Package leaflet: Information for the patient
ACTOFORAN® 100 mg powder for concentrate for solution for infusion
ACTOFORAN® 500 mg powder for concentrate for solution for infusion
pemetrexed
PACKAGE LEAFLET: INFORMATION FOR THE USER

Actoforan®
pemetrexed for injection
100mg and 500mg Vials

Package leaflet: Information for the user
ACTOFORAN® 100 mg powder for concentrate for solution for infusion ACTOFORAN® 500 mg powder for concentrate for solution for infusion pemetrexed
Read all of this leaflet carefully before you start receiving this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What ACTOFORAN is and what it is used for

ACTOFORAN is a medicine used in the treatment of cancer.
ACTOFORAN is given in combination with cisplatin, another anti-cancer medicine, as treatment for malignant pleural mesothelioma, a form of cancer that affects the lining of the lung, to patients who have not received prior chemotherapy.
ACTOFORAN is also given in combination with cisplatin for the initial treatment of patients with advanced stage of lung cancer.
ACTOFORAN can be prescribed to you if you have lung cancer at an advanced stage if your disease has responded to treatment or it remains largely unchanged after initial chemotherapy.
ACTOFORAN is also a treatment for patients with advanced stage of lung cancer whose disease has progressed after other initial chemotherapy has been used.

2. What you need to know before you use ACTOFORAN

Do not use ACTOFORAN
- if you are allergic (hypersensitive) to pemetrexed or any of the other ingredients of this medicine (listed in section 6).
- if you are breast-feeding; you must discontinue breast-feeding during treatment with ACTOFORAN.
- if you have recently received or are about to receive a vaccine against yellow fever.

Warnings and precautions
Talk to your doctor or hospital pharmacist before receiving ACTOFORAN.
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 ACTOFORAN.
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 receive ACTOFORAN. 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 ACTOFORAN.
If you have been recently vaccinated, please tell your doctor, as this can possibly cause bad effects with ACTOFORAN.
If you have heart disease or a history of 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 ACTOFORAN.
Children and adolescents
There is no relevant use of ACTOFORAN in the pediatric population
Other medicines and ACTOFORAN
Please tell your doctor 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 ACTOFORAN 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.
Please tell your doctor or hospital pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
Pregnancy
If you are pregnant, think you may be pregnant or are planning to have a baby, tell your doctor. The use of ACTOFORAN should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking ACTOFORAN during pregnancy. Women must use effective contraception during treatment
with ACTOFORAN.
Breast-feeding
If you are breast-feeding, tell your doctor.
Breast-feeding must be discontinued during ACTOFORAN treatment.
Fertility
Men are advised not to father a child during and up to 6 months following treatment with ACTOFORAN and should therefore use effective contraception during treatment with ACTOFORAN 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 spermstorage before starting your therapy.

Driving and usingmachines
ACTOFORAN may make you feel tired. Be careful when driving a car or using machines.
ACTOFORAN contains sodium
ACTOFORAN 500 mg contains approximately 54 mg sodium per vial. To be taken into consideration by patients on a controlled sodium diet.
ACTOFORAN 100 mg contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially ‘sodium-free’.

3. How to use ACTOFORAN

The dose of ACTOFORAN is 500 milligrams for every square metre 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 ACTOFORAN powder with 9 mg/ml (0.9 %) sodium chloride solution for injection before it is given to you.
You will always receive ACTOFORAN by infusion into one of your veins. The infusion will last approximately 10 minutes.
When using ACTOFORAN 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 ACTOFORAN has finished. The infusion of cisplatin will last approximately 2 hours. You should usually receive your infusion once every 3 weeks.
Additionalmedicines:
Corticosteriods: your doctor will prescribe you steroid tablets (equivalent to 4 milligram of dexamethasone twice a day) that you will need to take on the day before, on the day of, and the day after ACTOFORAN 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 1000 micrograms) that you must take once a day while you are taking ACTOFORAN. You must take at least 5 doses during the seven days before the first dose of ACTOFORAN. You
must continue taking the folic acid for 21 days after the last dose of ACTOFORAN. You will also receive
an injection of vitamin B12 (1000 micrograms) in the week before administration of ACTOFORAN and then approximately every 9 weeks (corresponding to 3 courses of ACTOFORAN treatment). Vitamin B12 and
folic acid are given to you to reduce the possible toxic effects of the anticancer treatment.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
You must contact your doctor immediately if you notice any of the following:
Fever or infection (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 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 haemoglobin 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 very 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).
Side effects with ACTOFORAN may include:
Very common (may affect more than 1 in 10 people)
Low white blood cells
Low haemoglobin level (anaemia)
Low platelet count
Diarrhoea
Vomiting
Pain, redness, swelling or sores in your mouth
Nausea
Loss of appetite
Fatigue (tiredness)
Skin rash
Hair loss
Constipation
Loss of sensation
Kidney: abnormal blood tests
Common (may affect up to 1 in 10 people)
Allergic reaction: skin rash / burning or prickling sensation
Infection including sepsis
Fever
Dehydration
Kidney failure
Irritation of the skin and itching
Chest pain
Muscle weakness
Conjunctivitis (inflamed eye)
Upset stomach
Pain in the abdomen
Taste change
Liver: abnormal blood tests
Watery eyes
Increased skin pigmentation
Uncommon (may affect up to 1 in 100 people)
Acute renal failure
Fast heart rate

