Two new lipid-regulating drugs

**Question 1**

Mr TA is a 67-year-old ex-smoker with poorly controlled familial hypercholesterolaemia (FH) despite treatment with a high-intensity statin and ezetimibe. He has read about two new lipid-regulating drugs, evolocumab and alirocumab, and discusses their potential risks and benefits with his specialist. Which one of the following statements about evolocumab and alirocumab is correct?

- Both drugs are licensed for treating primary hypercholesterolaemia and mixed dyslipidaemia
- Both drugs can be administered daily or weekly
- Both drugs are administered by intramuscular injection
- Both drugs are monoclonal antibodies that target high-density lipoprotein (HDL)-cholesterol
- Neither drug should be given with a statin or other lipid lowering drugs

**Answer:** a. In adults with primary hypercholesterolaemia or mixed dyslipidaemia, evolocumab and alirocumab are both indicated as an adjunct to diet in combination with a statin and/or other lipid-lowering therapies. In patients unable to tolerate statins, they are given alone or in combination with other lipid-lowering therapies.

**Question 2**

Evolocumab and alirocumab are the first in a novel class of lipid-regulating drugs, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. How are PCSK9 inhibitors thought to exert a lipid lowering effect?

- Inhibit microsomal triglyceride transfer protein
- Inhibit intestinal absorption of cholesterol
- Inhibit apolipoprotein B-100 synthesis
- Inhibit cholesteryl ester transfer protein
- Regulate recycling of low-density lipoprotein (LDL)-receptors on the surface of liver cells

**Answer:** e. PCSK9 is a protein that regulates the recycling of LDL-receptors on the surface of liver cells and decreases the ability of the liver to clear LDL-cholesterol from the blood. Evolocumab and alirocumab bind to PCSK9 and increase recycling of LDL-receptors leading to reduced LDL-cholesterol concentrations.

**Question 3**

Current guidance from the National Institute for Health and Care Excellence (NICE) on the management of FH in adults recommends the use of a statin as initial treatment. What percentage reduction in LDL-cholesterol (LDL-C) over pretreatment levels does NICE recommend?

- >60%
- >50%
- >40%
- >30%
- >20%

**Answer:** b. Statins are recommended as initial treatment for all adults with FH. The NICE guidance suggests using a high-intensity statin with the aim of achieving >50% reduction in LDL-C over pretreatment levels.
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**Question 4**

In a network meta-analysis of 17 randomised controlled trials, compared with ezetimibe, by how much did treatment with a PCSK9 inhibitor reduce LDL-cholesterol?

- a. 12%
- b. 23%
- c. 36%
- d. 45%
- e. 57%

**Answer:** c. A network meta-analysis of 17 randomised controlled trials involving 13,083 adults with primary hypercholesterolaemia found that treatment with a PCSK9 inhibitor significantly reduced LDL-C by 57% compared with placebo (p<0.001) and 36% compared with ezetimibe (p<0.001).

**Question 5**

Mr TA is concerned about adverse effects. Which one of the following common adverse effects was reported for both evolocumab and alirocumab?

- a. Urticaria
- b. Nausea
- c. Headache
- d. Eczema
- e. Influenza

**Answer:** c. The most commonly reported adverse effects in trials of evolocumab, occurring in up to about 5% of people, were nasopharyngitis, upper respiratory tract infections, headache, back pain, arthralgia, influenza and nausea. The most common adverse effects of alirocumab were nasopharyngitis, injection site reactions, upper respiratory tract symptoms, headache, myalgia, arthralgia and pruritis.