SLiMS Supplement 1 – PCSK9 Inhibitors

Alirocumab (Praluent, Sanofi) and Evolocumab (Repatha, Amgen) are monoclonal antibodies that target Proprotein Convertase Subtilisin/Kextin type 9 (PCSK9). This enzyme binds to the LDL receptor causing it to be degraded. PCSK9 Inhibitors therefore block this process, increasing the number of LDL receptors, and lowering LDL levels in the blood.

Alirocumab and Evolocumab are recommended as treatment options for primary hypercholesterolaemia or mixed dyslipidaemia only if LDL concentrations are persistently above the thresholds specified in the table below despite maximal tolerated Lipid-lowering therapy ie

- maximum dose has been reached
- further titration is limited by intolerance

Statin intolerance is defined as the presence of clinically significant adverse effects that represent an unacceptable risk to the patient or that may reduce compliance with therapy

Table 1. LDL-C Concentrations above which PCSK-9 Inhibitors are recommended

	Without CVD	**With CVD**	
		High Risk CVD [1]	**Very High Risk CVD [2]**
Primary Non-Familial Hypercholesterolaemia or Mixed Dyslipidaemia	Not recommended at any LDL-C level	Recommended only if LDL–C persistently > 4 mmol/L	Recommended only if LDL–C persistently > 3.5mmol/L
Primary Heterozygous Familial Hypercholesterolaemia	Recommended only if LDL-C persistently > 5 mmol/L	Recommended only if LDL–C persistently > 3.5mmol/L	

[1] High Risk CVD

History of :- Acute coronary syndrome (eg MI or unstable angina requiring hospitalization)
Coronary or other arterial revascularization procedures
Chronic heart disease
Ischaemic stroke
Peripheral arterial disease

[2] Very High Risk CVD

Recurrent cardiovascular events
Cardiovascular events in more than one vascular bed (ie polyvascular disease)

Patients who fulfill these criteria should be referred to the Lipid Clinic for the initiation of PCSK9 Inhibitor therapy

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