Package leaflet: Information for the user

Bugvi 5 mg/ml poeder voor dispersie voor infusie

paclitaxel

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1.What <Invented name> is and what it is used for

What <Invented name> is
<Invented name> contains, as its active substance, paclitaxel attached to the human protein albumin, in the form of tiny particles known as nanoparticles. Paclitaxel belongs to a group of medicines called “taxanes” used for cancer treatment.
- Paclitaxel is the part of the medicine that affects the cancer; it works by stopping cancer cells from dividing – this means that they die.
- Albumin is the part of the medicine that helps paclitaxel dissolve in the blood and get across the walls of the blood vessels into the tumour. This means that other chemicals that can cause side effects that can be life threatening are not needed. Such side effects occur far less with <Invented name>.

What <Invented name> is used for
<Invented name> is used to treat the following types of cancer:

<u>Breast cancer</u>
- Breast cancer which has spread to other parts of the body (this is called “metastatic” breast cancer).
- <Invented name> is used for metastatic breast cancer when at least one other therapy has been tried but has not worked and you are unsuitable for treatments containing a group of medicines called “anthracyclines”.
- People with metastatic breast cancer who received <Invented name> where another therapy had failed, were more likely to experience a reduction in tumour size, and lived longer than people who took an alternative therapy.

<u>Pancreatic cancer</u>
- <Invented name> is used together with a medicine called gemcitabine if you have metastatic cancer of the pancreas. People with metastatic pancreatic cancer (pancreatic cancer that has spread to other parts of the body) who received paclitaxel with gemcitabine in a clinical trial lived longer than people who had only received gemcitabine.

Lung cancer
- <Invented name> is also used together with a medicine called carboplatin if you have the most common type of lung cancer, called “non-small cell lung cancer”.
- <Invented name> is used in non-small cell lung cancer where surgery or radiotherapy would not be suitable to treat the disease.

2. What you need to know before you are given <Invented name>

DO NOT use <Invented name>
- if you are allergic (hypersensitive) to paclitaxel or any of the other ingredients of this medicine (listed in section 6)
- if you are breast-feeding
- if you have a low white blood cell count (baseline neutrophil counts < 1 500 cells/mm^3 - your doctor will advise you on this)

Warnings and precautions
Talk to your doctor or nurse before using <Invented name>
- if you have poor kidney function
- if you have severe liver problems
- if you have heart problems

Talk to your doctor or nurse if you experience any of these conditions whilst being treated with <Invented name>, your doctor may wish to stop treatment or reduce the dose:
- if you experience any abnormal bruising, bleeding, or signs of infections such as a sore throat or a fever
- if you experience numbness, tingling, pricking sensations, sensitivity to touch, or muscle weakness
- if you experience breathing problems, like shortness of breath or dry cough

Children and adolescents
<Invented name> is only for adults and should not be taken by children and adolescents aged below 18 years.

Other medicines and <Invented name>
Tell your doctor if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, including herbal medicines. This is because <Invented name> can affect the way some other medicines work. Also, some other medicines can affect the way <Invented name> works.

Take care and speak to your doctor when taking <Invented name> at the same time as any of the following:
- medicines for treating infections (i.e. antibiotics such erythromycin, rifampicin, etc.; ask your doctor, nurse or pharmacist if you are unsure whether the medicine you are taking is an antibiotic), including medicines for treating fungal infections (e.g. ketoconazole)
- medicines used to help you stabilise your mood also sometimes referred to as anti-depressants (e.g. fluoxetine)
- medicines used to treat seizures (epilepsy) (e.g. carbamazepine, phenytoin)
- medicines used to help you lower blood lipid levels (e.g. gemfibrozil)
- medicine used for heartburn or stomach ulcers (e.g. cimetidine)
- medicines used to treat HIV and AIDS (e.g. ritonavir, saquinavir, indinavir, nelfinavir, efavirenz, nevirapine)
- a medicine called clopidogrel used to prevent blood clots

Pregnancy, breast-feeding and fertility
Paclitaxel may cause serious birth defects and should therefore not be used if you are

pregnant. Your doctor will arrange a pregnancy test before starting treatment with <Invented name>.

Women of childbearing age should use effective contraception during and up to 1 month after receiving treatment with <Invented name>.

Do not breast feed when taking <Invented name> as it is not known if the active ingredient paclitaxel passes into breast milk.

