Tablet Press EXTRA

The prescribing newsletter for GPs, nurses and pharmacists
NHS Northamptonshire

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Lipid modification (NICE CG181; 2014)

In July 2014 NICE issued a revised clinical guideline on lipid modification http://www.nice.org.uk/guidance/CG181 which differs substantially from their previous 2008 guidance. Some of the main differences include offering statins to people at ≥10% risk of a CV event over the next 10 years (previously ≥20%), the use of atorvastatin 20mg/day for primary prevention and atorvastatin 80mg/day for secondary prevention. Since this new guidance has caused some controversy in professional journals and lay media about the risk and benefits of "medicalising" patients at 10-20% risk and the use of higher intensity statins it has been suggested that prescribers might find a summary of the main differences and the rationale useful.

Within the guidelines statins have been arranged into 3 groups according to how much they reduce low density lipoprotein cholesterol e.g. low intensity (20%–30%), medium intensity (31%–40%) and high intensity (above 40%). See table below

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%[2]	43%	48%	53%	–

Primary prevention

- Before starting treatment for primary prevention:
  - discuss the benefits of lifestyle modification and optimise the management of all other modifiable CVD risk factors. Recognise that people may need support to change their lifestyle. Offer people the opportunity to have their CVD risk assessed again after making lifestyle changes.
  - take at least one sample for a full lipid profile; measure total cholesterol, HDL and non-HDL cholesterol (total cholesterol – HDL cholesterol) and triglyceride concentrations. A fasting sample is NOT needed.
- If patients (including adults with type 2 diabetes) have a ≥10% 10-year risk of developing CVD despite attempts at lifestyle modifications **"offer*" atorvastatin 20mg**. For people ≥85 years consider atorvastatin 20mg as statins may be of benefit in reducing the risk of non-fatal myocardial infarction, but be aware of factors that may make treatment inappropriate.
- **Adults with type 1 diabetes** – **"consider**"** atorvastatin 20mg for the primary prevention of CVD in all patients. **"Offer"** atorvastatin 20mg for the primary prevention of CVD to adults with type 1 diabetes who:
  - Are aged >40 years, OR
  - have had diabetes for >10 years, OR
  - have established nephropathy, OR
  - have other CVD risk factors. Start treatment with atorvastatin 20mg.
- **Adults with CKD – "Offer"** atorvastatin 20mg

Secondary prevention

- Take a full lipid profile but do NOT delay statin treatment to manage modifiable risk factors.
- Start treatment in people with CVD with **atorvastatin 80mg**. Use a lower dose of atorvastatin if any of the following apply:
  - potential drug interactions,
  - high risk of adverse effects,
  - patient preference.

This edition is also available on PathfinderRF
http://nww.pathfinder-rf.northants.nhs.uk/nene

- people with CKD (initial dose should be 20mg)

Baseline monitoring and follow-up:

➢ **Creatinine Kinase**

- Before offering a statin, ask the person if they have had persistent generalised unexplained muscle pain, whether this was associated, or not, with previous lipid-lowering therapy. If they have, measure CK levels.
  - if CK levels are >5 times the upper limit of normal, re-measure CK after 7 days.
  - If CK levels are still 5 times the upper limit of normal, do not start statin treatment.
  - if CK levels are raised but <5 times the upper limit of normal, start statin treatment at a lower dose.
- Do NOT measure CK levels in asymptomatic people who are being treated with a statin.

➢ **Liver transaminase enzymes**

Measure liver transaminase enzymes (alanine aminotransferase or aspartate aminotransferase) within 3 months of starting treatment and at 12 months, but not again unless clinically indicated.

➢ **Lipid**.

- Measure total cholesterol, HDL cholesterol and non-HDL cholesterol (calculated) in all people before starting statin treatment.
- Refer to a lipid specialist if they have
  - total cholesterol >7.5mmol/litre AND a family history of premature coronary heart disease OR total cholesterol >9.0mmol/litre.
  - triglyceride concentration of >20mmol/litre (not due to excess alcohol or poor glycaemic control).
  - two (second one "fasting") triglyceride concentrations (between 5 days and 2 weeks) between 10 and 20mmol/litre.
- Re-measure after 3 months of statin treatment and **aim for a >40% reduction in non-HDL cholesterol.**

Note – Reducing non-HDL by >40% reduction is the **"aim"** of treatment, rather than a "target". This is because any statin at any dose reduces CVD risk. Furthermore there can be a significant variation between individual lipid measurements (CI ~14%). As such patients should only be "**considered**" for an increased dose (if started on less than atorvastatin 80mg) if they have a higher risk because of comorbidities (risk score or clinical judgement). The vast majority of patients taking atorvastatin 20mg will have a greater than >40% non-HDL reduction (see table above) therefore adherence to lipid lowering treatment and "diet and lifestyle measures" should be discussed if this is not achieved, prior to considering a dose increase.

