Package leaflet: Information for the user

KANJINTI 150 mg powder for concentrate for solution for infusion
KANJINTI 420 mg powder for concentrate for solution for infusion

trastuzumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 pharmacist.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What KANJINTI is and what it is used for

KANJINTI contains the active substance trastuzumab, which is a monoclonal antibody. Monoclonal antibodies attach to specific proteins or antigens. Trastuzumab is designed to bind selectively to an antigen called human epidermal growth factor receptor 2 (HER2). HER2 is found in large amounts on the surface of some cancer cells where it stimulates their growth. When trastuzumab binds to HER2 it stops the growth of such cells and causes them to die.

Your doctor may prescribe KANJINTI for the treatment of breast and gastric cancer when:

- You have early breast cancer, with high levels of a protein called HER2.
- You have metastatic breast cancer (breast cancer that has spread beyond the original tumour) with high levels of HER2. KANJINTI may be prescribed in combination with the chemotherapy medicine paclitaxel or docetaxel as first treatment for metastatic breast cancer or it may be prescribed alone if other treatments have proved unsuccessful. It is also used in combination with medicines called aromatase inhibitors with patients with high levels of HER2 and hormone-receptor positive metastatic breast cancer (cancer that is sensitive to the presence of female sex hormones).
- You have metastatic gastric cancer with high levels of HER2, when it is in combination with the other cancer medicines capecitabine or 5-fluorouracil and cisplatin.

2. What you need to know before you are given KANJINTI

In order to improve the traceability of this medicine, your doctor or pharmacist should record the tradename and the lot number of the product you have been given in your patient file. You may also wish to make a note of these details in case you are asked for this information in the future.

Do not use KANJINTI if:

- you are allergic to trastuzumab, to murine (mouse) proteins, or to any of the other ingredients of this medicine (listed in section 6).
- you have severe breathing problems at rest due to your cancer or if you need oxygen treatment.

Warnings and precautions

Your doctor will closely supervise your therapy.

Heart checks

Treatment with KANJINTI alone or with a taxane may affect the heart, especially if you have ever used an anthracycline (taxanes and anthracyclines are two other kinds of medicine used to treat cancer). The effects may be moderate to severe and could cause death. Therefore, your heart function will be checked before, during (every three months) and after (up to two to five years) treatment with KANJINTI. If you develop any signs of heart failure (inadequate pumping of blood by the heart), your heart function may be checked more frequently (every six to eight weeks), you may receive treatment for heart failure or you may have to stop KANJINTI treatment.

Talk to your doctor, pharmacist or nurse before you are given KANJINTI if:

- you have had heart failure, coronary artery disease, heart valve disease (heart murmurs), high blood pressure, taken any high blood pressure medicine or are currently taking any high blood pressure medicine.
- you have ever had or are currently using a medicine called doxorubicin or epirubicin (medicines used to treat cancer). These medicines (or any other anthracyclines) can damage heart muscle and increase the risk of heart problems with KANJINTI.
- you suffer from breathlessness, especially if you are currently using a taxane. KANJINTI can cause breathing difficulties, especially when it is first given. This could be more serious if you are already breathless. Very rarely, patients with severe breathing difficulties before treatment have died when they were given trastuzumab.
- you have ever had any other treatment for cancer.

If you receive KANJINTI with any other medicine to treat cancer, such as paclitaxel, docetaxel, an aromatase inhibitor, capecitabine, 5-fluorouracil, or cisplatin you should also read the patient information leaflets for these products.

Children and adolescents

KANJINTI is not recommended for anyone under the age of 18 years.

Other medicines and KANJINTI

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or may take any other medicines.

It may take up to 7 months for KANJINTI to be removed from the body. Therefore you should tell your doctor, pharmacist or nurse that you have had KANJINTI if you start any new medicine in the 7 months after stopping treatment.

Pregnancy

- If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before taking this medicine.
- You should use effective contraception during treatment with KANJINTI and for at least 7 months after KANJINTI treatment has ended.
- Your doctor will advise you of the risks and benefits of taking KANJINTI during pregnancy. In rare cases, a reduction in the amount of (amniotic) fluid that surrounds the developing baby within the womb has been observed in pregnant women receiving trastuzumab. This condition may be harmful to your baby in the womb and has been associated with the lungs not developing fully resulting in foetal death.

Breast-feeding

Do not breast-feed your baby during KANJINTI therapy and for 7 months after the last dose as KANJINTI may pass to your baby through your breast milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

KANJINTI may affect your ability to drive a car or use machines. If during treatment you experience symptoms, such as chills or fever, you should not drive or use machines until these symptoms disappear.