Male patients are advised to use effective contraception and to avoid fathering a child during and up to six months after treatment and should seek advice on conservation of sperm prior to treatment because of the possibility of irreversible infertility due to therapy with <Invented name>.

Ask your doctor for advice before taking this medicine.

Driving and using machines
Some people may feel tired or dizzy after being given <Invented name>. If this happens to you, do not drive or use any tools or machines.

If you are given other medicines as part of your treatment, you should ask your doctor for advice on driving and using machines.

<Invented name> contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per ml ready to administer solution, that is to say essentially 'sodium-free'.

3. How to use <Invented name>

<Invented name> will be given to you by a doctor or nurse into a vein from an intravenous drip. The dose you receive is based on your body surface area and blood test results.

The usual dose is for breast cancer is 260 mg/m^2 of body surface area given over a 30 minute period.

The usual dose for advanced pancreatic cancer is 125 mg/m^2 of body surface area given over a 30 minute period.

The usual dose for non-small cell lung cancer is 100 mg/m^2 of body surface area given over a 30 minute period.

How often will you receive <Invented name>?
For treatment of metastatic breast cancer, <Invented name> is usually given once every three weeks (on day 1 of a 21-day cycle).

For treatment of advanced pancreatic cancer, <Invented name> is given on days 1, 8 and 15 of each 28-day treatment cycle with gemcitabine being given immediately after <Invented name>.

For treatment of non-small cell lung cancer <Invented name> is given once every week (i.e. on days 1, 8 and 15 of a 21-day cycle), with carboplatin being given once every three weeks (i.e. only on day 1 of each 21-day cycle), immediately after the <Invented name> dose has been given.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everyone gets them.

The **very common** side effects may affect more than 1 in 10 people
- loss of hair (the majority of cases of hair loss happened less than one month after starting paclitaxel. When it happens, hair loss is pronounced (over 50 %) in the majority of patients)
- rash
- abnormal decrease in the number of types of white blood cells (neutrophils, lymphocytes or leukocytes) in the blood
- deficiency of red blood cells
- reduction in the number of platelets in the blood
- effect on peripheral nerves (pain, numbness, tingling or loss of feeling)
- pain in a joint or joints
- pain in the muscles
- nausea, diarrhoea, constipation, sore mouth, loss of appetite
- vomiting
- weakness and tiredness, fever
- dehydration, taste disturbance, weight loss
- low levels of potassium in the blood
- depression, sleep problems
- headache
- chills
- difficulty breathing
- dizziness
- swelling of mucosal and soft tissues
- increased liver function tests
- pain in extremities
- cough
- abdominal pain
- nose bleeds

The **common** side effects may affect up to 1 in 10 people
- itching, dry skin, nail disorder
- infection, fever with decrease in the number of a type of white blood cell (neutrophils) in the blood, flushing, thrush, severe infection in your blood which may be caused by reduced white blood cells
- reduction in all blood cell counts
- chest or throat pain
- indigestion, abdominal discomfort
- stuffy nose
- pain in back, bone pain
- diminished muscular coordination or difficulty reading, increased or decreased tears, loss of eyelashes
- changes in heart rate or rhythm, heart failure
- decreased or increased blood pressure
- redness or swelling at the site where the needle entered the body
- anxiety
- infection in the lungs
- infection in the urinary tract
- obstruction in the gut, inflammation of the large bowel, inflammation of the bile duct
- acute kidney failure
- increased bilirubin in the blood
- coughing up blood

- dry mouth, difficulty swallowing
- muscle weakness
- blurred vision

The **uncommon** side effects may affect up to 1 in 100 people
- increased weight, increased lactate dehydrogenase in the blood, decreased kidney function, increased blood sugar, increased phosphorus in the blood
- decreased or lack of reflexes, involuntary movements, pain along a nerve, fainting, dizziness when standing up, shaking, facial nerve paralysis
- irritated eyes, painful eyes, red eyes, itchy eyes, double vision, reduced vision, or seeing flashing lights, blurred vision due to swelling of the retina (cystoid macular oedema)
- ear pain, ringing in your ears
- coughing with phlegm, shortness of breath when walking or climbing stairs, runny nose, or dry nose, decreased breath sounds, water on the lung, loss of voice, blood clot in the lung, dry throat
- gas, stomach cramps, painful or sore gums, rectal bleeding
- painful urination, frequent urination, blood in the urine, inability to hold your urine
- fingernail pain, fingernail discomfort, loss of fingernails, hives, skin pain, red skin from sunlight, skin discolouration, increased sweating, night sweats, white areas on the skin, sores, swollen face
- decreased phosphorus in the blood, fluid retention, low albumin in the blood, increased thirst, decreased calcium in the blood, decreased sugar in the blood, decreased sodium in the blood
- pain and swelling in the nose, skin infections, infection due to catheter line
- bruising
- pain at site of tumour, death of the tumour
- decreased blood pressure when standing up, coldness in your hands and feet
- difficulty walking, swelling
- allergic reaction
- decreased liver function, increased size of liver
- pain in the breast
- restlessness
- small bleedings in your skin due to blood clots
- a condition involving destruction of red blood cells and acute kidney failure

