Guidance For Managing Suspected Statin Intolerance

Background

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 compliance with therapy being compromised” (NICE, 2007)

Approximately 5-10% of patients will experience an adverse effect from a statin, although many of these will not necessitate stopping treatment. Side effects commonly include muscle pains, headache and gastrointestinal effects, and less commonly sleep disturbances, sexual dysfunction, depression, skin rashes and hair loss (see current BNF for full list). Serious adverse events such as rhabdomyolysis, myopathy and elevation of liver transaminase (greater than three times the upper limit of normal) are very rare.

What action should I take if I suspect statin intolerance?

Muscle symptoms

- **Consider other possible causes** e.g. rigorous exercise, infection, recent trauma, drug or alcohol addiction. Muscle symptoms are often generalised but commonly occur in thigh and shoulder muscles. **Statins do not cause joint pain or worsen osteoarthritis**.

- **Stop the statin and check creatinine kinase**. Discontinue statin if markedly elevated (more than 5 times the upper limit of normal). Baseline CK levels before initiating statins are useful, especially in Afro-Caribbean patients who may naturally have higher pre-treatment levels. Once CK levels return to normal and symptoms resolve, reintroduce the statin at a lower dose or try an alternate low dose statin with careful monitoring.

- **Myalgia: Stop and rechallenge**: If CK levels are not elevated, stop the statin for 2-3 weeks. If muscle symptoms do not fully resolve then the statin is unlikely to be responsible and should be restarted. (Muscular symptoms are very common!). If muscle symptoms resolve, rechallenge with the statin, should symptoms recur then the statin is a probable cause.

- **Check TFT** – hypothyroidism can cause myalgia or myopathy and attenuate statin muscle effect.

Liver symptoms

- **Stop the statin and check LFT**. Compare to baseline levels.

- **Consider other causes** of deranged LFT e.g. alcohol intake, fatty liver disease, cirrhosis, hepatitis, cancer etc. There is evidence of benefit of statins in these groups
and treatment should not be withheld. Specialist advice may be needed. If a causal relation between liver damage and statin therapy cannot be excluded, the statin should not be restarted, and specialist advice sought.

Other side effects

- **Stop and rechallenge:** stop the statin for 2-3 weeks and assess impact on symptoms. Most adverse effects should resolve in this time. If no improvement than statin should be restarted. If symptom resolves, rechallenge with the statin and if reoccurrence then the statin is a probable cause.

So, statin intolerance has been confirmed – what next?

**Serious adverse events** – liver dysfunction, rhabdomyolosis, or myopathy on 2 or more statins (confirmed by markedly elevated creatinine kinase levels) – refer for specialist advice

**All others- TRY AN ALTERNATE STATIN**

There is a limited evidence base which indicates switching to an alternate statin may be helpful. Nair et al (2008) retrospectively analysed outcomes for patients at Hull Royal Infirmary lipid clinic referred with a ‘statin intolerance’ 60% of these were able to tolerate an alternate statin – on average 2 switches were made to find a tolerated statin.

There is no good evidence to support the improved tolerability of one statin over another. A systematic trial of all available statins would be a reasonable approach. Cost effective generic statins should generally all be tried i.e. simvastatin, atorvastatin and pravastatin before high cost branded products i.e. rosuvastatin (unless a high intensity statin is desirable e.g. familial hypercholesterolaemia, recent acute coronary syndromes, diabetes with existing cardiovascular disease **and** atorvastatin is not tolerated **and** lower intensity statins are unlikely to produce the desired lipid lowering effects.)

**NOTE:** Ezetimibe should be considered only where patients are truly intolerant to all available statins or in combination with low dose statins for high risk patient groups unable to tolerate higher doses of a potent statin (atorvastatin or rosuvastatin). Ezetimibe currently has no outcome trials demonstrating effects such as reduction of heart attacks, strokes or lower risk of death. Statins have a strong evidence base and should be used first line at the optimal dose wherever possible (see CCG guideline for Management of Hyperlipidaemia in Primary Care). Ezetimibe should be used in combination with high dose statins in line with the local “Management of Hyperlipidaemia Guidelines.”