Product Name	Repatha®
Active substance	Evolocumab

Indication and conditions of use	<u>Authorized indication</u>
	Repatha® (evolocumab) has been granted marketing authorization by the European Commission on 17 July 2015, and is indicated:
	• in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
	  ○ in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
	  ○ alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.
	• in adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia (HoFH) in combination with other lipid-lowering therapies.
	
	<u>Intended indication for this Medical Need Program</u>
	Adults and adolescents (≥12 years old) with uncontrolled HoFH, despite treatment with a maximum tolerated and well monitored lipid lowering therapy (LLT).
	
	<u>Conditions of use</u>
	Repatha® is given as an injection under the skin (subcutaneous).
	
	For HoFH the recommended starting dose is 420 mg once monthly. After 12 weeks of treatment, dose frequency can be up titrated to 420 mg once every 2 weeks if a clinically meaningful response is not achieved. Patients on apheresis may initiate treatment with 420 mg every two weeks to correspond with their apheresis schedule.

Conditions, delays and further rules for participation of patients	Inclusion criteria
	Adults and adolescents (≥12 years old) with uncontrolled HoFH, despite treatment with a maximum tolerated and well monitored lipid lowering therapy (LLT):
	• Genetic confirmation of HoFH or
	• Untreated* LDL-C >500 mg/dL and
	  ○ Xanthoma before age of 10 years or
	  ○ Confirmed diagnosis of HeFH in both parents (untreated* LDL-C >250 mg/dL)
	
	* Measured or calculated with the correction factors published by Besseling J et al. *Atherosclerosis*. 2014;233:219-223.
	
	Patient (and if applicable, legal representative) must have been clearly and completely informed by the treating physician and patient (if applicable legal representative) must have signed the Informed Consent Form (ICF) before the start of the treatment.
	
	Exclusion criteria
	• Female of childbearing potential unwilling to use adequate contraception
	• Pregnant or breastfeeding, or planning pregnancy or breastfeeding at any time in the future
	• Serious Adverse Events likely to be drug related during prior treatment with a PCSK9 inhibitor
	• Concomitant treatment with mipomersen or lomitapide; or receiving other experimental drugs or devices
	• Known hypersensitivity to the active substance or to any of the excipients: proline, acetic acid (E260), polysorbate 80 (E433), sodium hydroxide (for pH adjustment), water (for injections)
	• Eligible for any clinical trial with a PCSK9 inhibitor and/or a clinical trial running in the envisaged indication of this program
	• Participation in any PSCK9 inhibitor study which is currently still ongoing in Belgium
	
	Delays and further rules for participation of patients
	The request has to be made by a specialist working in a hospital, to enable product delivery via the hospital pharmacy.
	Within 7 working days the requestor will be notified of the decision whether or not the patient can be included and within 10 working days the product will be delivered.
	
	Process to include patients:
	• Completed and signed Informed Consent Form (ICF)
	• Signed declaration and written request by the treating physician
	• Positive advice by the responsible physician
	• Confirmation of enrolment by the responsible of the program

Duration of the program	Repatha® (evolocumab) will be provided free of charge by Amgen on an individual patient basis following the criteria stated in this program from approval by the FAMHP until: • in the clinical judgment of the treating physician, the patient is no longer benefiting from continuation of the treatment, *or* • Repatha® (evolocumab) becomes commercially available in Belgium for the target population of this MNP, whichever is sooner. The program will be reviewed regularly by Amgen, who has the right to stop the program at any time. Treatment duration must be in line with the supporting clinical trials (e.g. for treatments which were tested on a limited timespan).
Conditions of distribution	Repatha® (evolocumab) will be requested by the treating physician. The responsible of the program only makes available the medicinal product to the treating physician if the advice of the responsible physician is positive. After approval of the request, a written confirmation will be sent to the treating physician. Treatment should be initiated under the direction of and supervised by the treating physician. Repatha® (evolocumab) will be delivered to the hospital pharmacist of the requesting physician. Each time, Repatha® (evolocumab) will be delivered for a period of 4 months (dosing regimen of 420 mg [3 SC injection] once every month) or 16 weeks (dosing regimen of 420 mg [3 SC injections] once every 2 weeks). If in the clinical judgment of the treating physician, the patient will benefit from continuation of the treatment, he/she can then submit a renewal request.

Responsible of the program	<u>Responsible of the program</u> Amgen N.V. / S.A. Arianelaan 5 1200 Brussels Phone: +32 2 775 27 11 <u>Responsible Physician</u> Dr. Jo Van der Veken Arianelaan 5 1200 Brussels <u>Point of Contact</u> Dr. Michiel Brutsaert Arianelaan 5 1200 Brussels Phone: +32 2 775 28 39 Email: michielb@amgen.com
Modalities for the disposal	Any unused or expired medication needs to be returned to Amgen or destroyed in an appropriate facility as soon as possible after the patient's discontinuation from this program. The medication delivered for an individual patient request in the context of this program can only be used for that particular patient.

The information for registration of suspected unexpected serious adverse reactions	The most commonly reported adverse drug reactions during primary hypercholesterolaemia and mixed dyslipidaemia pivotal trials, at the recommended doses, were nasopharyngitis (4.8%), upper respiratory tract infection (3.2%), back pain (3.1%), arthralgia (2.2%), influenza (2.3%), and nausea (2.1%). The safety profile in the HoFH population was consistent with that demonstrated in the primary hypercholesterolaemia and mixed dyslipidaemia population. Adverse reactions reported in pivotal, controlled clinical studies in patients with primary hypercholesterolaemia and mixed dyslipidaemia and HoFH are listed below: *Common (≥ 1/100 to < 1/10)* • Influenza • Nasopharyngitis • Upper respiratory tract infection • Rash • Nausea • Back pain • Arthralgia • Injection site reactions *Uncommon (≥ 1/1,000 to < 1/100)* • Urticaria Physicians are requested to report all adverse events (non-serious and serious), other safety findings and product complaints by OR faxing a completed, signed and dated Safety Report Form to the Amgen – Belgian Safety Department (Safety fax nr: 0800 80 877) within one working day OR mailing a completed, signed and dated Safety Report Form to the email svc-ags-in-be@amgen.com within one working day. The physician may be asked to provide follow-up information on the reported event.