PCSK9 Inhibitors in the Management of Hypercholesterolaemia

NHS Greater Glasgow and Clyde

Overview

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are an injectable class of monoclonal antibodies, approved for the management of primary hypercholesterolemia (heterozygous familial and non-familial) or mixed dyslipidaemia.

Mechanism of Action

Low-density lipoprotein (LDL) cholesterol is cleared from the plasma by binding to LDL receptors on the surface of hepatocytes. This receptor/particle is then taken into the hepatocyte, where the receptor is degraded by PCSK9. Inhibition of PCSK9 allows the receptor to be recycled back to the cell membrane, making more receptor available for clearance of LDL. PCSK9 inhibitors have been shown to reduce plasma LDL cholesterol by around 50-60%, compared with placebo.

Place in Therapy

Scottish Medicines Consortium accepts alirocumab and evolocumab for restricted use in NHS Scotland. Both medicines are on the West of Scotland Formulary Hypercholesterolaemia Pathway, for use in adult patients with or without a statin and/or ezetimibe and in accordance with the NHSGGC Coronary Heart Disease and Stroke, Primary and Secondary Prevention (cholesterol) (181) | Right Decisions guideline. Initiation is restricted to a consultant or specialist practitioner working within a multidisciplinary team.

The dose of alirocumab is 75mg every two weeks by subcutaneous injection; this may be increased to 150mg every two weeks, dependent on response. The dose of evolocumab is 140mg every two weeks by subcutaneous injection. Plasma concentrations of LDL cholesterol should be re-checked between four and eight weeks after initiation of therapy and following a dose change; this will be undertaken by specialists.

Role of Primary Care

While treatment will only be commenced on the advice of a lipid specialist, ongoing prescribing can be continued in primary care; typically once the patient has been stabilised on the medication. As with other recommendations originating from an outpatient clinic, the specialist will inform the patient's general practice of the clinical management plan. All treatment monitoring and adjustments will be undertaken by the specialist clinic.

Patient Support

Both companies producing PCSK9 inhibitors (Amgen® and Sanofi®) offer a patient support programme. Following PCSK9 inhibitor initiation, the lipid specialist will inform a support nurse accordingly. Nursing support can be provided virtually or in person, helping to ensure that the patient feels comfortable with self-injection and medication storage requirements. Lipid clinics are responsible for the supply and disposal of sharps bins; patients will be instructed to return sharps to the clinic at each appointment.

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