Product Name	KEYTRUDA
Active substance	Pembrolizumab – MK 3475
Indication and conditions of use	Keytruda for the treatment of unresectable or metastatic melanoma patients in first line therapy (or after first line BRAF-inhibitor) *form:* Powder for concentrate for solution for infusion. White to off-white lyophilised powder. *dosage:* 50 mg powder for concentrate for solution for infusion. After reconstitution, 1 mL of solution contains 25 mg of pembrolizumab. *route of administration:* KEYTRUDA should be administered by intravenous infusion over 30 minutes. *posology:* The recommended dose of KEYTRUDA is 2 mg/kg administered intravenously over 30 minutes every 3 weeks. Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity. Atypical responses (i.e., an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until disease progression is confirmed.
Conditions, delays and further rules for participation of patients	**Inclusion criteria** A patient must meet all of the following criteria to be eligible to participate in the MNP: 1) Patient with a diagnosis of unresectable (Stage III) or metastatic melanoma (Stage IV) that cannot be satisfactorily treated with the approved and commercially available alternative treatments because of efficacy and/or safety issue(s), including the following: Patient with documented BRAF-V600 mutation has been considered for the available ERK pathway inhibiting therapy 2) Patient is ≥18 years of age at signing of informed consent/assent. 3) Patient with an Eastern Cooperative Oncology Group (ECOG) Performance status of 0 or 1. 4) If female patient of child bearing potential : negative urine or serum pregnancy test. 5) Women of childbearing potential are willing to use effective contraception during treatment with pembrolizumab and for at least 4 months after the last dose of pembrolizumab 6) Patient has adequate organ function defined by the following hematological and biochemical criteria: a. AST and ALT ≤2.5 X ULN or ≤5 X ULN with liver metastases b. Serum total bilirubin ≤1.5 X ULN or direct bilirubin ≤ ULN for patient with total bilirubin levels >1.5 ULN

	c. Serum creatinine ≤1.5 X ULN d. Absolute neutrophil count ≥1,000 /mcL e. Platelets ≥75,000 /mcL f. Hemoglobin ≥9 g/dL or ≥ 5.6 mmol/L **Exclusion criteria** A patient meeting any of the following criteria is not eligible to participate in the MNP: 1) The patient has previously participated in a clinical trial with Keytruda or is eligible for a clinical trial running with Keytruda and/or a clinical trial running in the indication of the program 2) The patient is currently receiving or eligible for treatment with available ERK pathway inhibiting therapy 3) Patient has not recovered to Grade 0-1 from adverse events due to prior chemotherapy, radioactive, or biological cancer therapy (including mAb). 4) Patient has not recovered from minor or major surgery and is less than 4 weeks from major surgery prior to starting treatment with pembrolizumab. 5) History of life-threatening or severe immune-related adverse events on treatment with another immunotherapy (e.g., ipilimumab). 6) Patient is expected to require any other form of systemic antineoplastic therapy while receiving Keytruda. 7) History of clinically severe (e.g., requires chronic immunosuppressive therapy) autoimmune disease (e.g., ulcerative colitis, lupus). 8) History of pneumonitis, organ transplant, human immunodeficiency virus positive, active hepatitis B or hepatitis C. 9) Patient requires systemic steroids for management of immune-related adverse events experienced on another immunotherapy. 10) Active central nervous system metastases and/or carcinomatous meningitis. Note: Patients with untreated brain metastasis will be excluded. Patients with previously treated brain metastases may participate provided they are clinically stable. 11) Condition (including but not limited to psychiatric or substance abuse disorders) which would interfere with patient compliance or safety.

