessment tool)
- Age > 85 years
- eGFR < 60mL/min/1.73m^2 and/or albuminuria
- Adults with type 1 diabetes

‡ **Low CVD risk:**
- <10% over next 10 years

* For cardiovascular risk reduction, specialists may consider Icosapent ethyl in line with NICE TA 805 in patients that have a high risk of cardiovascular events and raised fasting triglycerides (≥1.7 mmol/L) and are taking statins, but only if they have:
- established cardiovascular disease (secondary prevention), defined as a history of any of the following:
  - acute coronary syndrome (such as myocardial infarction or unstable angina needing hospitalisation)
  - coronary or other arterial revascularisation procedures
  - coronary heart disease
  - ischaemic stroke
  - peripheral arterial disease, and
- low-density lipoprotein cholesterol (LDL-C) levels above 1.04 mmol/L and below or equal to 2.60 mmol/L.

Note: Icosapent ethyl is not licensed for the treatment of hypertriglyceridaemia.

Secondary causes of hypertriglyceridemia [1]

- Obesity, often in association with an elevation in serum cholesterol
- Diabetes mellitus, where there is a relationship to poor glycaemic control and, in type 2 diabetes, obesity
- Nephrotic syndrome, often in association with hypercholesterolemia, and renal failure
- Hypothyroidism, often in association with hypercholesterolemia
- Serum total cholesterol and triglyceride concentrations normally increase markedly during pregnancy
- Medicines:
  - Oestrogen replacement administered orally
  - Tamoxifen can cause marked hypertriglyceridemia in a minority of women
  - Beta blockers, with the exception of carvedilol
  - Immunosuppressive medications, such as glucocorticoids and cyclosporine
  - HIV antiretroviral regimens
  - Oral retinoids (e.g. isotretinoin)

Investigations for causes of hypertriglyceridemia

- Urine dipstick (nephrotic syndrome)
- Blood tests:
  - Lipid profile (total cholesterol, HDL, non-HDL and triglycerides)
  - Fasting glucose or HbA1c
  - Renal function
  - Thyroid function tests (TFTs)
  - Liver function (LFTs)

Prescribing information for icosapent ethyl (see SPC for further information)

- Cautions: patients with hepatic impairment, atrial fibrillation or flutter, increased risk of bleeding, hypersensitivity to fish/shellfish
- Contraindications: Patients with hypersensitivity to the active substance, soya, peanuts, sorbitol or maltitol.
- Very common (≥1/10) and common (≥1/100 to <1/10) adverse effects: Bleeding, atrial fibrillation/flutter, gout, constipation, eructation, rash, musculoskeletal pain, peripheral oedema
- Monitoring: At the time of approval no specific monitoring was required for icosapent ethyl. GP's should review their patients as per their normal practice. However, icosapent ethyl is a black triangle drug and any suspected adverse reactions should be reported using the Yellow Card Scheme.

Lifestyle advice

Lifestyle modifications to reduce triglyceride levels are similar to those recommended for individuals at high risk of cardiovascular disease[1] (full lifestyle advice published in NICE CG181[2])

- Cardioprotective diet including:
  - Restrict consumption of high glycaemic index/load foods as well as refined sugars, fruit juices, and high fructose beverages [1]
  - Increased consumption of oily fish [1,2] (pregnant women to limit their oily fish to no more than 2 portions per week and to avoid marlin, shark and swordfish[2])
  - People with very high triglycerides (>10mmol/L) may benefit from the specialist advice from a lipid clinic regarding a very low fat diet
- Physical activity (at least 150 minutes of moderate intensity aerobic activity or 75 minutes of vigorous intensity aerobic activity)
- Weight management for those who are who are overweight or obese
- Avoid binge drinking and limit alcohol intake to national recommended limits
- Smoking cessation (primarily CV protection)

Monitoring fibrate therapy

- Recheck lipid levels within 3 months of initiation, aiming for a triglyceride level <4.5 mmol/L
- Check serum creatinine at baseline, within 3 months of initiation of treatment and at least annually thereafter (more frequently if clinical indicated).
  - Hold treatment if creatinine levels >50% ULN (upper limit of normal)
  - Consider dose reduction if renal function declines in line with the SPC / BNF
- Monitor liver transaminase levels every 3 months during the first 12 months of treatment and thereafter periodically.
  - Discontinue therapy if AST or ALT levels increase to more than 3x ULN.
  - If symptoms indicative of hepatitis occur (e.g. jaundice, pruritus), and diagnosis is confirmed by laboratory testing, fenofibrate therapy should be discontinued
- Baseline CK should only be checked in those who may already be taking a medicine that will increase the risk of myopathy when used concomitantly with fibrate, such as statin therapy.
- Routine CK monitoring for asymptomatic individuals is not recommended. Monitor CK for patients with muscle weakness/pain to assess severity of muscle damage and aid the decision to continue treatment

For information on prescribing statins and lipid modification for the prevention of CVD see:

- North Central London Statin Prescribing & Lipid Modification Guideline for the Prevention of Cardiovascular Disease
  - https://www.ncl-mon.nhs.uk/wp-content/uploads/Guidelines/2_Lipid_modification_prevention_cardiovascular_disease.pdf

Advice and Guidance: Accessible via eRS: https://nww.ebs.ncrs.nhs.uk/. The Royal Free Lipid Centre supports Advice and Guidance and can be identified on eRS as *"Lipid Management Service-Cardiology-Royal Free Hospital-RAL"*

Acknowledgement: Sections of this guideline were taken, with permission, from the South East London APC 'Guidance for the Management of Hypertriglyceridaemia' (July 2018)

Expert opinion: There are no national guidelines available for the management of hypertriglyceridaemia therefore the pathway structure is based on expert opinion from Royal Free London NHS Foundation Trust Lipid Clinic.

References:

1. UpToDate. Hypertriglyceridemia. (2019).
2. National Institute for Health and Care Excellence. NG238: Cardiovascular disease: risk assessment and reduction, including lipid modification. (2023). Available at: https://www.nice.org.uk/guidance/ng238.