Product Name	Kyprolis®
Active substance	Carfilzomib
Indication and conditions of use	<u>Authorized Indication</u> Carfilzomib in combination with lenalidomide and dexamethasone (KRd) is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. <u>Indication under assessment</u> Carfilzomib in combination with dexamethasone (Kd) for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. <u>Intended Indication for this Medical Need Program</u> Carfilzomib in combination with dexamethasone (Kd) for the treatment of adult patients with relapsed multiple myeloma who did receive 3 or more prior therapies. <u>Conditions of use:</u> Carfilzomib (20/56 mg/m^2) in combination with dexamethasone is administered intravenously as a 30 minute infusion, on two consecutive days, each week for three weeks (days 1, 2, 8, 9, 15, and 16), followed by a 12-day rest period (days 17 to 28). Each 28-day period is considered one treatment cycle. Carfilzomib is administered at a starting dose of 20 mg/m^2 (maximum dose 44 mg) in cycle 1 on days 1 and 2. If tolerated, the dose should be increased to 56 mg/m^2 (maximum dose 123 mg) on day 8 of cycle 1. Treatment may be continued until disease progression or until unacceptable toxicity occurs. When carfilzomib is combined with dexamethasone alone, dexamethasone is administered as 20 mg PO or IV on days 1, 2, 8, 9, 15, 16, 22, and 23 of the 28 day cycles. Dexamethasone should be administered 30 minutes to 4 hours before carfilzomib.
Conditions, delays and further rules for participation of patients	<u>Inclusion Criteria</u> - Age ≥ 18 year - Ability to understand the informed consent and willingness to provide an informed consent signature - Signed and dated written informed consent available - In case clinical trials are running in the patient population of the MNP program, patients must be offered first the possibility to participate in such trials - Patients cannot be satisfactorily treated with the approved and commercially available alternative treatments, in accordance with clinical guidelines, because of efficacy and/or safety issues - Such as patients with a relapsed multiple myeloma o who did receive 3 or more prior therapies including (but not limited to) all of following therapies: 1. Lenalidomide 2. Pomalidomide 3. Bortezomib o and who cannot be retreated with lenalidomide <u>Exclusion criteria</u> - Eligibility for ARROW phase III trial with carfilzomib - Lactating or pregnant females - Hypersensitivity to the active substance (= carfilzomib) or other excipients - Cardiac comorbidities: 1. Myocardial infarction within 4 months prior to administration, 2. NYHA Class III or IV heart failure, 3. Uncontrolled angina, 4. Uncontrolled hypertension, 5. History of severe coronary artery disease, 6. Severe uncontrolled ventricular arrhythmias, 7. Sick sinus syndrome, 8. Electrocardiographic evidence of acute ischemia, 9. Grade 3 conduction system abnormalities unless subject has a pacemaker

	Process to include patients 1. Completed and signed ICF 2. Written request of the treating physician 3. Positive advice by the responsible physician 4. Confirmation of enrolment by the responsible of the program All requests will be treated as soon as possible, and at the latest within 10 working days after the request. Carfilzomib will be provided after approval of the request by the responsible physician for 2 treatment cycles. The need for up to additional treatment cycles is patient-dependent and will be determined by the treating physician.
Duration of the program	This program will start after its approval by the Belgian authorities (FAMHP). Carfilzomib will be provided free of charge by Amgen® on an individual patient basis following the criteria stated in this program: - Until, in the clinical judgement of the treating physician, the patient is no longer benefiting from continuation of the treatment. - Or, until one of the following stopping criteria for ending the MNP is met (whichever comes first): • Carfilzomib comes effectively available on the Belgian market in the Kd indication • EMA ultimately decides that the benefit/risk assessment is not supportive of registration of carfilzomib in the Kd indication • Amgen® decides to withdraw the registration dossier following an unfavourable benefit/risk profile of carfilzomib in the Kd indication - Or, at the latest until the end of January 2018 The program will be reviewed regularly by Amgen®, who has the right to stop the program at any time. Patients that were already included in the program, will be supported until the end of their treatment.
Conditions of distribution	Carfilzomib 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 and carfilzomib will be sent to the hospital pharmacy. Treatment should be initiated under the direction of and supervised by the treating physician.
Responsible of the program	Responsible of the program: Amgen N.V. / S.A. Arianelaan 5 1200 Brussels +32 2 775 27 11 Responsible physician: Dr. Jo Van der Veken Arianelaan 5 1200 Brussel Point of contact for this program: Dr. Sofie Vingerhoedt Arianelaan 5 1200 Brussel +32 2 775 28 60 sofiev@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 the compassionate use program. The medication delivered for an individual patient request in the context of a medical need program can only be used for that particular patient.
The information for registration of suspected unexpected serious adverse reactions	Physicians are requested to report all adverse events (non-serious and serious) and other safety findings 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. In addition to adverse events, product complaints will be collected during the program. Physicians are requested to report all product complaints by mailing a signed and

	completed product complaint form to the Amgen® NASCR Operations Representative (eu-qualcom@amgen.com) within one working day. In case of an adverse event, the treating physician will decide on the further treatment with carfilzomib, and on the actions needed to take. The *most serious adverse reactions* that may occur during carfilzomib treatment include: cardiac toxicity, pulmonary toxicities, pulmonary hypertension, dyspnoea, hypertension including hypertensive crises, acute renal failure, tumour lysis syndrome, infusion reactions, thrombocytopenia, hepatic toxicity, PRES (posterior reversible encephalopathy syndrome) and TTP/HUS (thrombotic thrombocytopenic purpura/haemolytic uremic syndrome). In clinical studies with carfilzomib, cardiac toxicity and dyspnoea typically occurred early in the course of carfilzomib therapy. The *most common adverse reactions* (occurring in > 20% of subjects) were: anaemia, fatigue, diarrhoea, thrombocytopenia, nausea, pyrexia, dyspnoea, respiratory tract infection, cough and peripheral oedema.