PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]FLUDARA®

Fludarabine phosphate tablets

Read this carefully before you start taking **FLUDARA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **FLUDARA**.

Serious Warnings and Precautions

FLUDARA should be prescribed by a healthcare professional experienced with the use of anticancer drugs.

The following are possible serious side effects:

- **Myelosuppression**: This is a decreased production of the blood cells by the bone marrow. It can affect:
    - your body's ability to protect against infections due to low white blood cells (neutropenia)
    - the ability of blood cells to carry oxygen due to low red blood cells (anemia), or
    - blood clotting due to low platelets (thrombocytopenia)

  Myelosuppression may result in death.
- **Central nervous system problems** including blindness, coma, and death at doses four times greater than the recommended dose for CLL. This has been rarely reported at the recommended dose for CLL.
- **Hemolytic anemia:** This is a low red blood cell count due to a breakdown of red blood cells. It may result in death.
- Lung toxicity resulting in death. This has happened when FLUDARA was used in combination with the medicine pentostatin (deoxycoformycin).

What is FLUDARA used for?

FLUDARA is used to treat adults with chronic lymphocytic leukemia (CLL) when other treatments have not worked.

How does FLUDARA work?

FLUDARA slows or stops the growth of cancer cells. It does this by interfering with the production of the cell's genetic material called DNA.

What are the ingredients in FLUDARA?

Medicinal ingredient: fludarabine phosphate

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, ferric oxide (yellow, red), hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, talc, titanium dioxide.

FLUDARA comes in the following dosage forms:

Tablet: 10 mg fludarabine phosphate

Do not use FLUDARA if:

- you are allergic to fludarabine or any of the ingredients of this medication
- you have severe kidney problems
- you have hemolytic anemia (when red blood cells are broken down rapidly)
- you are also using a medicine called pentostatin (deoxycoformycin)

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take FLUDARA. Talk about any health conditions or problems you may have, including if you:

- have problems with your immune system
- are not feeling very well
- have kidney problems
- have liver problems
- are over 75 years old
- need any vaccinations. Live vaccine should be avoided during and after treatment with FLUDARA.
- have skin cancer. FLUDARA may worsen skin cancer lesions or cause them to flare-up. New skin cancers have also been reported in patients during or after FLUDARA therapy.
- have an infection associated with decreased immune function.

Other warnings you should know about:

Pregnancy and breastfeeding:

Female patients:

- If you are pregnant, able to get pregnant or think you are pregnant, there are specific risks you should discuss with your healthcare professional.
- Do not use FLUDARA if you are pregnant. It may harm your unborn baby or make you lose the pregnancy. If you are able to become pregnant:
    - Avoid becoming pregnant while you are receiving FLUDARA. Use birth control during your treatment with FLUDARA. Continue using this birth control for at least 6 months after stopping treatment.
    - Tell your healthcare professional right away if you become pregnant during your treatment.
    - Do not breastfeed while you are receiving FLUDARA.

Male patients while taking FLUDARA and for at least 6 months after stopping treatment:

- Do not father a child.
- Use effective birth control each time you have sex with a woman who could get pregnant. Be sure to tell her you are taking FLUDARA and that there are risks to an unborn baby should she get pregnant.
- If your sexual partner gets pregnant during your treatment, tell your healthcare professional right away.

Fertility: FLUDARA might affect your ability to have a child in the future. Before you start FLUDARA, you should speak with your healthcare professional about ways to protect your eggs or sperm.

If you are planning a pregnancy after your FLUDARA treatments, you should speak with a Genetic Counselor.

Tumour Lysis Syndrome: When cancer cells are destroyed they release waste products into the blood. In some cases, FLUDARA may cause a rapid breakdown of cancer cells making it difficult for your body to get rid of these waste products. This is called Tumour Lysis Syndrome. It may cause nausea and vomiting, joint pain, kidney failure, and heart problems. Your healthcare professional may give you medications to stop this from happening.

Encephalopathy: This is a disease of the brain. It can occur during treatment or up to 4 or more years after FLUDARA has been stopped. It can be permanent, life-threatening, or cause death. Your healthcare professional will do assessments of your nervous system to monitor for encephalopathy. This might include scans like a MRI.

When you take FLUDARA, encephalopathy can occur:

- At the recommended dose. It happens most commonly;
    - when given with other drugs known to cause encephalopathy
    - when you have:
        - Head or total body radiation therapy
        - Hematopoietic Stem Cell transplantation
        - Graft versus host disease
        - Kidney disease
- At higher than recommended doses

Driving and using machines: FLUDARA can cause fatigue, weakness, vision problem, confusion, agitation and seizures. This may reduce your ability to drive or use machines. Do not drive or operate machinery if FLUDARA affects your alertness or your vision.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with FLUDARA:

- A medicine used to prevent blood clots called dipyridamole.
- A medicine used in the treatment of cancer called cytarabine.

How to take FLUDARA:

- Take it exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Swallow tablets whole with water. Tablets can be taken with or without food.
- Do not chew, break or crush tablets.
- FLUDARA is given in treatment cycles. These are 28 days long. You will take FLUDARA each day of the first 5 days of each 28-day cycle. The number of cycles you have will depend on how you respond and tolerate the treatment. Usually, six 28-day cycles are required.
- Pregnant women must not touch FLUDARA tablets.
- Keep FLUDARA in its protective packaging until use.

Usual dose: 40 mg / m^2 once a day each day for the first 5 days of each 28-day cycle

Your dose of FLUDARA will be based on your height and weight. Your healthcare professional will tell you how much FLUDARA to take. You may receive a lower dose if you have kidney problems.

