Product Name	Opdivo
Active substance	Nivolumab (BMS-936558)

Indication and conditions of use	Nivolumab (Opdivo)) is registered by the EMA for the treatment of advanced (non-resectable or metastatic) melanoma and certain types of advanced lung cancer, but not for renal cell cancer. On 25 February 2016, the Committee for Medicinal Products for Human Use (CHMP) adopted positive opinion recommending a new indication as follows: 'Opdivo as monotherapy is indicated for the treatment of advanced renal cell carcinoma after prior therapy in adults' Subjects with advanced clear-cell renal cell carcinoma who have received prior anti-angiogenic therapy can be eligible for treatment in this program (please see eligibility criteria). Eligible subjects will receive nivolumab administered IV over 60 minutes at 3 mg/kg every 2 weeks until progression or until there is reimbursement for nivolumab in RCC, or until 1 year after Marketing Authorisation for RCC, whichever comes first.

Conditions, delays and further rules for participation of patients	**Inclusion Criteria** **1. Signed Written Informed Consent** Before any program procedures are performed, the details of the program will be described to the patient, and the patient will be given a written informed consent document to read. If the patient agrees to participate in the program, consent will be indicated by signing and dating of the informed consent document in the presence of program personnel. The treating physician will be informed about the responsible physician's approval or rejection of the request within 7 working days. **2. Target Population** a) Subjects with histologically-confirmed unresectable or metastatic clear-cell renal cell carcinoma. b) Karnofsky Performance Score (KPS) ≥ 70% c) Patients cannot be satisfactorily treated with the approved and commercially available alternative treatment options, in accordance with clinical guidelines, because of efficacy and/or safety issues. Petients must have received at least 1 prior anti-angiogenic therapy regimen (including, but not limited to, sunitinib, sorafenib, pazopanib, axitinib, tivozanib, and bevacizumab) in the advanced or metastatic setting. Prior cytokine therapy (e.g. IL-2, IFN-alpha) or treatment with cytotoxic is also allowed as an option if in accordance with current guidelines. d) The patient is not eligible for a clinical trial running with nivolumab and/or a clinical trial running in the envisaged indication of this program A list of ongoing clinical trials running in the same indication can be found on the clinical trials website https://clinicaltrials.gov and www.clinicaltrialsregister.eu with the following advanced keywords search: "Renal AND cancer AND Belgium". Results of such search will be performed and communicated by B-MS to participating sites on a monthly basis. e) Prior radiotherapy or radiosurgery must have been completed at least 2 weeks prior to the first dose of Nivolumab f) Subjects must be anti-PD-1 treatment-naïve. g) Screening laboratory values must meet the following criteria and should be obtained prior to commencement of treatment: i) WBC ≥ 2000/µL ii) Neutrophils ≥1500/µL iii) Platelets ≥ 100 X 10^3/µL iv) Hemoglobin ≥ 9.0 g/dL v) Creatinine Serum creatinine ≤ 1.5 X ULN or CrCL > 40 mL/minute (using Cockcroft/Gault formula) Female CrCl = [(140- age in years) X weight in kg X 0.85) ÷ (72 X serum creatinine in mg/ dL)]

Male CrCl = [(140- age in years) X weight in kg X 1.00) ÷ (72 X serum creatinine in mg/ dL)]

vi) AST ≤ 3 X ULN

vii) ALT ≤ 3 X ULN

viii) Total bilirubin ≤ 1.5 X ULN (except subjects with Gilbert Syndrome who can have total bilirubin < 3.0 mg/dL)

h) Subject re-enrollment: This program permits the re-enrollment of a subject that has discontinued the program as a pre-treatment failure (ie, subject has not been treated). If re-enrolled, the subject must be re-consented.

3. Age and Reproductive Status

a) Men and women, aged ≥ 18 years

b) Nivolumab is not recommended during pregnancy and in women of childbearing potential not using effective contraception unless the clinical benefit outweighs the potential risk. Effective contraception should be used for at least 5 months following the last dose of Opdivo.