	12) Pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of treatment with Keytruda. 13) Inability to voluntarily agree to participate by signed informed consent/assent. 14) Active infection requiring systemic therapy. 15) Has received a live virus vaccine within 30 days of planned start of therapy. The patient is not eligible for a clinical trial running with Keytruda and/or a clinical trial running in the envisaged indication of this program. Patients should have been clearly and completely informed by the requesting physician and provided written consent, before the start of the treatment. <u>Specific timelines on the treatment of the request by the treating physician and other information that might be relevant for a patient</u> Treatment request will be answered within 7 working days by the treating physician

Duration of the program	The inclusion of patients will start as soon as the program is authorized. Pembrolizumab will be provided free of charge by MSD on an individual patient basis following the criteria stated in this program until the product will be commercially available and reimbursed in Belgium or until, in the clinical judgement of the treating physician, the patient is not longer benefiting from continuation of the treatment.
Conditions of distribution	Patients will have access to the medicinal product only at the hospital where the prescribing physician is working. Drug will be delivered by IDIS to the hospital pharmacy of the requesting physician within 5 working days after approval of initial request or after request for resupply.
Responsible of the program	Dr Isabelle Mayne (isabelle.mayne@merck.com)
Modalities for the disposal	Any unused medication needs to be destroyed in an appropriate facility 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.
The information for registration of suspected unexpected serious adverse reactions	Like all medicines, this medicine can cause side effects, although not everybody gets them. When you get KEYTRUDA, you can have some serious side effects. See section 2. The following side effects have been reported in clinical trials: **Very common (may affect more than 1 in 10 people)** - diarrhoea; nausea - itching; skin rash - joint pain - feeling tired **Common (may affect up to 1 in 10 people)** - decrease in the number of platelets (bruising or bleeding more easily) - feeling less hungry; weight loss; change in your sense of taste - dehydration; dry mouth - headache - numbness; tingling - weakness of your hands or feet - dry eye - dizziness or spinning sensation - hot flush - cough; shortness of breath

	- bloating; stomach pain; constipation; vomiting - hair loss; patches of skin which have lost colour; dry skin; itchy skin; excess sweating - red raised skin rash, sometimes with blisters, these may include widespread peeling of the skin - joint pain with swelling; back pain; muscle spasms; muscle weakness, pain, stiffness, aches or tenderness; pain in arms or legs - unusual tiredness or weakness; chills; flu-like illness; fever - swelling in the arms or legs - inflammation of the mucous membranes (e.g., the lining of the mouth or throat) - decrease in the number of red blood cells - increased liver enzyme levels in the blood - inflammation of the lungs or intestines; gland problems including thyroid and pituitary - reaction related to the infusion of the medicine **Uncommon (may affect up to 1 in 100 people)** - inflammation of the liver, kidneys, pancreas, or the eyes - type 1 diabetes - conjunctivitis; shingles; fungal infection; urinary tract infection; herpes of the mouth; infection of the hair roots - abnormal blood test results - feeling confused; trouble sleeping; feeling anxious; decreased sex drive; depression - decreased feeling or sensitivity; decreased feeling in arms or legs; restless legs syndrome; memory impairment; tremor; disturbance in attention; increased sensitivity; numbness, tingling and colour change in fingers and toes when exposed to the cold; temperature intolerance; trouble walking - eye pain, irritation, itchiness or redness; decreased or blurry eyesight; changes in eyesight; increased tears; eyelash discolouration; uncomfortable sensitivity to light - fluid around the heart; irregular heartbeat; low blood pressure - problems with your voice; wheezing; nosebleed; excessive runny nose; sneezing; face swelling - trouble swallowing; mouth pain; coughing up blood; haemorrhoids; tooth problems; flatulence; mouth ulcers; inflammation of the lips - blocked bile duct - redness, swelling, and/or pain on the palms of the hand and/or soles of the feet; acne-like skin problem; hair colour changes; small skin bumps, lumps or sores; increased sensitivity of skin to the sun; thickened, sometimes scaly, skin growth; tender, red bumps under the skin caused by inflammation; changes in hair growth - tumour pain; bone pain; neck pain; pain in jaw - kidney failure; difficulty urinating - pelvic pain; erectile dysfunction; heavy period

	Reporting of side effects If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Agence fédérale des médicaments et des produits de santé. Division Vigilance. EUROSTATION II. Place Victor Horta, 40/ 40. B-1060 Bruxelles. (Site internet: www.afmps.be , e-mail: patientinfo@fagg-afmps.be . By reporting side effects you can help provide more information on the safety of this medicine.