The **rare** side effects may affect up to 1 in 1 000 people
- skin reaction to another agent or lung inflammation following radiation
- blood clot
- very slow pulse, heart attack
- leaking of drug outside the vein
- a disorder of the electrical conduction system of the heart (atrioventricular block)

The **very rare** side effects may affect up to 1 in 10 000 people
- severe inflammation/eruption of the skin and mucous membranes (Stevens-Johnson syndrome, toxic epidermal necrolysis)

Not known side effects (frequency cannot be estimated from the available data)
- hardening/thickening of the skin (scleroderma)

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Invented name>

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 carton and the vial after EXP. The expiry date refers to the last day of that month.

Unopened vials: Keep the vial in the outer carton in order to protect from light.

After first reconstitution the dispersion should be used immediately. If not used immediately, the dispersion may be stored in a refrigerator (2 °C-8 °C) for up to 24 hours in the vial when kept in the outer carton in order to protect it from light.

The reconstituted dispersion in the intravenous drip may be stored in a refrigerator (2 °C-8 °C) for up to 24 hours protected from light.

The total combined storage time of reconstituted medicinal product in the vial and in the infusion bag when refrigerated and protected from light is 24 hours. This may be followed by storage in the infusion bag for 4 hours below 25 °C.

Your doctor or pharmacist is responsible for disposing of any unused <Invented name> correctly.

6. Contents of the pack and further information

What <Invented name> contains
The active substance is paclitaxel.
Each vial contains 100 mg of paclitaxel formulated as albumin bound nanoparticles.
After reconstitution, each ml of dispersion contains 5 mg of paclitaxel formulated as albumin bound nanoparticles.
The other ingredient is human albumin (containing sodium caprylate and N-acetyl-L-tryptophan).

What <Invented name> looks like and contents of the pack
<Invented name> is a white to yellow powder for dispersion for infusion. <Invented name> is available in glass vials containing 100 mg of paclitaxel formulated as albumin bound nanoparticles.
Each pack contains 1 vial.

Vergunning holder:
STADA Arzneimittel AG
Stadastr. 2 – 18
61118 Bad Vilbel
Duitsland

Fabrikant:
STADA Arzneimittel AG
Stadastr. 2 – 18
61118 Bad Vilbel
Duitsland

STADA Arzneimittel GmbH
Muthgasse 36/2
1190 Vienna
Oostenrijk

In het register ingeschreven onder
Bugvi 5 mg/ml poeder voor dispersie voor infusie RVG 129035

Dit medicijn is geregistreerd in lidstaten van de EEA onder de volgende namen:

Oostenrijk	Bugvi 5 mg/ml Pulver zur Herstellung einer Infusionsdispersion
België	Bugvi 5 mg/ml poeder voor dispersie voor infusie
Duitsland	Bugvi 5 mg/ml Pulver zur Herstellung einer Infusionsdispersion
Denemarken	Bugvi
Spanje	Bugvi 5 mg/ml polvo para dispersión para perfusión EFG
Finland	Bugvi 5 mg/ml infuusiokuiva-aine, dispersiota varten
Frankrijk	Bugvi 5 mg/ml, poudre pour dispersion pour perfusion
Hongarije	Bugvi 5 mg/ml por diszperziós infúzióhoz
IJsland	Bugvi 5 mg/ml innrennslisstofn, ördreifa
Luxemburg	Bugvi 5 mg/ml poudre pour dispersion pour perfusion
Nederland	Bugvi 5 mg/ml poeder voor dispersie voor infusie
Noorwegen	Bugvi 5 mg/ml til infusjonsvæske, dispersjon
Roemenië	Bugvi 5 mg/ml pulbere pentru dispersie perfuzabilă
Zweden	Bugvi 5 mg/ml pulver till infusionsvätska, dispension