3. How KANJINTI is given

Before starting the treatment your doctor will determine the amount of HER2 in your tumour. Only patients with a large amount of HER2 will be treated with KANJINTI. KANJINTI should only be given by a doctor or nurse. Your doctor will prescribe a dose and treatment regimen that is right for you. The dose of KANJINTI depends on your body weight.

It is important to check the product labels to ensure that the correct formulation is being given as prescribed. KANJINTI intravenous formulation is not for subcutaneous use and should be given as an intravenous infusion only.

KANJINTI intravenous formulation is given as an intravenous infusion ("drip") directly into your veins. The first dose of your treatment is given over 90 minutes and you will be observed by a health professional while it is being given in case you have any side effects. If the first dose is well tolerated the next doses may be given over 30 minutes (see section 2 under "Warnings and precautions"). The number of infusions you receive will depend on how you respond to the treatment. Your doctor will discuss this with you.

In order to prevent medication errors it is important to check the vial labels to ensure that the medicine being prepared and given is KANJINTI (trastuzumab) and not trastuzumab emtansine.

For early breast cancer, metastatic breast cancer and metastatic gastric cancer, KANJINTI is given every 3 weeks. KANJINTI may also be given once a week for metastatic breast cancer.

If you have metastatic or early breast cancer
You will be given KANJINTI on either a three-weekly or once weekly cycle.

- The recommended starting dose for the three-weekly cycle is 8 mg/kg body weight. This will then be reduced to a maintenance dose of 6 mg/kg body weight every three weeks, beginning three weeks after your first dose.
- The recommended starting dose for the once weekly cycle is 4 mg/kg body weight. This will then be reduced to a maintenance dose of 2 mg/kg body weight once weekly, beginning one week after the first dose.

If you have metastatic gastric cancer
The recommended starting dose is 8 mg/kg body weight. This will then be reduced to a maintenance dose of 6 mg/kg body weight every three weeks, beginning three weeks after your first dose.

If you miss a dose of KANJINTI

It is important for you to keep all your appointments to receive KANJINTI. If you miss an appointment, ask your doctor when to schedule your next dose.

If you stop using KANJINTI

Do not stop using this medicine without talking to your doctor first. All doses should be taken at the right time every week or every three weeks (depending on your dosing schedule). This helps your medicine work as well as it can.

It may take up to 7 months for KANJINTI to be removed from your body. Therefore your doctor may decide to continue to check your heart functions, even after you finish treatment.

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

4. Possible side effects

Like all medicines, KANJINTI can cause side effects, although not everybody gets them. Some of these side effects may be serious and may lead to hospitalisation.

During a KANJINTI infusion, chills, fever and other flu like symptoms may occur. These are very common (may affect more than 1 in 10 people). Other infusion-related symptoms are: feeling sick (nausea), vomiting, pain, increased muscle tension and shaking, headache, dizziness, breathing difficulties, wheezing, high or low blood pressure, heart rhythm disturbances (palpitations, heart fluttering or irregular heart beat), swelling of the face and lips, rash and feeling tired. Some of these symptoms can be serious and some patients have died (see section 2 under "Warnings and precautions").

These effects mainly occur with the first intravenous infusion ("drip" into your vein) and during the first few hours after the start of the infusion. They are usually temporary. You will be observed by a health care professional during the infusion and for at least six hours after the start of the first infusion and for two hours after the start of other infusions. If you develop a reaction, they will slow down or stop the infusion and may give you treatment to counteract the side effects. The infusion may be continued after the symptoms improve.

Occasionally, symptoms start later than six hours after the infusion begins. If this happens to you, contact your doctor immediately. Sometimes, symptoms may improve and then get worse later.

Serious side effects

Other side effects can occur at any time during treatment with trastuzumab, not just related to an infusion. **Tell a doctor or nurse straight away, if you notice any of the following side effects**:

- Heart problems can sometimes occur during treatment and occasionally after treatment has stopped and can be serious. They include weakening of the heart muscle possibly leading to heart failure, inflammation of the lining around the heart and heart rhythm disturbances. This can lead to symptoms such as breathlessness (including breathlessness at night), cough, fluid retention (swelling) in the legs or arms, palpitations (heart fluttering or irregular heart beat) (see section 2 under "Heart checks").

Your doctor will monitor your heart regularly during and after treatment but you should tell your doctor immediately if you notice any of the above symptoms.

