Patient Information Leaflet for FLUDARA

SCHEDULING STATUS

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

FLUDARA sterile lyophilised solid cake for solution

Read all of this this leaflet carefully before you receive FLUDARA.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **FLUDARA** 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.

1. WHAT FLUDARA CONTAINS

The active ingredient is 50 mg fludarabine phosphate per vial.

The other ingredients are mannitol and sodium hydroxide.

Contains sugar (50 mg mannitol per vial).

2. WHAT FLUDARA IS USED FOR

FLUDARA is a medication that stops the growth of new cancer cells. All cells of the body produce new cells like themselves by dividing. To do this the cell's genetic material (DNA) must be copied and reproduced. **FLUDARA** is taken up by the cancer cells and hinders the production of new DNA.

FLUDARA is used in the treatment of B-cell chronic lymphocytic leukaemia (B-CLL) in patients with sufficient healthy blood cell production.

3. BEFORE YOU RECEIVE FLUDARA

Your doctor will examine you and ask you about your medical history in order to decide whether you can receive **FLUDARA**.

Do not receive FLUDARA:

- If you are allergic (hypersensitive) to fludarabine phosphate or any of the other ingredients of **FLUDARA** (see **WHAT FLUDARA CONTAINS**).
- If you have severely reduced kidney function.
- If the number of your red blood cells is reduced due to breaking down of these cells.

FLUDARA is not recommended for use in children under the age of 18 since it has not been established if it is safe in children and adolescents.

Take special care with FLUDARA:

- **If your bone marrow is working very poorly, or if you have a poorly functioning or depressed immune system or a history of infections due to depressed immune system.** Tell your doctor if any of the conditions listed above apply before your treatment. Your doctor may decide not to give you **FLUDARA**, or may give you some additional treatment.
- **If you feel unwell, have unusual bruising, more bleeding than usual after an injury, or if you seem to be catching a lot of infections**. These may be signs of a reduction in the number of your blood cells, which may be caused either by the disease itself or the therapy. It can last for up to a year, independent of whether or not you had a treatment with **FLUDARA** before. You will have regular blood tests during treatment and you will be closely monitored while you are being treated with **FLUDARA**. Inform your doctor if any of these apply before you start treatment.
- **If during treatment your urine turns red to brownish, or you have a rash or any blisters on your skin**, inform your doctor immediately.
- During or after treatment with **FLUDARA** your body may produce an abnormal immune response and may attack substances or tissues normally present in your body (called

"autoimmune phenomenon"), or your red blood cells (called "autoimmune haemolysis"). These conditions can be life-threatening.

If this occurs your doctor will stop your treatment and you may receive further medication, such as transfusion of irradiated blood (see below) and adrenocorticoids.

- **If you notice any unusual symptoms of your nervous system such as disturbed vision, headache, confusion or seizures (fits)**, tell your doctor. When **FLUDARA** is used in the recommended dose symptoms of various forms of leukoencephalopathy have been reported: headache, nausea, vomiting, seizures (fits), visual disturbances (including vision loss), changes is mental state (abnormal thinking, confusion, altered consciousness, agitation), drowsiness, muscle weakness in your limbs (including irreversible partial or complete paralysis), uncontrolled leakage of urine (see **POSSIBLE SIDE EFFECTS**). If **FLUDARA** is used for a long time (more than 6 courses of therapy), its long-term effects on the central nervous system are not known. In patients on doses four times greater than recommended, blindness, coma and death have been reported. Some of these symptoms appeared delayed, up to 60 days after treatment had been stopped. In some patients receiving **FLUDARA** doses higher than the recommended dose, the symptoms of leukoencephalopathy may be irreversible, life-threatening or fatal. When leukoencephalopathy is suspected and confirmed, you doctor will stop and permanently discontinue your treatment with **FLUDARA**.
- **If you notice any pain in your side, blood in your urine or reduced amount of urine,** tell your doctor immediately. When your disease is very severe, your body may not be able to clear all the waste products from the cells destroyed by **FLUDARA**. This is called *tumour lysis syndrome* and can cause kidney failure and heart problems, from the first week of treatment. Your doctor will be aware of this and may give you other medicines to help prevent it. He/she may decide that you should start your therapy in hospital.
- **If you need a blood or blood products transfusion** and you are being treated with **FLUDARA**, you should receive blood or blood products that are irradiated.
- **If you notice any changes to your skin** either while you are receiving **FLUDARA** or after you have finished the therapy, inform your doctor.