Deze bijsluiter is voor het laatst aangepast in juni 2024

Medical or healthcare professionals

The following information is intended for medical or healthcare professionals only:

Instructions for use, handling and disposal

Preparation and administration precautions
Paclitaxel is a cytotoxic anticancer medicinal product and, as with other potentially toxic compounds, caution should be exercised in handling <Invented name>. Gloves, goggles and protective clothing should be used. If <Invented name> dispersion contacts the skin, the skin should be washed immediately and thoroughly with soap and water. If <Invented name> contacts mucous membranes, the membranes should be flushed thoroughly with water. <Invented name> should only be prepared and administered by personnel appropriately trained in the handling of cytotoxic agents. Pregnant staff should not handle <Invented name>.

Given the possibility of extravasation, it is advisable to closely monitor the infusion site for possible infiltration during administration of the medicinal product. Limiting the infusion of <Invented name> to 30 minutes, as directed, reduces the likelihood of infusion-related reactions.

Reconstitution of the product and administration
<Invented name> should be administered under the supervision of a qualified oncologist in units specialised in the administration of cytotoxic agents.

<Invented name> is supplied as a sterile lyophilised powder for reconstitution before use. After reconstitution, each ml of dispersion contains 5 mg of paclitaxel formulated as albumin bound nanoparticles. Reconstituted <Invented name> dispersion is administered intravenously using an infusion set incorporating a 15 µm filter.

Reconstitution of 100 mg
Using a sterile syringe, 20 ml of sodium chloride 9 mg/ml (0.9 %) solution for infusion should slowly be injected into the 100 mg vial of <Invented name> over a minimum of 1 minute.

The solution should be directed onto the inside wall of the vial. The solution should not be injected directly onto the powder as this will result in foaming.

Once the addition is complete, the vial should be allowed to stand for a minimum of 5 minutes to ensure proper wetting of the solid. Then, the vial should gently and slowly be swirled and/or inverted for at least 2 minutes until complete redispersion of any powder occurs. The generation of foam should be avoided. If foaming or clumping occurs, the dispersion should stand for at least 15 minutes until foam subsides.

The reconstituted dispersion should be milky and homogenous without visible precipitates. Some settling of the reconstituted dispersion may occur. If precipitates or settling are visible, the vial should be gently inverted again to ensure complete redispersion prior to use.

Inspect the dispersion in the vial for particulate matter. Do not administer the reconstituted dispersion if particulate matter is observed in the vial.

The exact total dosing volume of 5 mg/ml dispersion required for the patient should be calculated and the appropriate amount of reconstituted <Invented name> should be injected into an empty, sterile, PVC or non-PVC type intravenous bag.

The use of medical devices containing silicone oil as a lubricant (i.e. syringes and IV bags) to reconstitute and administer <Invented name> may result in the formation of proteinaceous strands. Administer <Invented name> using an infusion set incorporating a 15 µm filter to avoid

administration of these strands. Use of a 15 µm filter removes strands and does not change the physical or chemical properties of the reconstituted product.

Use of filters with a pore size less than 15 µm may result in blockage of the filter.

The use of specialised DEHP-free solution containers or administration sets is not necessary to prepare or administer <Invented name> infusions.

Following administration, it is recommended that the intravenous line be flushed with sodium chloride 9 mg/ml (0.9 %) solution for injection to ensure administration of the complete dose.

Any unused product or waste material should be disposed of in accordance with local requirements.

Stability
Unopened vials of <Invented name> are stable until the date indicated on the package when the vial is kept in the outer carton in order to protect from light. Neither freezing nor refrigeration adversely affects the stability of the product. This medicinal product does not require any special temperature storage conditions.

Stability of the reconstituted dispersion in the vial
Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C-8 °C in the original carton, protected from light.

Stability of the reconstituted dispersion in the infusion bag
Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C-8 °C followed by 4 hours at 25 °C, protected from light.

However, from a microbiological point of view, unless the method of reconstituting and filling of the infusion bags precludes the risks of microbial contamination, the product should be used immediately after reconstitution and filling of the infusion bags.

If not used immediately, in-use storage times and conditions are the responsibility of the user.

The total combined storage time of reconstituted medicinal product in the vial and in the infusion bag when refrigerated and protected from light is 24 hours. This may be followed by storage in the infusion bag for 4 hours below 25 °C.