PART III: CONSUMER INFORMATION

PrFLUDARA®

(fludarabine phosphate)

This leaflet is part III of a three-part "Product Monograph" published when FLUDARA was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about FLUDARA. Contact your doctor or pharmacist if you have any questions about the drug.

Please read this leaflet carefully before you start using FLUDARA. Keep this leaflet. You may need to read it again.

ABOUT THIS MEDICATION

What the medication is used for:
FLUDARA is an anticancer drug. It is taken by mouth as tablets.

FLUDARA (tablets) is used as a second line treatment in patients with chronic lymphocytic leukemia (CLL) who have failed other conventional treatments.

In CLL, too many abnormal lymphocytes are produced and lymph nodes start to grow in various regions of your body. The abnormal lymphocytes either do not work properly or are too young (immature) to fight infection well. If there are too many of these abnormal lymphocytes, they push aside healthy blood cells in the bone marrow where most of the new blood cells are formed. Without enough healthy blood cells, infections, anemia, bruising, excessive bleeding or even organ failure can result.

What it does:
All cells of the body produce new cells like themselves by dividing. For this purpose, the cells' genetic material (DNA) must be copied and reproduced. FLUDARA works by hindering the production of new DNA. Therefore, when the cells take up FLUDARA, it stops the growth of new cells. It has been discovered that FLUDARA works especially well against some cancers of the type of white blood cells called lymphocytes.

When it should not be used:
You must not use FLUDARA if any of the following apply to you:

- Allergy (hypersensitivity) to any of the ingredients of this medication
- Kidney function is severely reduced
- Low red blood cell count because of a certain type of anemia (hemolytic anemia). Your doctor will have told you if you have this condition.

FLUDARA should not be used with a drug called pentostatin (deoxycoformycin).

What the medicinal ingredient is:
fludarabine phosphate

What the nonmedicinal ingredients are:
colloidal silicon dioxide, croscarmellose sodium, ferric oxide (yellow, red), hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, talc, titanium dioxide.

What dosage forms it comes in:
FLUDARA is available as a tablet.
Each salmon-pink coloured tablet contains 10 mg of fludarabine phosphate. Tablets are supplied in blister packs packaged inside child-resistant containers.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

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

The following are possible serious side effects:

- Decreased production of the blood cells by the bone marrow (bone marrow suppression). The protection against infections, the ability of blood cells to carry oxygen, or blood clotting can be affected. It 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.
- Low red blood cell count due to a breakdown of red blood cells (hemolytic anemia) may result in death.
- Lung toxicity resulting in death when used in combination with pentostatin (deoxycoformycin).

BEFORE you use FLUDARA, talk to your doctor if you:

- have a low red blood cell count
- are not feeling very well
- have kidney problems
- have liver problems
- are over 75 years old
- have herpes zoster (shingles)
- need a blood transfusion
- are pregnant or intend to became pregnant.
- FLUDARA may harm an unborn child
- are breast feeding
- need any vaccinations. Live vaccine should be avoided during and after treatment with FLUDARA
- have had a skin cancer. The worsening or flare-up of pre-existing skin cancer lesions, as well as new onset

of skin cancer, has been reported in patients during or after FLUDARA therapy.
- have a disease associated with decreased immune function.

FLUDARA can harm an unborn baby. FLUDARA should not be used during pregnancy unless clearly necessary. If you are pregnant, it is important to discuss with your doctor prior to starting FLUDARA treatment.

Men and women who may still be fertile must use a reliable form of contraception during and for at least 6 months after stopping treatment. Women should avoid becoming pregnant while on FLUDARA therapy.

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 may cause nausea and vomiting, joint pain, kidney failure, and heart problems. Your physician may give you medications to stop this from happening.

Encephalopathy 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 irreversible, life-threatening, or cause death. 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

FLUDARA may reduce the ability to drive or use machines, since e.g., fatigue, weakness, visual disturbances, confusion, agitation and seizures have been observed. Do not drive or operate machinery if FLUDARA affects your alertness and your vision.

INTERACTIONS WITH THIS MEDICATION

This medicine should not be used with a drug called pentostatin (deoxycoformycin).

The effectiveness of FLUDARA may be reduced by medications containing dipyridamole and similar substances.

Tell your doctor if you are taking cytarabine.

If you are taking any other medicines regularly, tell your doctor.

PROPER USE OF THIS MEDICATION

Usual dose:
FLUDARA should be prescribed by a qualified physician experienced in the use of anticancer treatment. The dose you receive or should take varies with your body surface area.

Technically this is measured in square meters (m^2), but actually is worked out from your height and weight.

Usual starting dose: 40 mg/m^2 once a day for 5 consecutive days on a 28 day cycle.

Usually six 28 day cycles are required. The numbers of cycles are decided based on how you will respond and tolerate the treatment .

