PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

ALIMTA
100 mg
Powder for solution for infusion

Composition:
Each vial contains:
100 milligrams pemetrexed (as pemetrexed disodium)
After reconstitution, the solution contains 25 mg/ml of pemetrexed. Further dilution by a healthcare provider is required prior to administration.

For information on inactive ingredients and allergens - see section 2 "Important information about some of the ingredients of this medicine" and section 6 "Additional information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, please contact your doctor or pharmacist.
This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Alimta is a medicine used in the treatment of cancer.

Alimta in combination with cisplatin, is indicated for the treatment of patients with malignant pleural mesothelioma, whose disease is unresectable or who are otherwise not candidates for curatible surgery.
Alimta in combination with cisplatin is indicated for the first line treatment of patients with locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology.
Alimta is indicated as monotherapy for the second line treatment of patients with locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology.
Alimta is indicated as monotherapy for the maintenance treatment of locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy.

Therapeutic group: folic acid analogues.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- you are hypersensitive (allergic) to the active ingredient (pemetrexed) or any of the other ingredients that this medicine contains (listed in section 6).
- you are breastfeeding; you must discontinue breastfeeding during treatment with **Alimta.**

– you have recently received or are about to receive a vaccine against yellow fever. See also in section 2 under “Drug interactions/reactions”.

Special warnings regarding the use of this medicine
Before starting treatment with **Alimta**, tell your doctor if:

- you currently have or have previously had problems with your kidneys, talk to your doctor or hospital pharmacist, as you may not be able to receive **Alimta**.
- Before each infusion, you will have samples of your blood taken to evaluate if you have sufficient kidney and liver function and to check that you have enough blood cells to **determine the suitability of receiving the treatment of Alimta**. Your doctor may decide to change the dose or delay treating you depending on your general condition and if your blood cell counts are too low. If you are also receiving cisplatin, your doctor will make sure that you are properly hydrated and receive appropriate treatment before and after receiving cisplatin to prevent vomiting.
- you have had or are going to have radiation therapy, please tell your doctor, as there may be an early or late radiation reaction with **Alimta**.
- you have been recently vaccinated, please tell your doctor, as this can possibly cause bad effects with **Alimta**.
- you have a heart disease or a history of a heart disease, please tell your doctor.
- you have an accumulation of fluid around your lungs, your doctor may decide to remove the fluid before giving you **Alimta**.

Children and adolescents:
This medicine should not be used in children or adolescents, since there is no experience with this medicine in children and adolescents under 18 years of age.

Drug interactions/reactions
If you are taking or have recently taken other medicines, **including non-prescription medicines and nutritional supplements, inform the doctor or hospital pharmacist.**
Particularly if you are taking:
Any medicine for pain or inflammation (swelling), such as medicines called “nonsteroidal anti-inflammatory drugs” (NSAIDs), including medicines purchased without a doctor’s prescription (such as ibuprofen). There are many sorts of NSAIDs with different durations of activity. Based on the planned date of your infusion of **Alimta** and/or on the status of your kidney function, your doctor needs to advise you on which medicines you can take and when you can take them. If you are unsure, ask your doctor or pharmacist if any of your medicines are NSAIDs.

Pregnancy, breastfeeding and fertility

Pregnancy
If you are pregnant, think you may be pregnant or are planning a pregnancy, **tell your doctor**. The use of **Alimta** should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking **Alimta** during pregnancy. Women must use effective contraception during treatment with **Alimta** and for 6 months after receiving the last dose.

Breastfeeding
If you are breastfeeding, tell your doctor .
Breastfeeding must be discontinued during treatment with **Alimta**.

Fertility

Men are advised not to father a child during and up to 3 months following treatment with **Alimta** and should therefore use effective contraception during treatment with **Alimta** and for up to 3 months afterwards. If you would like to father a child during the treatment or in the 3 months following receipt of treatment, seek advice from your doctor or pharmacist. **Alimta** can affect your ability to have children. Talk to your doctor to seek advice about sperm storage before starting your therapy.

Driving and using machines
Alimta may make you feel tired. Be careful when driving a car or using machines.

Important information about some of the ingredients of this medicine
Alimta 100 mg contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THIS MEDICINE?

