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| Product Name | Kyprolis® |
| Active substance | Carfilzomib |
| Indication and conditions of use | <u>Authorized Indication</u><br>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.<br><br><u>Intended Indication for this Medical Need Program</u><br>Carfilzomib in combination with dexamethasone and lenalidomide (KRd) for the treatment of adult patients with relapsed multiple myeloma who did receive at least one prior therapy.<br><br><u>Conditions of use</u><br>Carfilzomib (20/27 mg/m$^2$) in combination with dexamethasone is administered intravenously as a 10 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 27 mg/m$^2$ (maximum dose 60 mg) on day 8 of cycle 1. Treatment with carfilzomib combined with lenalidomide and dexamethasone for longer than 18 cycles should be based on an individual benefit-risk assessment, as the data on the tolerability and toxicity of carfilzomib beyond 18 cycles are limited.<br>In combination with carfilzomib, lenalidomide is administered as 25 mg orally on days 1-21 and dexamethasone is administered as 40 mg orally or intravenously on days 1, 8, 15, and 22 of the 28 day cycles. Appropriate dose reduction for the starting dose of lenalidomide should be considered according to the recommendations in the current lenalidomide summary of product characteristics, for example for patients with baseline renal impairment. Dexamethasone should be administered 30 minutes to 4 hours before carfilzomib. |
| Conditions, delays and further rules for participation of patients | <u>Inclusion Criteria</u><br>- Age ≥ 18 year<br>- Ability to understand the informed consent and willingness to provide an informed consent signature<br>- Signed and dated written informed consent available<br>- 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<br>- 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<br>- Such as patients with a relapsed multiple myeloma who did receive at least 1 prior therapy<br><br><u>Exclusion criteria</u><br>- Eligibility for ARROW phase III trial with carfilzomib<br>- Lactating or pregnant females<br>- Women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme of lenalidomide are met<br>- Hypersensitivity to the active substance (= carfilzomib) or other excipients<br>- Cardiac comorbidities:<br>1. Myocardial infarction within 4 months prior to administration<br>2. NYHA Class III or IV heart failure,<br>3. Uncontrolled angina,<br>4. Uncontrolled hypertension,<br>5. History of severe coronary artery disease,<br>6. Severe uncontrolled ventricular arrhythmias,<br>7. Sick sinus syndrome,<br>8. Electrocardiographic evidence of acute ischemia,<br>9. Grade 3 conduction system abnormalities unless subject has a pacemaker<br><br><u>Process to include patients</u><br>1. Completed and signed ICF<br>2. Written request of the treating physician |

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| | 3. Positive advice by the responsible physician<br>4. Confirmation of enrolment by the responsible of the program<br><br>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).<br><br>Carfilzomib will be provided free of charge by Amgen® on an individual patient basis following the criteria stated in this program:<br>- Until, in the clinical judgement of the treating physician, the patient is no longer benefiting from continuation of the treatment.<br>- Or, until one of the following stopping criteria for ending the MNP is met (whichever comes first):<br>• Carfilzomib comes effectively available on the Belgian market in the KRd indication<br>• Amgen® decides to stop the development of carfilzomib following an unfavourable benefit/risk profile of carfilzomib in the KRd indication<br>- Or, at the latest until the end of January 2017<br><br>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:<br>Amgen N.V. / S.A.<br>Arianelaan 5<br>1200 Brussels<br>+32 2 775 27 11<br><br>Responsible physician:<br>Dr. Jo Van der Veken<br>Arianelaan 5<br>1200 Brussel<br><br>Point of contact for this program:<br>Dr. Sofie Vingerhoedt<br>Arianelaan 5<br>1200 Brussel<br>+32 2 775 28 60<br>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), 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.<br>The physician may be asked to provide follow-up information on the reported event.<br><br>In case of an adverse event, the treating physician will decide on the further treatment with carfilzomib, and on the actions needed to take.<br><br>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 |

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| | 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.<br><br>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. |