PATIENT INFORMATION LEAFLET

Please read this leaflet carefully before using TYSABRI.

In addition to this leaflet you will be given a Patient Alert Card, which contains important safety information that you need to know before you are given TYSABRI (pronounced tie-SA-bree) and during treatment with TYSABRI.

- Keep this leaflet and the Patient Alert Card. You may need to read them again.
- It is important that you keep the Alert Card with you during treatment and for six months after the last dose of TYSABRI, since side-effects may occur even after you have stopped treatment.
- If you have any further questions, please ask your doctor or your pharmacist.
- This leaflet will explain about side-effects that some patients experience on TYSABRI. If you have any worrying side-effects, or if you notice any side-effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.
- TYSABRI has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

Scheduling Status: Schedule 4

Proprietary name, Strength and Pharmaceutical Form:

TYSABRI concentrate for solution for infusion (each ml of concentrate contains 20 mg of natalizumab). Each 15 ml vial of concentrate contains 300 mg natalizumab.

1. WHAT TYSABRI CONTAINS

Active ingredient: natalizumab

Inactive ingredients: sodium phosphate, monobasic, monohydrate; sodium phosphate, dibasic, heptahydrate; sodium chloride; polysorbate 80; water for injections.

2. WHAT TYSABRI IS USED FOR

TYSABRI is used to treat multiple sclerosis (MS).

The symptoms of MS vary from patient to patient, and you may experience some or none of them. Symptoms can include; walking problems, numbness in the face, arms or legs, problems seeing things, tiredness, feeling off-balance or light headed, bladder and bowel problems, difficulty in thinking and concentrating, depression, acute or chronic pain, sexual problems, and stiffness and

muscle spasms. When the symptoms flare up, it is called a relapse (also known as an exacerbation or an attack). When a relapse occurs, you may notice the symptoms suddenly, within a few hours, or slowly progressing over several days. Your symptoms will then usually improve gradually (this is called a remission).

MS causes inflammation in the brain that damages the nerve cells. In TYSABRI the active ingredient is natalizumab, a protein similar to your own antibodies. It stops the cells that cause inflammation from going into your brain. This reduces nerve damage caused by MS.

It is important to continue with your medicine for as long as you and your doctor decide that it is helping you.

Will TYSABRI always work?

In patients who use TYSABRI, over time the body's natural defence may stop TYSABRI from working properly (the body develops antibodies to TYSABRI). Your doctor can decide whether TYSABRI is not working properly for you by testing your blood and will stop TYSABRI, if necessary.

3. BEFORE YOU RECEIVE TYSABRI

Before you start treatment with TYSABRI, it is important that you and your doctor have discussed the benefits you would expect to receive from this treatment and the risks that are associated with it.

You should not receive TYSABRI:

- If you are allergic (hypersensitive) to natalizumab or any of the other ingredients of TYSABRI.
- If your doctor has told you that you have PML (progressive multifocal leukoencephalopathy). PML is a rare infection of the brain.
- If your doctor tells you that you have a serious problem with your immune system (due to disease for example, leukaemia or HIV or due to a medicine you are taking or have previously taken).
- If you are taking medicines that cannot be used with TYSABRI (see Using other medicines, below).
- If you have cancer (unless it is a type of skin cancer called basal cell carcinoma).
- If you are under 18 years of age.
- If you are planning to become pregnant, are pregnant or are breastfeeding an infant.

Take special care with TYSABRI:

There have been cases of a rare brain infection called PML (progressive multifocal leukoencephalopathy) that have occurred in patients who have been given TYSABRI. PML may lead to severe disability or death. The risk of PML increases the longer that you are on treatment especially if you have been on treatment for more than two years. It is not known if the chance of getting PML continues to rise, remains the same, or falls after you have been on TYSABRI for more than three years. The risk of PML is at least tripled if you have previously taken a medicine that weakens your immune system. In patients with PML a reaction known as IRIS (Immune Reconstitution Inflammatory Syndrome) is likely to occur after treatment for PML, as TYSABRI is removed from your body. IRIS may lead to your condition getting worse, including worsening of brain function.

The symptoms of PML may be similar to an MS relapse (e.g. weakness or visual changes). Therefore, if you believe your MS is getting worse or if you notice any new symptoms, it is very important that you speak to your doctor as soon as possible.

Speak with your partner or caregivers and inform them about your treatment. Symptoms might arise that you might not become aware of by yourself, such as changes in mood or behaviour, memory lapses, speech and communication difficulties, which your doctor may need to investigate further to rule out PML.

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.

Serious infections may occur with TYSABRI. If you develop any infection, or if you develop symptoms like an unexplained fever, severe diarrhoea, prolonged dizziness / headache / stiff neck, weight loss, or listlessness, or other symptoms potentially associated with an infection whilst receiving TYSABRI, speak to your doctor as soon as possible and show the Patient Alert Card and this package leaflet to him.

Pregnancy and breastfeeding:

You should not use TYSABRI if you are pregnant. Be sure to tell your doctor immediately if you are pregnant, think you may be pregnant, or if you are planning to become pregnant.

Do not breastfeed whilst using TYSABRI. You should discuss with your doctor whether you choose to breastfeed or to use TYSABRI.

