

Patient Information Leaflet for FLUDARA ORAL

SCHEDULING STATUS

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

FLUDARA ORAL film coated tablet

Read all of this this leaflet carefully before you take FLUDARA ORAL.

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

The active ingredient is 10 mg fludarabine phosphate per film coated tablet.

The other ingredients are colloidal silicon dioxide, croscarmellose sodium, red ferric oxide, yellow ferric oxide, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, talc and titanium dioxide.

Contains sugar (74,75 mg lactose monohydrate per tablet).

2. WHAT FLUDARA ORAL IS USED FOR

FLUDARA ORAL 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 ORAL** is taken up by the cancer cells and hinders the production of new DNA.

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

3. BEFORE YOU TAKE FLUDARA ORAL

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

Do not take FLUDARA ORAL:

- If you are allergic (hypersensitive) to fludarabine phosphate or any of the other ingredients of **FLUDARA ORAL** (see **WHAT FLUDARA ORAL 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 ORAL 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 ORAL:

- **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 ORAL**, or may give you some additional treatment.
- **If you feel unwell, have unusual bruising, more bleeding than usual after 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 ORAL** before. You will have regular blood tests during treatment and you will be closely monitored while you are being treated with **FLUDARA ORAL**. 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 ORAL** 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 ORAL** 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 in 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 ORAL** 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 ORAL** doses higher than the recommended dose, the symptoms of leukoencephalopathy may be irreversible, life-threatening or fatal. When leukoencephalopathy is suspected and confirmed, your doctor will stop and permanently discontinue your treatment with **FLUDARA ORAL**.
- **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 ORAL**. 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 ORAL**, you should receive blood or blood products that are irradiated.
- **If you notice any changes to your skin** either while you are taking **FLUDARA ORAL** 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 take **FLUDARA ORAL** or afterwards. You may also develop skin cancer during or after **FLUDARA ORAL** 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 ORAL** 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 ORAL**.
- **If you need a vaccination, check with your doctor**, because live vaccinations should be avoided during and after treatment with **FLUDARA ORAL**.
- **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 ORAL** at all (see **Do not take FLUDARA ORAL** and **HOW TO TAKE FLUDARA ORAL**).
- **FLUDARA ORAL may cause more vomiting and nausea** (being or feeling sick) than **FLUDARA** given intravenously. If this is a problem when you take **FLUDARA ORAL**, your doctor will consider switching your treatment to the intravenous **FLUDARA**.

Elderly patients and FLUDARA ORAL:

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

Children:

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

Taking FLUDARA ORAL with food and drink:

FLUDARA ORAL can be taken with or without food.

Pregnancy and breastfeeding:

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

Pregnancy

FLUDARA ORAL 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 ORAL**. It is not known whether **FLUDARA ORAL** appears in the breast milk. However, in animal studies the active ingredients of **FLUDARA ORAL**, fludarabine phosphate, and/or its metabolites were found in breast milk.

Breastfeeding should be discontinued for the duration of **FLUDARA ORAL** treatment.

Males

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

Driving or using machinery:

FLUDARA ORAL 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 ORAL**. Do not try to drive, operate machinery, or do anything else that requires your attention until you know how **FLUDARA ORAL** affects you.

Important information about some of the ingredients of FLUDARA ORAL:

FLUDARA ORAL contains lactose monohydrate which may have an effect on the control of your blood sugar if you have diabetes mellitus. Patients with rare hereditary conditions of lactose or galactose intolerance should not take **FLUDARA ORAL**.

Using other medicines with FLUDARA ORAL:

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 efficacy of **FLUDARA ORAL**.
- Cytarabine, used to treat cancers of white blood cells.

4. HOW TO TAKE FLUDARA ORAL

Do not share medicines prescribed for you with any other person. Always take **FLUDARA ORAL** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

FLUDARA ORAL can be taken either on an empty stomach or together with food. Swallow the tablets whole with water. Do not chew or break tablets.

How long the treatment with **FLUDARA ORAL** lasts depends on how successful it is, and how well you tolerate **FLUDARA ORAL**. 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 ORAL treatment:

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

How FLUDARA ORAL should be handled:

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

If you take more FLUDARA ORAL than you should:

In the event of overdose, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

POSSIBLE SIDE EFFECTS

FLUDARA ORAL can have side effects.

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

If any of the following happens, stop taking **FLUDARA ORAL** 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 ORAL**. 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 ORAL** 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 cell 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 ORAL** 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 ORAL

- 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 ORAL

Packs containing 10, 15, 20 or 25 tablets. The outer cartons contain child-resistant containers with 2, 3, 4 or 5 metallic foil blisters of 5 tablets each.

8. IDENTIFICATION OF FLUDARA ORAL

Salmon-pink capsule-shaped film coated tablets with "LN" in a regular hexagon embossed on one side.

9. REGISTRATION NUMBER

36/26/0422

10. NAME AND ADDRESS OF THE REGISTRATION HOLDER

sanofi-aventis south africa (pty) ltd

Sanofi House

2 Bond Street

Midrand

+27 (0)11 256 3700

11. DATE OF PUBLICATION

Date of registration: 11 February 2005

Date of revision: 10 July 2018