

## Early Access to Medicines Scheme – Treatment protocol – Information for patients

### Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation) to UK patients that have a high unmet clinical need. The medicines included in the scheme are those that are intended to treat, diagnose or prevent seriously debilitating or life threatening conditions where there are no adequate treatment options. More information about the scheme can be found

here: <http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

The information below is intended for you, the patient, and is provided by the pharmaceutical company that manufactures the medicine. This medicine does not yet have a drug licence (also called a marketing authorisation). More information about medicines licensing can be found here:

<http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/MymedicineFromlaboratorytopharmacyshelf/Licensingmarketingauthorisation/index.htm>

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. Informed consent should be obtained from you prior to treatment.

This information is provided to help you decide with your doctor on whether to use the medicine and helps explain how to use the medicine in accordance with the pharmaceutical company's instructions for safe and proper use. Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine outweigh any potential risks.

## Information for the Patient

### Nivolumab 10 mg/mL concentrate for solution for infusion

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

#### What is in this leaflet

1. What nivolumab is and what it is used for
2. What you need to know before you use nivolumab
3. How to use nivolumab
4. Possible side effects
5. How to store nivolumab
6. Contents of the pack and other information

#### 1. What nivolumab is and what it is used for

Nivolumab is a medicine which is being used in the Early Access to Medicines Scheme (EAMS) to treat advanced melanoma (a type of skin cancer) in adults. It contains the active substance nivolumab, which is a monoclonal antibody, a type of protein designed to recognise and attach to a specific target substance in the body.

Nivolumab attaches to a target protein called programmed death-1 receptor (PD-1) that can switch off the activity of T cells (a type of white blood cell that forms part of the immune system, the body's natural defences). By attaching to PD-1, nivolumab blocks its action and prevents it from switching off your T cells. This helps increase their activity against the melanoma cells.

#### 2. What you need to know before you use nivolumab

You should not be given nivolumab

- if you are **allergic** to nivolumab or any of the other ingredients of this medicine (listed in section 6 "Contents of the pack and other information"). **Talk to your doctor** if you are not sure.

#### Warnings and precautions

Talk to your doctor before using nivolumab as it may cause:

- **Problems with your lungs** such as breathing difficulties or cough. These may be signs of inflammation of the lungs (pneumonitis or interstitial lung disease).
- **Diarrhoea** (watery, loose or soft stools) or any symptoms of **inflammation of the intestines** (colitis), such as stomach pain and mucus or blood in stool.
- **Inflammation of the liver (hepatitis)**. Signs and symptoms of hepatitis may include abnormal liver function tests, eye or skin yellowing (jaundice), pain on the right side of your stomach area, or tiredness.
- **Inflammation or problems with your kidneys**. Signs and symptoms may include abnormal kidney function tests, or decreased volume of urine.
- **Problems with your hormone producing glands** (including the pituitary, the thyroid and adrenal glands) that may affect how these glands work. Signs and symptoms that these glands are not working properly may include fatigue (extreme tiredness), weight change or headache and visual disturbances.
- **Diabetes** (symptoms include excessive thirst, the passing of a greatly increased amount of urine, increase in appetite with a loss of weight, feeling tired, drowsy, weak, depressed, irritable and generally

- unwell) or **diabetes ketoacidosis** (acid in the blood produced from diabetes).
- **Inflammation of the skin** that can lead to rash and itching.

**Tell your doctor immediately** if you have any of these signs or symptoms or if they get worse. **Do not try to treat your symptoms with other medicines on your own.** Your doctor may

- give you other medicines in order to prevent complications and reduce your symptoms,
- withhold the next dose of nivolumab,
- or stop your treatment with nivolumab altogether.

Please note that these signs and symptoms are **sometimes delayed**, and may develop weeks or months after your last dose. Before treatment, your doctor will check your general health. You will also have **blood tests** during your treatment.

**Check with your doctor or nurse before you are given nivolumab if:**

- you have an **autoimmune disease** (a condition where the body attacks its own cells);
- you have **melanoma of the eye**;
- you were previously given ipilimumab, another medicine for treating melanoma, and experienced **serious side effects** because of that medicine.