Always use the medicine according to the doctor's instructions. You should check with your doctor or pharmacist if you are not sure about the dose and manner of treatment with this medicine. The dosage and manner of treatment will be determined by the doctor only.
The usual dosage is:

The dose of **Alimta** is 500 milligrams for every square meter of your body's surface area. Your height and weight are measured to work out the surface area of your body. Your doctor will use this body surface area to work out the right dose for you. This dose may be adjusted, or treatment may be delayed depending on your blood cell counts and on your general condition. A hospital pharmacist, nurse or doctor will have mixed the **Alimta** powder with 9 mg/ml (0.9%) sodium chloride solution for injection before it is given to you.

You will always receive **Alimta** by infusion into one of your veins. The infusion will last approximately 10 minutes.

When using **Alimta** in combination with cisplatin:
The doctor or hospital pharmacist will work out the dose you need based on your height and weight. Cisplatin is also given by infusion into one of your veins, and is given approximately 30 minutes after the infusion of **Alimta** has finished. The infusion of cisplatin will last approximately 2 hours.

You should usually receive your infusion once every 3 weeks.

Additional medicines given during treatment:

Corticosteriods: your doctor will prescribe you steroid tablets (equivalent to 4 milligrams of dexamethasone twice a day) that you will need to take on the day before, on the day of, and the day after **Alimta** treatment. This medicine is given to you to reduce the frequency and severity of skin reactions that you may experience during your anticancer treatment.

Vitamin supplementation: your doctor will prescribe you oral folic acid (vitamin) or a multivitamin containing folic acid (350 to 1,000 micrograms) that you must take once a day while you are taking **Alimta**. You must take at least 5 doses during the seven days before the first dose of **Alimta**. You must continue taking the folic acid for 21 days after the last dose of **Alimta**. You will also receive an injection of vitamin B_{12} (1,000 micrograms) in the week before administration of

Alimta and then approximately every 9 weeks (corresponding to 3 courses of **Alimta** treatment). Vitamin B_{12} and folic acid are given to you to reduce the possible toxic effects of the anticancer treatment.

Do not exceed the recommended dose.
If you have accidentally taken a higher dose or if you have taken an overdose or if a child has accidentally swallowed the medicine, contact a doctor or hospital emergency room immediately and bring the medicine package with you.
Treatment should be continued as recommended by your doctor.
Do not take medicines in the dark! Check the label and the dose each time you take your medicine. Wear glasses if you need them.
If you have further questions regarding the use of this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of **Alimta** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

You must contact your doctor immediately if you notice any of the following:
- Fever or infection (respectively, common or very common): if you have a temperature of 38ºC or greater, sweating or other signs of infection (since you might have less white blood cells than normal which is very common). Infection (sepsis) may be severe and could lead to death.
- If you start feeling chest pain (common) or having a fast heart rate (uncommon).
- If you have pain, redness, swelling or sores in your mouth (very common).
- Allergic reaction: if you develop a skin rash (very common) / burning or prickling sensation (common), or fever (common). Rarely, skin reactions may be severe and could lead to death. Contact your doctor if you get a severe rash, or itching, or blistering (Stevens-Johnson Syndrome or Toxic epidermal necrolysis).
- If you experience tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less hemoglobin than normal which is very common).
- If you experience bleeding from the gums, nose or mouth or any bleeding that would not stop, reddish or pinkish urine, unexpected bruising (since you might have less platelets than normal which is common).
- If you experience sudden breathlessness, intense chest pain or cough with bloody sputum (uncommon) (may indicate a blood clot in the blood vessels of the lungs).

Additional side effects

Very common side effects (may affect more than 1 in 10 people)
Infection; pharyngitis (a sore throat); low number of neutrophil granulocytes (a type of white blood cell); low white blood cells; low hemoglobin level; pain, redness, swelling or sores in your mouth; loss of appetite; vomiting; diarrhea; nausea; skin rash; flaking skin; abnormal blood tests showing reduced functionality of kidneys; fatigue (tiredness).