Identifying people for cardiovascular risk assessment in primary care

- For primary prevention of CVD use a systematic strategy to identify people who are likely to be at high risk. Do NOT use opportunistic assessment as the main strategy to identify CVD risk in unselected people.
- Prioritise people for a full formal risk assessment if their estimated 10-year risk of CVD is ≥10%. People aged >40 years should have their estimate of CVD risk reviewed on an ongoing basis.
- Use the QRISK2 risk assessment tool to assess CVD risk:
  - for primary prevention of CVD in people ≤84 years.
  - in people with type 2 diabetes. Do NOT use a risk assessment tool to assess CVD risk in people with type 1 diabetes (see above).
  - with an eGFR >60ml/min/1.73m2 and/or albuminuria (see above).
- Measure both total and HDL cholesterol to achieve the best estimate of CVD risk.
- Offer people information about their absolute risk of CVD and the absolute benefits and harms of an intervention over a 10-year period. Set aside adequate time during the consultation to provide information on risk assessment and to allow any questions to be answered.

Note - NICE expects that there will be a discussion with the patient about the risks and benefits of the intervention; a patient decision aid is available https://www.nice.org.uk/news/blog/should-i-be-taking-statins to facilitate discussions with patients about these. Accept that the patient may have different views from healthcare professionals about the balance of risks, benefits and consequences of treatments. The patient has the right to decide not to have a treatment, even if you do not agree with their decision, as long as they have the capacity to make an informed decision and have been given and understand the information needed to do this. If a person declines treatment, record this and advise them that their CVD risk should be reassessed again in the future

People currently taking other doses of statins
For people stable on a low or middle-intensity statin (e.g. simvastatin 40mg or atorvastatin 10mg) discuss the likely additional benefits and potential risks of changing to a high-intensity statin at their next routine medication review and agree with the person if a change is needed.

Adverse effects
Muscle-related problems are the most frequently reported side effect of statins. The following statin incidences have been estimated based on RCTs, cohort studies, published case and spontaneous reports:

- mild muscle pain: 190 cases per 100,000 patient years
- myopathy: 5 cases per 100,000 patient years
- rhabdomyolysis: 1.6 cases per 100,000 patient years

Many people who take statins experience muscle pain from time to time. However high quality evidence from RCTs shows that, overall, there is no clinical difference between statins and placebo. Real-world experience can add value, but is prone to biases. Some factors e.g. raised CK, history of muscle pain or cramps etc. increase the risk of muscle-related side effects for individual people. NICE advises that patients should have their CK level measured and be asked specifically about previous muscle symptoms prior to starting statins in order to try to identify those at greatest risk of muscle-related side effects so steps can be taken to reduce the risk i.e. start statin at a lower dose.

Some people who take statins develop diabetes. An extra 3 people (9 rather than 6 people) out of 100 taking atorvastatin 80mg daily over an average of 5 years will develop diabetes. However as the reduction in vascular risk from a statin outweighs the risk of diabetes NICE advises that an increase in HbA1c is not a reason to stop it.

Cost-effectiveness
The Guideline Development Group (GDG) concluded that atorvastatin 20mg was the most clinically effective option for primary prevention of CVD and so should be recommended. Furthermore despite atorvastatin 80mg not being licensed for secondary prevention it was considered to be very likely to be cost effective for all secondary prevention when compared with atorvastatin 20mg. The GDG did consider that high-intensity statins may increase the rate of adverse events but concluded that they would still be cost effective versus medium-intensity treatment.

Ezetimibe
People with primary hypercholesterolaemia (heterozygous familial and non-familial) should be considered for ezetimibe treatment as per NICE technology appraisal 132 (2008).

Ezetimibe is not routinely recommended by NICE as a treatment for patients **without** heterozygous hypercholesterolaemia. However prescribers may want to **"consider"** ezetimibe for patients if:

- statins are contra-indicated
- they cannot tolerate statins e.g. generic simvastatin, generic atorvastatin and rosuvastatin. Prior approval requests for Lipitor or rosuvastatin will be approved if generic simvastatin or atorvastatin calcium trihydate (same salt as Lipitor) have been tried.
- they are on statin treatment, but non-HDL intensity is not appropriately controlled e.g. patients who can only tolerate a low or medium intensity statin and their reduction in non-HDL is <40% and it is considered beneficial for a second lipid modifying drug to be added.

Note - There remains no published evidence that ezetimibe, alone or added to a statin, reduces the risk of CVD or mortality compared with an active comparator. The IMPROVE-IT study (ClinicalTrials.gov Identifier: NCT00202878) has been completed, but the results have not been yet been published in full in a peer reviewed journal

Fibrates, nicotinic acid, a bile acid sequestrant or omega-3 fatty acid compounds
Do NOT routinely offer fibrates, nicotinic acid, a bile acid sequestrant or omega-3 fatty acid compounds.
Note - In Northamptonshire **new** initiations of these drugs should only be on the recommendation of a consultant lipidologist.

NICE uses 'offer**' when it is confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective*

***NICE uses '**consider**' when it is confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective*