Name of the drug	**Entresto®**
Active substance	The active substance of the proposed treatment is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin receptor developed by Novartis Pharma. Entresto® is a salt complex that comprises the anionic molecular moieties sacubitril and valsartan, sodium and water molecules in the ratio 6:6:18:15, respectively.
Indication	Symptomatic chronic heart failure with reduced ejection fraction (HF-rEF) in adult patients.
Conditions of use	**Dose, route of administration:** Entresto® will be provided in 3 doses: Entresto® 24mg sacubitril and 26mg valsartan film-coated tablets, Entresto® 49mg sacubitril and 51mg valsartan mg film-coated tablets, Entresto® 97mg sacubitril and 103mg valsartan film-coated tablets. Patient will be requested to take 1 tablet of Entresto®, 2 times a day (orally). The treatment plan is based on a titration with increasing dose levels of Entresto® to ensure safety and tolerability of the dose administered. The patient will take Entresto® in addition to his/her background heart failure therapy, except for angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs), which will be replaced by Entresto®.
Conditions, delays and further rules for participation of patients	The aim of this Medical Need Program (MNP) is to make Entresto® available to a group of patients who suffer from symptomatic chronic heart failure with reduced ejection fraction and, in the opinion and the clinical judgement of the treating physician, would benefit from a treatment with the product which is not yet commercially available for that given indication. The disease for which the drug is requested is a chronic disease or severely affects patient's health or is life-threatening and cannot be satisfactorily treated by the drugs currently marketed and approved for the treatment in this indication. Entresto® will only be made available after approval by the responsible physician of an individual request submitted by the treating physician within 2 or 3 weeks depending on the availability of the treating physician. The initiation and conduct of the treatment with Entresto® for a particular patient will fall under the full and only responsibility of the treating physician. Patients should have been clearly and completely informed by the requesting physician and provided written consent. **<u>Inclusion criteria</u>** Patients eligible for inclusion in this program have to fulfill the following criteria: - Entresto® is indicated in adult patients (≥ 18 years) for treatment of symptomatic chronic HF-rEF. - The patient is not eligible for a clinical trial running with Entresto® and/or a clinical trial running in the envisaged indication of this program. - The patient cannot be satisfactorily treated with the approved and commercially available alternative treatments, in accordance with clinical guidelances, because of efficacy and/or safety issues.

	<u>Exclusion criteria</u> Patients fulfilling any of the following criteria are not eligible for inclusion in this program: - Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 of the SmPC - Concomitant use with ACEis (see sections 10.3.5 and 10.3.6 of the MNP Protocol). Entresto® must not be administered until 36 hours after discontinuing ACEi therapy. - Known history of angioedema related to previous ACEi or ARB therapy (see section 10.3.5 of the MNP Protocol). - Hereditary or idiopathic angioedema (see section 10.3.5 of the MNP Protocol). - Concomitant use with aliskiren-containing medicinal products in patients with diabetes mellitus or in patients with renal impairment (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m^2) (see sections 10.3.5 and 10.3.6 of the MNP Protocol). - Severe hepatic impairment, biliary cirrhosis and cholestasis (see section 10.3.1 of the MNP Protocol). - Second and third trimester of pregnancy (see section 10.3.7 of the MNP Protocol).
Duration of the program	Entresto® will be provided free of charge by Novartis Pharma on an individual patient basis following the criteria stated in this program until the product will be commercially available in Belgium or until, in the clinical judgement of the treating physician, the patient is no longer benefiting from continuation of the treatment, whichever is sooner. Inclusion in this program will end when drug reimbursement is obtained or on 1 May 2017 in case of reimbursement refusal for this indication or if new scientific data emerge. Patients who are included in this program until that time and do not meet reimbursement criteria or in case when drug reimbursement is not obtained, will be further treated with Entresto® for as long as treatment with Entresto® is beneficial. If the FAMHP after evaluation concludes that Entresto® no longer meets the criteria of the Medical Need product, this program will end as well. The treating physician can also decide according to his clinical judgment to discontinue treatment, if the patient is no longer benefiting from continuation of the treatment. The patient can also decide at any time to end his/her participation.
Conditions of distribution	All documents related to this Medical Need Program will be archived by Novartis Pharma in Belgium for at least 10 years. The demands for patient inclusion with annexes should be archived by the responsible physician for at least 10 years. For submission of a request, the following steps have to be taken: - An unsolicited request by the treating physician for individual patient