FLUDARA tablets can be taken on an empty stomach or with food. Swallow the tablets whole with water. **Do not chew, break or crush the tablets**.

FLUDARA tablets must not be removed from their packaging until ready to use.

FLUDARA tablets must not be touched by pregnant women. Unused FLUDARA tablets should be returned to a pharmacist for safe disposal.

Overdose:
If you take more FLUDARA than you should, talk to your doctor, nurse, pharmacist, or call your local poison control centre right away.

In case of drug overdose, contact a health care practitioner, 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, ask your doctor how to continue with the treatment. Do not take a double dose**.**

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The following side effects have been reported very commonly:
- decreased production of the blood cells by the bone marrow (bone marrow suppression) which may cause:
  - increased risk of serious infections such as pneumonia or viral infections (like latent viral reactivation, e.g., Herpes zoster virus, Epstein-Barr virus, Progressive multifocal leucoencephalopathy)
  - anemia (reduced number of red blood cells)
  - abnormal bleeding or bruising
- fever
- feeling tired

- feeling weak
- cough
- nausea
- vomiting
- diarrhea

The following side effects have been reported commonly:

- loss of appetite
- numb or weak limbs
- 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 (edema)

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

The following side effects have been reported uncommonly:

- bleeding in the digestive system
- confusion
- pulmonary injury, with symptoms such as difficulty breathing and shortness of breath
- pain in your side, blood in your urine, or a reduced amount of urine
- red or purple discolorations on the skin caused by bleeding underneath the skin

The following side effects have been reported rarely:

- coma
- seizures
- agitation
- blindness
- pain in the eye
- heart failure
- irregular heartbeat
- inflammation of the bladder
- skin and/or mucous membrane reaction with redness, inflammation, blistering and erosion (e.g., Stevens-Johnson syndrome, Lyell's syndrome or toxic epidermal necrosis)
- skin cancer
- Epstein-Barr virus associated lymphoproliferative disorder (disorders of the lymph system due to a viral infection)

The following side effects for which frequency is unknown:

- bleeding (hemorrhage) including the following:
  - bleeding from a ruptured blood vessel in the brain (cerebral hemorrhage),
  - lung bleeding (pulmonary hemorrhage),
  - eye bleeding (includes retinal hemorrhage)

When used at doses four times greater than the recommended dose for chronic lymphocytic leukemia (CLL), a third of patients experienced severe central nervous system effects including blindness, coma, and death. Such effects are rare (coma, seizures and agitation) or uncommon (confusion) but have been reported in patients who receive the recommended dose for CLL. These effects usually begin from three to eight weeks after treatment has been given but may occur earlier or later.

If you notice any unwanted effects, or if you are unsure about the effect of this product, please inform your doctor.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		**Talk with your doctor or pharmacist**		**Stop taking drug and call your doctor or pharmacist**
		Only if severe	**In all cases**	
Common	vomiting, diarrhea / dehydration (lasting more than 24 hours)		✓	
	cough, trouble breathing, fever / pneumonia		✓	
	fever, chills, feeling unwell, pain / infection		✓	
	numb or weak limbs / motor disturbances		✓	
	blurred vision / changes in vision		✓	
Uncommon	difficulty breathing, rash, itching / allergic reaction			✓
	pain in your side, blood in your urine/ infection		✓	
	tar-coloured or bloody stool / bleeding in the digestive system		✓	
	chest pain / heart failure, irregular heartbeat		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	extreme fatigue, unusual bruising, excessive bleeding after injury / reduction in blood cell production by the bone marrow		✓	
	yellowing of the skin or eyes and/or red-brown urine / rapid breakdown of red blood cells (also called hemolytic anemia)		✓	
	confusion / severe central nervous system effects		✓	
	loss of hearing		✓	
Rare	coma, seizures, agitation / severe central nervous system effects		✓	
	red and flaky skin / severe skin disorder			✓
	pain in your eyes, blindness		✓	
Unknown frequency	Headache with nausea and vomiting, seizure, visual disturbances (vision loss), confusion, muscle spasm , drowsiness			✓

This is not a complete list of side effects. For any unexpected effects while taking FLUDARA, contact your doctor or pharmacist.

HOW TO STORE IT

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

Store FLUDARA tablets between 15ºC and 30ºC. Do not freeze.

Store FLUDARA out of the reach of children and pets.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

Toll-free telephone:	866-234-2345
Online:	www.healthcanada.gc.ca/medeffect
Complete a Canada Vigilance Reporting form and:	
Fax toll-free	1-866-678-6789
Mail to	Canada Vigilance Program Health Canada Postal Locator 0701E Ottawa, Ontario K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals, can be found at: www.sanofi.ca or by contacting the sponsor, sanofi-aventis Canada Inc., at: 1-800-265-7927

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