- **If you have or have had skin cancer** it may worsen or flare up again while you receive **FLUDARA** or afterwards. You may also develop skin cancer during or after **FLUDARA** therapy as it reduces your body's defence mechanism.
- **Men and women who are fertile must use effective contraception** during treatment and for at least 6 months afterwards. It cannot be ruled out that **FLUDARA** may harm an unborn baby.
- **If you are breastfeeding your baby or consider breastfeeding your baby,** you should not start it or continue while on treatment with **FLUDARA**.
- **If you need a vaccination, check with your doctor,** because live vaccinations should be avoided during and after treatment with **FLUDARA**.
- **If you have kidney problems,** you will have regular blood and/or laboratory tests to check your kidney function. If your kidney problems are severe, you will not be prescribed **FLUDARA** at all (see **Do not receive FLUDARA** and **HOW FLUDARA IS ADMINISTERED**).

Elderly patients and FLUDARA:

People who are 65 years or older will have regular tests for kidney function. People over 75 years will be closely monitored.

Children:

FLUDARA is not recommended for use in children under the age of 18 since safety and efficacy have not been established.

Receiving FLUDARA with food and drink:

FLUDARA can be administered without regard to food.

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your healthcare provider for advice before receiving **FLUDARA**.

Pregnancy

FLUDARA should not be used during pregnancy because animal studies and very limited experiences in humans have shown a possible risk of abnormalities in the unborn baby as well as early pregnancy loss or premature delivery.

- If you are pregnant or you think you may be pregnant, tell your doctor immediately.
- If you are a woman who can become pregnant, use effective contraceptive methods during treatment and for at least 6 months afterwards.

Breastfeeding

You should not start or continue breastfeeding your baby during your treatment with **FLUDARA**. It is not known whether **FLUDARA** appears in the breast milk. However, in animal studies the active ingredients of **FLUDARA**, fludarabine phosphate, and/or its metabolites were found in breast milk. Breastfeeding should be discontinued for the duration of **FLUDARA** treatment.

Males

Men who are receiving **FLUDARA** and who can become fathers must use effective contraception during treatment and for at least 6 months afterwards.

Driving or using machinery:

FLUDARA may impair your ability to drive and use machinery. Some people get tired, feel weak, have disturbed vision, become confused or agitated, or have seizures while they are treated with **FLUDARA**. Do not try to drive, operate machinery, or do anything else that requires your attention until you know how **FLUDARA** affects you.

Important information about some of the ingredients of FLUDARA:

FLUDARA contains less than 1 mmol sodium per vial.

FLUDARA contains mannitol which may have a mild laxative effect.

Using other medicines with FLUDARA:

Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

It is especially important to tell your doctor about:

- Pentostatin (deoxycoformycin), also used to treat B-cell chronic lymphocytic leukaemia. Taking these two medicines together can lead to severe lung complications.
- Dipyridamole, used to prevent excessive blood clotting, or other similar medicines. They may reduce the effectiveness of **FLUDARA**.
- Cytarabine, used to treat cancers of white blood cells.

4. HOW FLUDARA IS ADMINISTERED

FLUDARA should be administered under supervision of a doctor qualified and experienced in the use of cancer (anti-neoplastic) therapy. The dose you receive depends on how big you are. It varies with your body surface area. This is measured in square meters (m^2) and is calculated from your weight and height.

FLUDARA is given in the form of a solution directly in the bloodstream through a vein (as an injection or infusion over approximately 30 minutes).

How long the treatment with **FLUDARA** lasts depends on how successful it is, and how well you tolerate **FLUDARA**. If side effects are a problem, the repeat course may be delayed and/or the dosage may be decreased. You will have blood tests after every treatment course. Your individual dose will be carefully adjusted according to the number of your blood cells and your response to the therapy. If the number of your blood cells is too low, your next treatment cycle may be postponed for up to two weeks or your dose may be decreased.

Repeat treatment option after initial FLUDARA treatment:

If you have responded well to **FLUDARA** once, you have a good chance of doing so again at a later stage.

How FLUDARA should be handled:

Due to the toxic nature of an anti-cancer medication, such as **FLUDARA**, special protective recommendations for handling are advised. Please consult your doctor. **FLUDARA** must not be touched by pregnant women.

If you receive more FLUDARA than you should:

Since a healthcare professional will administer **FLUDARA**, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

5. POSSIBLE SIDE EFFECTS

FLUDARA can have side effects.

Not all side effects reported for **FLUDARA** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving **FLUDARA**, please consult your doctor qualified and experienced in the use of **FLUDARA**.