#### **Children and adolescents**

Nivolumab should not be used in children and adolescents below 18 years of age.

#### **Other medicines and nivolumab**

**Before you are given nivolumab, tell your doctor** if you are taking any medicines that suppress your immune system, such as corticosteroids, since these medicines may interfere with the effect of nivolumab. However, once you are treated with nivolumab, your doctor may give you corticosteroids to reduce any possible side effects that you may have during your treatment and this will not impact the effect of the medicine.

**Tell your doctor** if you are taking or have recently taken any other medicines. **Do not take any other medicines** during your treatment without talking to your doctor first.

#### **Pregnancy and breast-feeding**

**Tell your doctor** if you are pregnant or think you might be, if you are planning to become pregnant, or if you are breast-feeding.

**Do not use nivolumab if you are pregnant** unless your doctor specifically tells you to. The effects of Nivolumab in pregnant women are not known, but it is possible that the active substance, nivolumab, could harm an unborn baby.

- You must use **effective contraception** while you are being treated with nivolumab, if you are a woman who could become pregnant.
- If you become pregnant while using nivolumab **tell your doctor**.

It is not known whether nivolumab gets into breast milk. A risk to the breast-fed infant cannot be excluded. **Ask your doctor** if you can breast-feed during or after treatment with nivolumab.

#### **Driving and using machines**

Nivolumab is unlikely to affect your ability to drive or use machines; however, use caution when performing these activities until you are sure that nivolumab does not adversely affect you.

#### **Nivolumab contains sodium**

**Tell your doctor** if you are on a low-sodium (low-salt) diet before you are given nivolumab. This medicine contains 2.5 mg sodium per mL of concentrate.

### 3. How to use nivolumab

#### How much nivolumab is given

The amount of nivolumab will be given will be calculated based on your body weight. The recommended dose is 3 mg of nivolumab per kilogram of your body weight.

Depending on your dose, the appropriate amount of nivolumab will be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection or glucose 50 mg/mL (5%) solution for injection before use. More than one vial of nivolumab may be necessary to obtain the required dose.

#### How nivolumab is given

You will receive treatment with nivolumab in a hospital or clinic, under the supervision of an experienced doctor.

Nivolumab will be given to you as an infusion (a drip) into a vein (intravenously) over a period of 60 minutes, every 2 weeks. Your doctor will continue giving you nivolumab for as long as you keep benefitting from it or until you no longer tolerate the treatment.

#### If you miss a dose of nivolumab

It is very important for you to keep all your appointments to receive nivolumab. If you miss an appointment, ask your doctor when to schedule your next dose.

#### If you stop using nivolumab

Stopping your treatment may stop the effect of the medicine. Do not stop treatment with nivolumab unless you have discussed this with your doctor.

If you have any further questions about your treatment or on the use of this medicine, ask your doctor.

### 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Your doctor will discuss these with you and will explain the risks and benefits of your treatment.

**Be aware of important symptoms of inflammation.** Nivolumab acts on your immune system and may cause inflammation in parts of your body. Inflammation may cause serious damage to your body and some inflammatory conditions may be life-threatening and need treatment or withdrawal of nivolumab.

The following side effects have been reported in clinical trials with nivolumab:

#### Very common (may affect more than 1 in 10 people)

- Diarrhoea (watery, loose or soft stools), nausea
- Skin rash, itching
- Feeling tired or weak

#### Common (may affect up to 1 in 10 people)

- Infections of the upper respiratory tract
- Underactive thyroid gland, which can cause tiredness or weight gain, overactive thyroid gland, which can cause rapid heart rate, sweating and weight loss
- High sugar levels in the blood (hyperglycaemia)
- Low levels of sodium in the blood (hyponatraemia), decreased appetite
- Inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; headache, dizziness
- High blood pressure (hypertension)
- Inflammation of the lungs (pneumonitis), characterised by coughing and difficulty breathing, shortness of breath (dyspnoea), cough
- Inflammation of the intestines (colitis), mouth ulcers and cold sores (stomatitis), vomiting, stomach pain,

constipation

- Skin colour change in patches (vitiligo), dry skin, redness of the skin, unusual hair loss or thinning
- Pain in the muscles, bones and joints
- Fever, oedema (swelling)
- Allergic reaction, reactions related to the infusion of the medicine