Overdose:

If you think you, or a person you are caring for, have taken too much FLUDARA, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose or vomit after taking a tablet, contact your healthcare professional. Do not take 2 doses at the same time to make up for a missed dose**.**

What are possible side effects from using FLUDARA?

These are not all the possible side effects you may have when taking FLUDARA. If you experience any side effects not listed here, tell your healthcare professional.

- fever
- feeling tired
- feeling weak
- cough
- nausea
- vomiting
- diarrhea
- loss of appetite
- visual problems (blurred vision)
- inflammation or sores of the mouth, lips and digestive track
- skin rash
- generally feeling unwell
- chills
- build-up of fluid in the body (swelling)
- bruising

Prolonged vomiting, diarrhea, or mouth sores may limit your fluid intake. This can make you prone to dehydration. Contact your doctor if these symptoms last for 24 hours.

FLUDARA can cause abnormal blood test results. Your healthcare professional will do blood tests during your treatment. These will tell your healthcare professional how FLUDARA is affecting your blood.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Myelosuppression (decreased blood cell production including: **neutropenia** (low white blood cell count), **anemia** (low red blood cell count) **thrombocytopenia** (low platelet count)**:** any unusual bruising, more bleeding than usual after injury, frequent infections. This may also lead to an increased risk of (serious) infections, caused by organisms, that usually do not cause disease in healthy persons (opportunistic infections) including a late reactivation of viruses, for example herpes zoster.		✓	
Pneumonia (lung infection): cough, trouble breathing, chest pain with or without fever		✓	
COMMON			
Infection: fever, chills, feeling unwell, pain		✓	
Peripheral neuropathy: pain, numbness or weakness in the arms and / or legs, dropping things from your hands, trouble with tasks like walking, picking up items, or moving your limbs.		✓	
Richter's Syndrome (rare type of lymphoma): Rapid and dramatic increase in the size of the lymph nodes in the neck, abdomen, armpit or groin; night sweats, weight loss, fever, palpitations, fatigue, shortness of breath, dizziness		✓	
UNCOMMON			
Allergic reaction: difficulty breathing, rash, itching			✓
Tumour Lysis Syndrome (the sudden, rapid death of cancer cells due to treatment): pain in your side, blood in your urine, a reduced amount of urine		✓	
Bleeding in the digestive system: tar-coloured or bloody stool		✓	
Hemolytic Anemia (rapid breakdown of red blood cells): yellowing of the		✓	

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
skin or eyes and/or red-brown urine			
Confusion: problems with short-term memory, difficulty carrying out tasks, poor attention span, unclear speech and difficulty in following a conversation		✓	
Autoimmune reactions: (when the immune system mistakenly attacks our own cells): can lead to various symptoms depending on the affected part of the body, such as fatigue, dizziness or light-headedness, low grade fever, muscle aches, swelling, skin rash.		✓	
Lung injury: difficulty breathing and shortness of breath			✓
RARE			
Heart Failure: palpitations (you suddenly become aware of your heartbeat), irregular heartbeat, chest pain.		✓	
Epstein Barr Virus-associated lymphoproliferative disorder (disorders of the lymph system due to a viral infection): fever, sore throat, swollen lymph nodes, spleen or liver enlargement, jaundice, high white blood cell count, low red blood cell count, abnormal bleeding or bruising, excessive bleeding, unintentional weight loss, night sweats, loss of appetite, weakness, dizziness, bone pain, rashes, frequent infections, headaches, seizures, confusion, nausea and vomiting		✓	
Coma: prolonged state of unconsciousness		✓	
Seizures: temporary confusion, a staring spell, jerking movements of the arms and legs that can't be controlled, Loss of consciousness or awareness, Cognitive or emotional changes.		✓	
Agitation: feeling of aggravation, annoyance, restlessness, or nervousness		✓	
Lyell's syndrome, Stevens-Johnson syndrome, Toxic Epidermal Necrolysis (severe skin			✓

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
reactions): redness, inflammation, blistering, tissue break down			
Pain in your eyes/Blindness (lack of vision)			✓
Cystitis (inflammation of the bladder): feeling the need to urinate more often, sudden desire to pee, pain/ burning with urination, dark or foul-smelling pee		✓	
UNKNOWN FREQUENCY			
Neurological Disorders: headache with nausea and vomiting, seizure, visual disturbances (vision loss), confusion, muscle spasm, drowsiness			✓
Hemorrhage including • **Cerebral hemorrhage** (bleeding in the brain): sudden headache, nausea, loss of consciousness • **Pulmonary hemorrhage:** (bleeding in lung): coughing, which may bring up blood or clots, weakness, dizziness, fainting • **Retinal hemorrhage:** (bleeding in the eye): sudden vision loss, blurry vision, blind spots, flashes or floaters			✓
Transfusion-associated severe allergic reaction: back pain, dark urine, chills, fainting or dizziness, fever, flank pain, skin flushing, shortness of breath or itching.			✓
Skin cancer: a pearly or waxy bump, flesh-colored or brown scar-like lesion, bleeding or scabbing sore that heals and returns, firm and red nodule, flat lesion with a scaly and crusted surface, large brownish spot with darker speckles, a mole that changes in appearance or that bleeds, painful lesion that itches or burns. Usually occurs in sun-exposed areas of your body, such as your neck or face		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Please note the expiry date on the pack. Do not use after this date.

Store FLUDARA between 15°C and 30°C. Do not freeze.

Any unused FLUDARA should be returned to a pharmacist for safe disposal.

Keep out of reach and sight of children.

If you want more information about FLUDARA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.sanofi.ca, or by calling 1-800-265-7927.

This leaflet was prepared by sanofi-aventis Canada Inc.

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