	supply of Entresto® will be collected in writing (fax or e-mail) together with a motivation to enrol the patient within this program. The physician also completes the declaration form including the fact that he is personally responsible for the use of the medical need medication, that the patient has chronic heart failure with reduced ejection fraction that cannot be treated with the current marketed products in this indication and that the patient will be informed in a clear and complete manner and sign the informed consent form accordingly. The treated physician will also sign the protocol signature page to confirm that he is trained on the protocol by reading it carefully. - Before submission of a request, the patient has to be informed correctly by the physician regarding the benefits, use and risks of this treatment. The patient has to give his/her consent by signing the informed consent form. The physician has to make sure that patient is eligible for this program based on the inclusion and exclusion criteria described above (see section 5 of the MNP Protocol) and is not eligible for an ongoing clinical study. - The unsolicited request form, the declaration form of the physician and the protocol signature page have to be sent to Novartis Pharma Belgium (by fax 02/246 16 55 or by e-mail ETA-ETR.genmed@novartis.com). - The responsible physician of the medical department of Novartis Belgium checks the completeness and feasibility of the application and gives a reasoned advice about the eligibility of the patient for treatment and inclusion in this program. The responsible of the program will make the medicinal product available following the disposable modalities to the treating physician. - The maximum duration between initial request for participation to the program, and decision on inclusion of the patient into the program will be maximum 4 weeks. The requesting physician will be asked to state that the requested starting dose is in accordance with the SmPC. The delivery of medication will take 1 week. - The medication is sent to the hospital pharmacy of the treating physician or to the general practitioner. - Patients can decide at all times to stop his/her participating in this program. The treating physician can also decide to stop treatment when he/she is convinced that continuation of the treatment is harmful for the patient. The coded patient data (initials and year of birth) will be kept by the sponsor in a central registry together with the tracking information on the drug supply. A waiver for a centre registry with nominative data was submitted to the FAMHP.
Responsible of the program	**<u>Responsible of the program</u>** Novartis Pharma N.V. Contact Person: Dr. Stefaan Vancayzeele Chief Scientific Officer

	Medialaan 40 bus 1 B-1800 Vilvoorde Tel: +32 (0) 246 1759 Email: stefaan.vancayzeele@novartis.com **<u>Responsible physician for this program</u>** Dr. Ann Fieuw Therapeutic Area Head Cardio-metabolic Novartis Pharma N.V. Medialaan 40 bus 1 B-1800 Vilvoorde Tel: +32 (0)2 246 1821 Email : ann.fieuw@novartis.com
Modalities for the disposal	Any unused medication needs to be returned to Novartis Pharma and destroyed as soon as possible after the patient's discontinuation from the Medical Need Program. The medication delivered for an individual patient request in the context of the Medical Need Program can only be used for that particular patient. Novartis has a contractual agreement with Movianto, a local third party warehouse, which ensures the disposal of Entresto®, medicinal product object of this MNP, and which also collects Entresto®, medicinal product object of this MNP, for further destruction by Indaver. Please contact Novartis Belgium (0032 2 246 18 17) to make the practical arrangements for drug return to: Movianto Belgium an Owens & Minor Company Waterkeringstraat 1 B-9320 Aalst, Belgium
Information regarding possible adverse effects	**Side effects which have been reported in patients taking Entresto® :** The most commonly reported adverse reactions during treatment with Entresto® were hypotension, hyperkalaemia and renal impairment (see section 10.3.5 of the MNP Protocol). Angioedema was reported in patients treated with Entresto®. **Very common** (may affect more than 1 in 10 people): low blood pressure (dizziness, light-headedness), high level of potassium in the blood (shown in a blood test) , decreased renal function (renal impairment) **Common** (may affect up to 1 in 10 people): cough, dizziness, diarrhea, low level of red blood cells (shown in a blood test), tiredness, (acute) renal failure (severe kidney disorder), low level of potassium in the blood (shown in a blood test), headache, fainting, weakness, feeling sick (nausea), low blood pressure (dizziness, light-headedness) when switching from sitting or lying to standing position, gastritis (stomach pain, nausea), spinning sensation, low level of sugar in the blood (shown in a blood test) **Uncommon** (may affect up to 1 in 100 people): allergic reaction with rash and itching, dizziness when switching from sitting to standing position.