Inflammation of the lining of the oesophagus (gullet) has been experienced with ACTOFORAN/ radiation
therapy.
Colitis (inflammation of the lining of the large bowel, which may be accompanied by intestinal or rectal bleeding) Interstitial pneumonitis (scarring of the air sacs of the lung) Oedema (excess fluid in body tissue, causing swelling)Some patients have experienced a heart attack, stroke or “mini-stroke” while receiving ACTOFORAN usually in combination with another anticancer therapy.
Pancytopenia- combined low counts of white cells, red cells and platelets.
Radiation pneumonitis (scarring of the air sacs of the lung associated with radiation therapy) may occur in patients who are also treated with radiation either before, during or after their ACTOFORAN
therapy.
Extremity pain, low temperature and discolouration have been reported.
Blood clots in the lung blood vessels (pulmonary embolism).
Rare (may affect up to 1 in 1,000 people)
Radiation recall (a skin rash like severe sunburn) which can occur on skin that has previously been exposed to radiotherapy, from days to years after the radiation.
Bullous conditions (blistering skin diseases)- including Stevens-Johnson syndrome and Toxic epidermal necrolysis.
Immune mediated haemolytic anaemia (antibody-mediated destruction of red blood cells).
Hepatitis (inflammation of the liver).
Anaphylactic shock (severe allergic reaction).
Not known: frequency cannot be estimated from the available data
Lower limb swelling with pain and redness
Increased urine output
Thirst and increased water consumption
Hypernatraemia – increased sodium in blood
Inflammation of the skin, mainly of the lower limb with swelling, pain and redness
You might have any of these symptoms and/or conditions. You must tell your doctor as soon as possible when you start experiencing any of these side effects.
If you are concerned about any side effects, talk to your doctor.
Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store ACTOFORAN

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the label and carton.
This medicine does not require any special storage conditions.
Reconstituted and Infusion Solutions: The product should be used immediately. 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.
This medicine is for single use only; any unused solution must be disposed of in accordance with local requirement.

6. Contents of the pack and other information

What ACTOFORAN contains
The active substance is pemetrexed.
ACTOFORAN 100 mg: Each vial contains 100 milligrams of pemetrexed (as pemetrexed disodium).
ACTOFORAN 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.
The other ingredients are mannitol, hydrochloric acid and sodium hydroxide.
What ACTOFORAN looks like and contents of the pack
ACTOFORAN is a powder for concentrate for solution for infusion in a vial. It is a white to either light yellow or green-yellow lyophilised powder.
Each pack of ACTOFORAN consists of one ACTOFORAN vial.

Not all pack sizes may be marketed.

MarketingAuthorisation Holder
Manufactured in India by:
TAJ PHARMACEUTICALS LTD.
Mumbai, India
at SURVEY NO.188/1 TO 189/1,190/1 TO 4,
ATHIYAWAD, DABHEL, DAMAN- 396210 (INDIA)

This leaflet was last revised in May 2019.

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The following information is intended for medical or healthcare professionals only:
Instructions for use, handling and disposal.
1. Use aseptic techniques during the reconstitution and further dilution of pemetrexed for intravenous infusion administration.
2. Calculate the dose and the number of ACTOFORAN vials needed. Each vial contains an excess of pemetrexed to facilitate delivery of the label amount.
3. ACTOFORAN 100 mg:
Reconstitute each 100 mg vial with 4.2 ml of 9 mg/ml (0.9%) sodium chloride solution for injection, without preservative, resulting in a solution containing 25 mg/ml pemetrexed.
ACTOFORAN 500 mg:
Reconstitute each 500 mg vial with 20 ml of 9 mg/ml (0.9%) sodium chloride solution for injection, without preservative, resulting in a solution containing 25 mg/ml pemetrexed.
Gently swirl each vial until the powder is completely dissolved. The resulting solution is clear and ranges in colour from colourless to yellow or green-yellow without adversely affecting product quality. The pH of the reconstituted solution is between 6.6 and 7.8. Further dilution is required.
4. The appropriate volume of reconstituted pemetrexed solution must be further diluted to 100 ml with 9 mg/ml (0.9 %) sodium chloride solution for injection, without preservative, and administered as an intravenous infusion over 10 minutes.
5. Pemetrexed infusion solutions prepared as directed above are compatible with polyvinyl chloride and polyolefin lined administration sets and infusion bags. Pemetrexed is incompatible with diluents containing calcium, including lactated Ringer’s Injection and Ringer’s Injection.
6. Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.
7. Pemetrexed solutions are for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.
Preparation and administration precautions: As with other potentially toxic anticancer agents, care should be exercised in the handling and preparation of pemetrexed infusion solutions. The use of gloves is recommended. If a pemetrexed solution contacts the skin, wash the skin immediately and thoroughly with soap and water. If pemetrexed solutions contact the mucous membranes, flush thoroughly with water.
Pemetrexed is not a vesicant. There is not a specific antidote for extravasation of pemetrexed. There have been a few reported cases of pemetrexed extravasation, which were not assessed as serious by the investigator. Extravasation should be managed by local standard practice as with other non-vesicants.

Actoforan®
pemetrexed for injection
100mg and 500mg Vials

TAJ PHARMA