Driving and using machinery:
TYSABRI is not expected to have an effect on your ability to drive or to operate machines. If you are concerned, discuss this with your doctor.

Using other medicines with TYSABRI:
Please tell your doctor if you are taking or have recently taken any other medicines, including complementary or traditional medicines. The use of TYSABRI with these medicines may cause undesirable interactions. You may not be able to use TYSABRI with some medicines that affect your immune system. Please consult your doctor, pharmacist or other healthcare professional for advice.

4. HOW TYSABRI WILL BE ADMINISTERED

TYSABRI will be prepared and given to you by a doctor.

The adult dose is 300 mg given once every 4 weeks.

TYSABRI must be diluted before it is given to you. It is given as a drip into a vein (by intravenous infusion), usually in your arm. This takes about 1 hour.

A few patients have had an allergic reaction to TYSABRI. Your doctor will check for allergic reactions during the infusion and for 1 hour afterwards.
It is important to continue with your medicine for as long as you and your doctor decide that it is helping you. Continuous dosing with TYSABRI is important, especially during the first four months of treatment. This is because patients who received up to three doses of TYSABRI and then had a gap in treatment of three months or more, were more likely to have an allergic reaction when resuming treatment.

If you have the impression that the effect of TYSABRI is too strong or too weak, talk to your doctor or pharmacist.

If you miss your dose of TYSABRI:

TYSABRI is given by your doctor once every four weeks through a needle placed into your vein. If you miss your usual dose of TYSABRI, contact your doctor immediately and arrange with your doctor to receive the dose as soon as possible. You can then continue to receive your dose of TYSABRI every 4 weeks.

5. POSSIBLE SIDE-EFFECTS

TYSABRI can cause side-effects. If you have any worrying side-effects, including any not listed in this leaflet, please tell your doctor, nurse or pharmacist as soon as possible.

Speak to your doctor or nurse immediately if you notice any of the following:

Signs of allergy to TYSABRI, during or shortly after your infusion:

- Itchy rash (hives)
- Swelling of your face, lips or tongue
- Difficulty breathing.
- Chest pain or discomfort
- Increase or decrease in your blood pressure (your doctor or nurse will notice this if they are monitoring your blood pressure).

Signs of a possible liver problem:

- Yellowing of your skin and the whites of your eyes
- Unusual darkening of the urine.

TYSABRI can also have other side-effects.

Side-effects are listed below by how frequently they have been reported in clinical trials:

Common side-effects that may occur in less than 10 in 100 patients:

- Urinary tract infection
- Sore throat and runny or blocked up nose
- Shivering
- Itchy rash (hives)
- Headache

- Dizziness
- Feeling sick (nausea)
- Being sick (vomiting)
- Joint pain
- Fever
- Tiredness.

Uncommon side-effects that may occur in less than 1 in 100 patients:

- Severe allergy (hypersensitivity).

Rare side-effects that may occur in less than 1 in 1000 patients:

- Unusual infections (so-called "Opportunistic infections")
- Progressive multifocal leukoencephalopathy (PML), a rare brain infection.

What to do if your MS gets worse or you notice new symptoms

There have been reports of a rare brain infection called PML (progressive multifocal leukoencephalopathy) that have occurred in patients who have been given TYSABRI. PML usually leads to severe disability or death.

The symptoms of PML may be similar to an MS relapse.

- Therefore, if you believe your MS is getting worse or if you notice any new symptoms, it is important that you speak to your doctor as soon as possible.
- Discuss your treatment with your partner or caregivers. They might see new symptoms that you might not notice such as changes in mood or behaviour, memory lapses, speech and communication difficulties, which your doctor may need to investigate further to rule out PML.
- Show the Alert Card and this package leaflet to any doctor involved with your treatment, not only to your neurologist.

Serious infections may occur with TYSABRI. The symptoms of infections include:

- an unexplained fever
- severe diarrhoea
- shortness of breath
- prolonged dizziness

– headache
– stiff neck
– weight loss
– listlessness.

- Speak to your doctor as soon as possible if you think you have an infection.
- Show the Alert Card and this package leaflet to any doctor involved with your treatment, not only to your neurologist.

You will also find this information in the Patient Alert Card you have been given by your doctor.

6. STORING AND DISPOSING OF TYSABRI

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN

Unopened vial:

Store in a refrigerator (2 °C to 8 °C).

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Do not use TYSABRI after the expiry date stated on the label and carton.

Diluted solution:

After dilution, immediate use is recommended. If not used immediately, the diluted solution must be stored at 2 °C – 8 °C and infused within 8 hours of dilution.

Do not use TYSABRI if you notice particles in the liquid and/or the liquid in the vial is discoloured.

7. PRESENTATION OF TYSABRI

15 ml TYSABRI is filled in a type I clear glass vial with a grey bromobutyl rubber stopper and an aluminium seal with a royal blue plastic flip-off cap. Pack size is one vial per carton.

8. IDENTIFICATION OF TYSABRI

Colourless, clear to slightly cloudy solution. No visible particles.

9. REGISTRATION NUMBER

42/30.1/0765.

10. NAME AND ADDRESS OF REGISTRATION HOLDER

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11. DATE OF PUBLICATION

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