If any of the following happens, stop receiving **FLUDARA** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing.
- Rash or itching.
- Fainting.
- Yellowing of the skin and eyes, also called jaundice.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to **FLUDARA**. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Symptoms of leukoencephalopathy, such as headache, feeling sick (nausea) and vomiting, visual disturbances including vision loss, changes in mental status (abnormal thinking, confusion, altered consciousness, agitation), drowsiness, muscle weakness in your limbs (including irreversible partial or complete paralysis), uncontrolled leakage of urine.
- Bleeding in the brain (with symptoms such as severe headache, difficulty speaking or walking, vision problems, confusion, seizures/fits).
- Inflammation of the bladder, which can cause pain when passing urine, and can lead to blood in the urine (haemorrhagic cystitis).
- Difficulty breathing, coughing associated with blood discharge, or chest pain with or without fever. These may be signs of lung problems.
- Palpitations (if you suddenly become aware of your heartbeat) or chest pain. These may be signs of heart problems.

These are all serious side effects. You may need urgent medical attention.

The following side effects have been identified as **frequent** in patients receiving **FLUDARA** treatment:

- Infections or opportunistic infections (infections due to depressed immune system) e.g. herpes zoster virus, Epstein-Barr virus (disorders of the lymph system due to viral infection), progressive multi-focal leukoencephalopathy (a serious viral infection of the brain), pneumonia (inflammation of the lungs).
- Myelodysplastic syndrome (disorders of the stem cells in the bone marrow causing symptoms such as shortness of breath, weakness, pale skin colour, easy bruising or unexplained bleeding) and acute myeloid leukaemia (a cancer of the myeloid line of blood cells causing symptoms such as fever, shortness of breath, easy bruising or unexplained bleeding, weakness, weight loss and loss of appetite).

- Neutropenia (decrease in number of white blood cells), anaemia (reduction in the number of red blood cells), thrombocytopenia (reduction in the number of platelets in the blood, with a possibility of bruising and bleeding).
- Myelosuppression (bone marrow suppression presenting with symptoms such as tiredness, frequent infections and unexplained bleeding or bruising).
- Anorexia (an eating disorder).
- Visual disturbances.
- Peripheral neuropathy (damage to the nervous system with a tingling, pins and needles sensation in the hands, feet, legs or arms).
- Cough.
- Nausea (feeling sick), vomiting (being sick), diarrhoea, stomatitis (pain and swelling in the mouth).
- Rash.
- Fever, fatigue (feeling tired), weakness, chills, general discomfort, swelling.

The following side effects have been identified as **less frequent** in patients receiving **FLUDARA** treatment:

- Stevens-Johnson syndrome or toxic epidermal necrolysis (severe skin disorders with painful rashes that spread and form blisters).
- Seizures (fits).
- Abnormal bleeding.
- Blood in the urine.
- Confusion.
- Feeling agitated.
- Eye disorders (partial or complete loss of vision).
- Lymphoproliferative disorder (a condition in which certain white blood cells or lymphocytes are produced in excessive quantities causing symptoms such as enlarged lymph nodes or an enlarged spleen).

- Autoimmune disorder (condition that occurs when your immune system mistakenly attacks and destroys healthy body tissue causing symptoms such as rheumatoid arthritis, skin conditions (white patches, redness, irritation or flaky silver patches), inflammatory bowel diseases (stomach upset) or diabetes).
- Changes in your liver or pancreatic enzyme levels (causing symptoms such as jaundice, fatigue, nausea, vomiting, pain of your stomach area, mental changes or itching).
- Changes in the levels of potassium (too high levels of potassium causing symptoms such as muscle fatigue, weakness, abnormal heartbeat and nausea), phosphates (too high levels of phosphate causing symptoms such as muscle cramps, tiredness, shortness of breath, nausea, vomiting or trouble sleeping), calcium (too low levels of calcium causing symptoms such as muscle spasms, numbness or tingling of your hands, face or feet, hallucinations or loss of memory) or uric acid (too high levels of uric acid causing symptoms such as gout) in your blood.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF FLUDARA

- Store at or below 30 °C.
- Do not remove from outer carton until required for use.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the label or carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

7. PRESENTATION OF FLUDARA

1 vial containing 50 mg.

5 vials containing 50 mg each.

8. IDENTIFICATION OF FLUDARA

Sterile white lyophilised solid cake or powder supplied in clear glass single dose vials of 10 mL capacity.

9. REGISTRATION NUMBER

28/26/0605

10. NAME AND ADDRESS OF THE REGISTRATION HOLDER

sanofi-aventis south africa (pty) ltd

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11. DATE OF PUBLICATION

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