

**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

ALIMTA

500 mg

Powder for solution for infusion

The active ingredient is pemetrexed.

Alimta 100 mg: Each vial contains 100 milligrams of pemetrexed (as pemetrexed disodium).

Alimta 500 mg: Each vial contains 500 milligrams of 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.

Inactive ingredients and allergens: See section 6 "Additional information" and section 2 "Important information about some of the ingredients of this medicine".

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 curative 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 Alimta if:

- you are hypersensitive (allergic) to 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.
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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.

If 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**.

If you have been recently vaccinated, please tell your doctor, as this can possibly cause bad effects with **Alimta**.

If you have a heart disease or a history of a heart disease, please tell your doctor.

If you have an accumulation of fluid around your lungs, your doctor may decide to remove the fluid before giving you **Alimta**.

Children and adolescents:

There is no relevant use of **Alimta** in the pediatric population in malignant pleural mesothelioma and non-small cell lung cancer.

Interactions/Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or 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**.

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 6 months following treatment with **Alimta** and should therefore use effective contraception during treatment with **Alimta** and for up to 6 months afterwards. If you would like to father a child during the treatment or in the 6 months following receipt of treatment, seek advice from your doctor or pharmacist. You may want to seek counselling on 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'.

Alimta 500 mg contains 54 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.7% of the recommended maximum daily dietary intake of sodium for an adult.

3. HOW SHOULD YOU USE 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:

Corticosteroids: 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 B₁₂ (1,000 micrograms) in the week before administration of **Alimta** and then approximately every 9 weeks (corresponding to 3 courses of **Alimta** treatment).

Vitamin B₁₂ and folic acid are given to you to reduce the possible toxic effects of the anticancer treatment.

Do not exceed the recommended dose.

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 38°C 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 Alimta 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 numbers of the medicine in the National Drug Registry of the Ministry of Health:

Alimta 100 mg: 138-86-31721-00

Alimta 500 mg: 131-45-31049-00/1

Revised in December 2020.