Exclusion Criteria

a) Any active known or suspected autoimmune disease. However, subjects with vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.

b) Any history of or current CNS metastases

c) Any condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days prior to the first dose of Nivolumab. However, inhaled steroids and adrenal replacement steroid doses > 10 mg daily prednisone equivalent are permitted in the absence of active autoimmune disease.

d) Uncontrolled adrenal insufficiency.

e) Any known active chronic liver disease.

f) Prior malignancy active within the previous 3 years except for locally curable cancers that have been apparently cured, such as basal or squamous cell skin cancer, superficial bladder cancer, or carcinoma in situ of the prostate, cervix or breast.

g) Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS).

h) Any positive test for hepatitis B or hepatitis C virus indicating acute or chronic infection.

i) Known medical condition (e.g. a condition associated with diarrhea or acute diverticulitis) that, in the physician's opinion, would increase the risk associated with MNP participation or Nivolumab administration

j) Prior treatment with an anti-PD-1, or anti-PD-L1, or any medicine specifically targeting T-cell co-stimulation or checkpoint pathways.

k) Major surgery (e.g. nephrectomy) less than 28 days prior to the first dose of Nivolumab. Minor surgery less than 14 days prior to the first dose of Nivolumab.

l) Presence of toxicities attributed to prior anti-cancer therapy other than alopecia that have not resolved to Grade 1 (NCI CTCAE version 4) or baseline before administration of Nivolumab.

1. Physical and Laboratory Test Findings

Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS)

2. Allergies and Adverse Drug Reaction

History of severe hypersensitivity reactions to other monoclonal antibodies

History of allergy or intolerance (unacceptable adverse events) to study drug components or Polysorbate-80-containing infusions

3. Sex and Reproductive Status

WOCBP who are pregnant or breastfeeding

Women with a positive pregnancy test at enrollment or prior to administration of study medication

Women of Childbearing Potential

A woman of childbearing potential (WOCBP) is defined as any female who has experienced menarche and who has not undergone surgical sterilization (hysterectomy or bilateral oophorectomy) or is not postmenopausal. Menopause is defined clinically as 12 months of amenorrhea in a woman over age 45 in the absence of other biological or physiological causes. In additional, women under the age of 55 must have a documented serum follicle stimulating hormone, (FSH) level > 40 mIU/mL to confirm menopause.

Concomitant Treatments

Prohibited and/or Restricted Treatments

Live vaccines should be avoided, whenever possible, while on nivolumab treatment.

The following medications are prohibited during the program (unless utilized to treat a drug-related adverse event):

1) Immunosuppressive agents (except to treat a drug-related adverse event)
2) Systemic corticosteroids > 10 mg daily prednisone equivalent (except to treat drug-related AEs)

	Any concurrent antineoplastic therapy (ie, chemotherapy, hormonal therapy, immunotherapy, non-palliative radiation therapy, or standard or investigational agents for treatment of cancer) Patients may continue to receive hormone replacement therapy if initiated prior to first dose of treatment, or use in the treatment of a drug related AE (e.g. endocrinopathy)

Duration of the program	Nivolumab will be provided free of charge by Bristol-Myers Squibb on an individual patient basis following the criteria stated in this program until nivolumab will be reimbursed in this indication in Belgium or until, in the clinical judgement of the treating physician, the patient is no longer benefiting from continuation of the treatment, until disease progression or unacceptable toxicity,or until the non-squamous lung cancer MNP will close, whichever is sooner. In case of reimbursement, no new patients will be allowed to enter the program, AND patients that are receiving treatment as part of the program will be switched to receive commercial supply. In case of one year after inclusion of renal cell cancer in the nivolumab label (and thus no reimbursement), no new patients will be allowed to enter the program, BUT patients that are receiving treatment as part of the program will continue to receive the treatment until the criteria for discontinuation have been met (progression of the disease or unacceptable toxicity) or reimbursement will have been obtained. Bristol-Myers Squibb can decide at any moment to terminate enrolment of new patients to the program.
Conditions of distribution	If the patient is eligible and the inclusion approved by the responsible physician, then the patient can receive the nivolumab infusion from the treating physician.
Responsible of the program	Dr. Muriel Sterckx SA Bristol-Myers Squibb Belgium NV Parc de l'Alliance Avenue de Finlande, 4 B-1420 Braine l'Alleud Phone : 0032 477 251 045 Email: muriel.sterckx@bms.com
Modalities for the disposal	Unused or expired medication will be destroyed at the hospital pharmacy according to local regulations.

The information for registration of suspected unexpected serious adverse reactions	The most common side effects of nivolumab are: • Fatigue • Skin reactions: including rash, itching, hives, redness, and dry skin • Diarrhea • Nausea • Abdominal pain • Decreased appetite • Low red blood cells • Fever • Joint pain of stiffness The treating physician should report any adverse event to the below contact person. Adverse Events Reporting Contact: Mrs. Patricia VANDAMME, Head of Country Pharmacovigilance Belgium Avenue de Finlande, 4 1420 Braine-l'Alleud Fax number: 02 352 75 66 Email: safety_belgium@bms.com