STATINS

- competitively inhibit (HMG CoA) reductase [especially in the liver]
- are effective at lowering LDL-cholesterol
- are less effective than the fibrates in reducing triglyceride concentration
- Reduce CVD events and total mortality irrespective of the initial cholesterol conc

CONSIDER STATINS IN/FOR

- all with symptomatic cardiovascular disease
- history of angina or MI
- occlusive arterial disease
- peripheral vascular disease
- non-haemorrhagic stroke
- transient ischaemic attacks
- *all* over 40 years with diabetes mellitus (type 1 and 2)
- younger patients with diabetes [if there is target-organ damage, poor glycaemic control (HbA_{1c} > 9%), low HDL, raised triglyceride concentration, hypertension, or a family history of premature CVD.
- prevention of CVD events in asymptomatic individuals who are at increased risk
- TC /HDL ratio > 6

CAUTIONS

- hypothyroidism should be managed adequately before starting a statin
- history of liver disease
- high alcohol intake
- hepatic impairment
- unexplained persistent elevations in serum transaminases
- avoid in pregnancy
- breastfeeding – see BNF

MEASURE LIVER ENZYMES

- before treatment
- repeat within 3 months
- repeat at 12 months of starting treatment
- repeat if indicated at other times [signs or symptoms suggestive of hepatotoxicity]

Serum transaminases **< 3 times the upper limit** → **do not** routinely exclude statins.

Serum transaminases **> 3 times the upper limit** → **discontinue** statin.

Use with caution in those with risk factors for myopathy or rhabdomyolysis

Patients should be advised to report unexplained muscle pain.

Avoid in acute porphyria [but rosuvastatin is thought to be safe].

SIDE-EFFECTS

Include:

- myalgia, myopathy, myositis, and rhabdomyolysis [rare]
- altered liver function tests
- rarely cause hepatitis and jaundice
- pancreatitis and hepatic failure [very rare]
- gastro-intestinal disturbances
- sleep disturbance
- very rare - interstitial lung disease; [symptoms - dyspnoea, cough, and weight loss]
- hyperglycaemia and the development of diabetes mellitus [esp in those already at risk]

MUSCLE EFFECTS

likelihood increases with

- higher doses
- fibrate therapy [gemfibrozil is specifically mentioned in the BNF]
- lipid-lowering doses of nicotinic acid
- fusidic acid
- drugs that increase the plasma-statin concentration [macrolides like erythromycin, clarithromycin and azithromycin , imidazole and triazole antifungals, and ciclosporin]
- certain patients [see below]

Patients at increased risk of muscle toxicity:

- personal or family history of muscular disorders
- previous history of muscular toxicity
- high alcohol intake
- renal impairment
- hypothyroidism
- the elderly

In patients at increased risk of muscle effects, a statin should not usually be started if the baseline creatine kinase > 5 times the upper limit of normal

(some patients may present with an extremely elevated baseline creatine kinase concentration, due to e.g. a physical occupation, or rigorous exercise—specialist advice should be sought regarding consideration of statin therapy in these patients).

If muscular symptoms or raised creatine kinase occur during treatment

exclude other possible causes first

(e.g. rigorous physical activity, hypothyroidism, infection, recent trauma, and drug or alcohol addiction).

If statin is suspected to be the cause of myopathy

Stop if CK > 5 times upper limit of normal

Stop if muscular symptoms are severe

If symptoms resolve and CK returns to normal → reintroduce at a lower dose monitor closely;

Do not discontinue in the event of small, asymptomatic elevations of CK.

Routine monitoring of CK is unnecessary in asymptomatic patients.