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) for the treatment of patients with this specific type of cancer - classical Hodgkin lymphoma. It is however authorised for the treatment of patients with other types of cancer (melanoma, non-small cell lung cancer and renal cell carcinoma) under the name Opdivo®.

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
nivolumab

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.
- It is important that you keep the Alert Card with you during treatment.
- 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

Nivolumab is a medicine used to treat classical Hodgkin lymphoma that has come back after or has not responded to previous therapies, including an autologous stem-cell transplant (a transplant of your own blood-producing cells) 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 lymphoid cancer 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 **diabetic 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 been told that your **cancer has spread to your brain;**
- you have any history of **inflammation of the lungs**;
- you have been taken **medicines to suppress your immune system.**

Complications of stem cell transplant that uses donor stem cells (allogeneic) after treatment with Nivolumab. These complications can be severe and can lead to death. Your healthcare provider will monitor you for signs of complications if you have an allogeneic stem cell transplant.

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 and for at least 5 months following the last dose of 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.

You will also find this information in the Patient Alert Card you have been given by your doctor. It is important that you keep this Alert Card and show it to your partner or caregivers.

3. How to use Nivolumab

How much Nivolumab is given
The amount of Nivolumab you 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
- Allergic reaction, reactions related to the infusion of the medicine
- 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)
- Decreased appetite

- Inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; headache, dizziness
- Dry eyes
- 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, dry mouth
- Skin colour change in patches (vitiligo), dry skin, redness of the skin, unusual hair loss or thinning
- Pain in the muscles, bones and joints, inflammation of the joints
- Fever, oedema (swelling)

Uncommon (may affect up to 1 in 100 people)
- Serious lung infection (pneumonia), bronchitis
- Increase in some white blood cells
- 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)
- Dehydration, increased acid levels in the blood
- Inflammation of the liver (hepatitis), blockage of bile ducts
- Damage to nerves causing numbness and weakness (polyneuropathy), 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, blurred vision
- Fast heart rate
- Inflammatory disease of blood vessels
- Fluid around the lungs
- Inflammation of the pancreas, gastritis (inflammation of the stomach)
- 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), hives (itchy, bumpy rash)
- Inflammation of muscles causing pain or stiffness
- Inflammation of the kidney, kidney failure
- Pain, chest pain

Rare (may affect up to 1 in 1000 people)
- A disease causing the inflammation or enlargement of a lymph node (Kikuchi lymphadenitis)
- 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)
- Changes in the rhythm or rate of the heart beat, abnormal heart rhythm
- Fluid in the lungs
- Ulcer of the small intestines
- Severe and possibly fatal peeling of the skin (toxic epidermal necrolysis)
- Myopathy (aching muscles, muscle tenderness or weakness, not caused by exercise)

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
- Increased or decreased amount of calcium or potassium
- Increased or decreased blood levels of magnesium or sodium
- Decrease in body weight

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 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 packs containing 1 vial of 10 mL.

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Additional information:

- **Informed Consent Form** – This document will be explained to the patient thoroughly before their treatment commences. The patient will be requested to sign the form and a copy will be given to them to keep.

- **Patient Alert card** - This will be given to all patients 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 highlight 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 (HCP) first.

Contact information:

Bristol-Myers Squibb Medical Information on 0800 731 1736 or medical.information@bms.com