#### **Uncommon (may affect up to 1 in 100 people)**

- Decreased secretion of hormones produced by adrenal glands (glands situated above the kidneys), underactive function (hypopituitarism) or inflammation (hypophysitis) of the pituitary gland situated at the base of the brain, swelling of the thyroid gland, acid in the blood produced from diabetes (diabetic ketoacidosis), diabetes
- A temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain-Barré syndrome); loss of the protective sheath around nerves (demyelination); a condition in which the muscles become weak and tire easily (myasthenic syndrome); inflammation of the nerves caused by the body attacking itself, causing numbness, weakness, tingling or burning pain
- Inflammation of the eye, which causes pain and redness, vision problems or blurry vision
- Changes in the rhythm or rate of the heart beat
- Inflammation of the pancreas
- Severe condition of the skin that causes red, often itchy spots, similar to the rash of measles, which starts on the limbs and sometimes on the face and the rest of the body (erythema multiforme); skin disease with thickened patches of red skin, often with silvery scales (psoriasis); skin condition of the face where the nose and cheeks are unusually red (rosacea)
- Inflammation of the kidney, kidney failure.

**Tell your doctor immediately** if you get any of the side effects listed above. Do not try to treat your symptoms with other medicines on your own.

#### **Changes in test results**

Nivolumab may cause changes in the results of tests carried out by your doctor. These include:

- Abnormal liver function tests (increased amounts of the liver enzymes aspartate aminotransferase, alanine aminotransferase or alkaline phosphatase in your blood, higher blood levels of the waste product bilirubin)
- Abnormal kidney function tests (increased amounts of creatinine in your blood)
- A decreased number of red blood cells (which carry oxygen), white blood cells (which are important in fighting infection) or platelets (cells which help the blood to clot)
- An increased level of the enzyme that breaks down fats and of the enzyme that breaks down starch.

### **5. How to store nivolumab**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the vial label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Store in the original package in order to protect from light.

Do not store any unused portion of the infusion solution for reuse. Any unused medicine or waste material should be disposed of in accordance with local requirements.

## 6. Contents of the pack and other information

### What nivolumab contains

- The active substance is nivolumab.  
Each mL of concentrate for solution for infusion contains 10 mg of nivolumab.  
Each vial contains or 100 mg (in 10 mL) of nivolumab.
- The other ingredients are sodium citrate dihydrate, sodium chloride (see section 2 "nivolumab contains sodium"), mannitol (E421), pentetic acid, polysorbate 80, sodium hydroxide, hydrochloric acid and water for injections.

### What nivolumab looks like and contents of the pack

Nivolumab concentrate for solution for infusion (sterile concentrate) is a clear to opalescent, colourless to pale yellow liquid that may contain few light particles.

It is available in pack containing 1 vial of 10 mL.

Not all pack sizes may be marketed.

### Scientific Opinion Holder

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### Additional information:

Before starting treatment, the scheme will be explained thoroughly to all patients and the patient will be provided with the following two documents:

- **Informed Consent Form**  
This is a description of the scheme, which the patient will be requested to sign and a copy will be given to them to keep.
- **Patient Alert card**  
This will be given to the patient after signing the Informed Consent Form. It is a wallet-sized card to be carried at all times. It contains important information on the main symptoms of the important adverse reactions and highlights the importance of notifying their treating physician immediately if symptoms occur, persist or worsen and also the importance of not attempting to self-treat any symptoms without consulting with their healthcare professional first.

### Contact information:

Bristol-Myers Squibb Medical Information on 0800 731 1736 or [medical.information@bms.com](mailto:medical.information@bms.com)