Common side effects (may affect up to 1 in 10 people)
Blood infection; fever with low number of neutrophil granulocytes (a type of white blood cell); low platelet count; allergic reaction; loss of body fluids; taste change; damage to the motor nerves which may cause muscle weakness and atrophy (primary in the arms and legs); damage to the sensory nerves that may cause loss of sensation, burning pain and unsteady gait; dizziness;

inflammation or swelling of the conjunctiva (the membrane that lines the eyelids and covers the white of the eye); dry eyes; watery eyes; dryness of the conjunctiva (the membrane that lines the eyelids and covers the white of the eye) and cornea (the clear layer in front of the iris and pupil); swelling of the eyelids; eye disorder with dryness, tearing, irritation, and/or pain; cardiac failure (condition that affects the pumping power of your heart muscles); irregular heart rhythm; indigestion; constipation; abdominal pain; liver: increases in the chemicals in the blood made by the liver; increased skin pigmentation; itchy skin; rash on the body where each mark resembles a bullseye; hair loss; hives; kidney stop working; reduced functionality of kidney; fever; pain; excess fluid in body tissue, causing swelling; chest pain; inflammation and ulceration of the mucous membranes lining the digestive tract.

Uncommon side effects (may affect up to 1 in 100 people)
Reduction in the number of red, white blood cells and platelets; stroke; type of stroke when an artery to the brain is blocked; bleeding inside the skull; angina (chest pain caused by reduced blood flow to the heart); heart attack; narrowing or blockage of the coronary arteries; increased heart rhythm; deficient blood distribution to the limbs; blockage in one of the pulmonary arteries in your lungs; inflammation and scarring of the lining of the lungs with breathing problems; passage of bright red blood from the anus; bleeding in the gastrointestinal tract; ruptured bowel; inflammation of the lining of the esophagus; inflammation of the lining of the large bowel, which may be accompanied by intestinal or rectal bleeding (seen only in combination with cisplatin); inflammation, edema, erythema, and erosion of the mucosal surface of the esophagus caused by radiation therapy; inflammation of the lung caused by radiation therapy.

Rare side effects (may affect up to 1 in 1,000 people)
Destruction of red blood cells; anaphylactic shock (severe allergic reaction); inflammatory condition of the liver; redness of the skin; skin rash that develops throughout a previously irradiated area.

Very rare side effects (may affect up to 1 in 10,000 people)
Infections of skin and soft tissues; Stevens-Johnson syndrome (a type of severe skin and mucous membranes reaction that may be life threatening); toxic epidermal necrolysis (a type of severe skin reaction that may be life threatening); autoimmune disorder that results in skin rashes and blistering on the legs, arms, and abdomen; inflammation of the skin characterized by the presence of bullae which are filled with fluid; skin fragility, blisters and erosions and skin scarring; redness, pain and swelling mainly of the lower limbs; inflammation of the skin and fat beneath the skin (pseudocellulitis); inflammation of the skin (dermatitis); skin to become inflamed, itchy, red, cracked, and rough; intensely itchy spots.

Not known: frequency cannot be estimated from the available data
Form of diabetes primarily due to pathology of the kidney; disorder of the kidneys involving the death of tubular epithelial cells that form the renal tubules.

If a side effect occurs, if any of the side effects worsen, or if you are suffering from a side effect not mentioned in this leaflet, consult the doctor.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link “Reporting side effects due to drug treatment” that can be found on the Homepage of the Ministry of Health’s website (www.health.gov.il), which refers to the online form for reporting side effects, or by entering the following link:
https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use this medicine after the expiry date (exp. date) which is stated on the vial and carton. The expiry date refers to the last day of that month.
  Storage conditions
- Store below 25˚C.
  Reconstituted and Infusion Solutions: From a microbiological point of view, the product should be used immediately. If not used immediately and when prepared as directed, chemical and physical in-use stability of reconstituted and infusion solutions of pemetrexed were demonstrated for 24 hours at refrigerated temperature (2˚C-8˚C).
- This medicine is for single use only; any unused solution must be disposed of in accordance with local requirement.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, Alimta also contains:
mannitol, hydrochloric acid, sodium hydroxide, water for injection, nitrogen.

What the medicine looks like and contents of the pack:
Alimta is a powder for solution for infusion in a vial. It is a white to either light yellow or green-yellow lyophilized powder.
Each pack of **Alimta** consists of one **Alimta** vial .

License Holder and address: Eli Lilly Israel Ltd., 4 HaSheizaf St., P.O.B 4246, Ra'anana 4366411.

Manufacturer and address: Lilly France S.A.S., Fegersheim, France.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 138-86-31721-00

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