## Evolocumab for familial hypercholesterolaemia

<table>
<thead>
<tr>
<th>Title</th>
<th>Evolocumab for familial hypercholesterolaemia</th>
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<tr>
<td>Areas where Protocol/Guideline applicable e.g. District, Hospital, ITU, Ward</td>
<td>SESLHD</td>
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<tr>
<td>Areas where Protocol/Guideline not applicable</td>
<td>Paediatrics</td>
</tr>
</tbody>
</table>
| Authorised Prescribers | Cardiologists, neurologists, endocrinologists for initiation  
All prescribers for continuation |

### Indication for use

Approved for use in accordance with PBS criteria:
Familial homozygous hypercholesterolaemia
- The treatment must be in conjunction with dietary therapy and exercise;

AND
- The condition must have been confirmed by genetic testing; OR
- The condition must have been confirmed by a Dutch Lipid Clinic Network Score of at least 7;

AND
- Patient must have an LDL cholesterol level in excess of 3.3 mmol/L after at least three months of treatment at a maximum tolerated dose of an HMG CoA reductase inhibitor (statin), in conjunction with dietary therapy and exercise; OR
- Patient must have an LDL cholesterol level in excess of 3.3 mmol/L after having developed a clinically important product-related adverse event during treatment with an HMG CoA reductase inhibitor (statin) necessitating a withdrawal of statin treatment; OR
- Patient must have an LDL cholesterol level in excess of 3.3 mmol/L and must be one in whom treatment with an HMG CoA reductase inhibitor (statin) is contraindicated.
Clinical condition

- Known hypersensitivity to evolocumab or any of the excipients found in evolocumab.
### Precautions

**Allergic Reactions**
Hypersensitivity reactions (e.g., rash, urticaria) have been reported, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment, treat according to the standard of care, and monitor until signs and symptoms resolve.

**Concomitant lipid-lowering therapies**
When using evolocumab in combination with statins or other lipid-lowering therapies (e.g., ezetimibe), the prescriber should refer to the Contraindications and Precautions sections of the product information for these medications.

**Low LDL-C levels**
Although adverse consequences of very low LDL-C were not identified in the clinical trials, the long term effects of very low levels of LDL-C induced by evolocumab are unknown.

**Immunogenicity**
The presence of anti-evolocumab (present in 0.1% of patients) binding antibodies did not impact the pharmacokinetic profile, clinical response, or safety of evolocumab.

**Effects on fertility**
No data are available on the effect of evolocumab on human fertility.

**Use in pregnancy**
Pregnancy Category: B1
When evolocumab is administered with a statin or other lipid-lowering therapies (e.g. ezetimibe) in women of childbearing potential, refer to the pregnancy section of the prescribing information for those medications.

**Use in lactation**
It is not known whether evolocumab is present in human milk.

**Paediatric use**
The safety and effectiveness of evolocumab have not been established in paediatric patients with primary hypercholesterolaemia and mixed dyslipidaemia. Long term safety has not been established in children.

**Use in the elderly**
No overall differences in safety or efficacy were observed between the elderly (age >75) and younger patients.
### Genotoxicity
The mutagenic potential of evolocumab has not been evaluated; however, monoclonal antibodies are not expected to alter DNA or chromosomes.

### Hepatic impairment
No dose adjustment is necessary in patients with mild to moderate hepatic impairment (Child-Pugh A or B). Evolocumab has not been studied in patients with severe hepatic impairment (Childs-Pugh C).

### Renal impairment
No dose adjustment is necessary in patients with Chronic Kidney Disease (CKD) stages 2 and 3 (mild to moderate renal impairment) with eGFR < 90 to 30 mL/min/1.73m2. Evolocumab has not been studied in patients with CKD stages 4 and 5 (severe and very severe) with eGFR < 30 mL/min/1.73m2.

### Place in Therapy
Second line. Evolocumab is recommended to be used in conjunction with diet and exercise and maximum tolerating statin (in patients who are not statin intolerant) or with other lipid lowering therapy in statin intolerant patients.

### Drugs recommended for co-administration or used in combination
Recommended use for evolocumab is in combination with other lipid-lowering therapies, for example:
- Statins – rosvastatin, simvastatin, atorvastatin, fluvastatin, pravastatin (no statin dose adjustments are necessary when used in combination with evolocumab)
- Ezetimibe/statin combination
- Bile-acid sequestrants

### Dosage
420 mg once monthly
The dose can be increased to 420 mg every 2 weeks if a clinically meaningful response is not achieved in 12 weeks.

n.b. dose may vary for other non-formulary indications (e.g. primary hypercholesterolaemia). Refer to Product Information in these circumstances

### Duration of therapy
No specified duration – chronic therapy

### Important Drug Interactions
No formal drug-drug interaction studies have been conducted for evolocumab

The pharmacokinetic interaction between statins and evolocumab was evaluated in the evolocumab clinical trials. An approximate 20% increase in the clearance of evolocumab was observed in patients co-administered with statins. This increased clearance is in part mediated by statins increasing the concentration of PCSK9 which did not adversely impact the pharmacodynamic effect of evolocumab on lipids. No statin dose adjustments are necessary when used in combination with evolocumab.
**Prescribing Protocol SESLHDPR/594**

**Evolocumab for Familial hypercholesterolaemia**

| Administration instructions | Subcutaneous administration delivered by an individual trained to administer the product with three SureClick® pre-filled pens administered consecutively within 30 minutes. The injections may be administered in the thigh or abdomen or a carer may inject in the upper arm. Injection sites should be rotated and injections should not be given into areas where the skin is tender, bruised, red or hard. Injection site reactions have been reported in patients treated with evolocumab (3.0% control vs 3.3% evolocumab). The most common injection site reactions were erythema, pain and bruising. Most of these reactions were mild in severity. |
| Monitoring requirements | |
| Safety | Advise patient of the signs and symptoms of hypersensitivity reactions |
| Effectiveness | LDL cholesterol as part of biochemical lipid profile testing – initially at 6 weeks then six monthly. |
| Management of complications | Hypersensitivity reactions (eg, rash, urticaria) have been reported in patients treated with evolocumab, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with evolocumab, treat according to the standard of care, and monitor until signs and symptoms resolve. |
| Basis of Protocol/Guideline (including sources of evidence, references) | Evolocumab Product Information |
| Groups consulted in development of this protocol | |

**AUTHORISATION**

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**GOVERNANCE**

| Enactment date | August 2017 |
| Expiry date: (maximum 36 months from date of original approval) | August 2019 |
### Prescribing Protocol SESLHDPR/594
**Evolocumab for Familial hypercholesterolaemia**

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<thead>
<tr>
<th>Ratification date by SESLHD QUM Committee</th>
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<td>Chairperson, QUM Committee</td>
<td>Prof George Rubin</td>
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<td>Approved Protocol/Guideline distributed</td>
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<tr>
<td>Version Number</td>
<td>1.0</td>
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