- Tumour lysis syndrome (a group of metabolic complications occurring after cancer treatment characterised by high blood levels of potassium and phosphate, and low blood levels of calcium). Symptoms may include kidney problems (weakness, shortness of breath, fatigue and confusion), heart problems (fluttering of the heart of a faster or slower heartbeat), seizures, vomiting or diarrhoea and tingling in the mouth, hands or feet.

If you experience any of the above symptoms when your treatment with KANJINTI has finished, you should see your doctor and tell them that you have previously been treated with KANJINTI.

Very common side effects (may affect more than 1 in 10 people):
- infections
- diarrhoea
- constipation
- heartburn (dyspepsia)
- fatigue
- skin rashes
- chest pain
- abdominal pain
- joint pain
- low counts of red blood cells and white blood cells (which help fight infection) sometimes with fever
- muscle pain
- conjunctivitis
- watery eyes
- nose bleeds
- runny nose
- hair loss
- tremor
- hot flush
- dizziness
- nail disorders
- weight loss
- loss of appetite
- inability to sleep (insomnia)
- altered taste
- low platelet count
- bruising
- numbness or tingling of the fingers and toes
- redness, swelling or sores in your mouth and/or throat
- pain, swelling, redness or tingling of hands and/or feet
- breathlessness
- headache
- cough
- vomiting
- nausea

Common side effects (may affect up to 1 in 10 people):
- allergic reactions
- throat infections
- bladder and skin infections
- shingles
- inflammation of the breast
- inflammation of the liver
- kidney disorders
- increased muscle tone or tension (hypertonia)
- pain in the arms and/or legs
- itchy rash
- sleepiness (somnolence)
- haemorrhoids
- itchiness
- dry mouth and skin
- dry eyes
- sweating
- feeling weak and unwell
- anxiety
- depression
- abnormal thinking
- asthma
- infection of lungs
- lung disorders
- back pain
- neck pain
- bone pain
- acne
- leg cramps

Uncommon side effects (may affect up to 1 in 100 people):
- deafness
- bumpy rash
- blood infection

Rare side effects (may affect up to 1 in 1,000 people):
- muscle weakness
- jaundice
- inflammation or scarring of the lungs

Other side effects that have been reported (frequency cannot be estimated from the available data):
- abnormal or impaired blood clotting
- anaphylactic reactions
- high potassium levels
- swelling of the brain
- swelling or bleeding at the back of the eyes
- shock
- swelling of the lining of the heart
- slow heart rate
- abnormal heart rhythm
- respiratory distress
- respiratory failure
- acute accumulation of fluid in the lungs
- acute narrowing of the airways
- abnormally low oxygen levels in the blood
- difficulty in breathing when lying flat
- liver damage/failure
- swelling of the face, lips and throat
- kidney failure
- abnormally low levels of fluid around baby in womb
- failure of the lungs of the baby to develop in the womb
- abnormal development of the kidneys of the baby in the womb

Some of the side effects you experience may be due to your underlying cancer. If you receive KANJINTI in combination with chemotherapy, some of them may also be due to the chemotherapy.

If you get any side effects, talk to your doctor, pharmacist or nurse.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. 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 KANJINTI

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

Store in a refrigerator (2°C - 8°C). Do not freeze the reconstituted solution. Store in the original package in order to protect from light.

Infusion solutions should be used immediately after dilution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user, and would not normally be longer than 24 hours at 2°C - 8°C. Do not use KANJINTI if you notice any particulate matter or discolouration prior to administration.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What KANJINTI contains

- The active substance is trastuzumab. Each vial contains either:
  - 150 mg trastuzumab that has to be dissolved in 7.2 mL of water for injection, or
  - 420 mg trastuzumab that has to be dissolved in 20 mL of water for injection.
- The resulting solution contains approximately 21 mg/mL trastuzumab.
- The other ingredient(s) are histidine, histidine monohydrochloride, trehalose dihydrate, polysorbate 20.

What KANJINTI looks like and contents of the pack

KANJINTI is a powder for concentrate for solution for intravenous infusion, which is supplied in a glass vial with a rubber stopper containing either 150 mg or 420 mg of trastuzumab. The powder is a white to pale yellow pellet. Each carton contains 1 vial of powder.

Site of Manufacture of the Drug Product
Amgen Technology (Ireland) Unlimited Company
Pottery Road, Dun Laoghaire,
Co. Dublin, Ireland

Marketing Authorisation Holder and Manufacturer
Amgen Europe B.V.
Minervum 7061,
NL-4817 ZK Breda,
The Netherlands

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

THIS MEDICINE

Is a product, which affects your health, and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicine.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.

The following information is intended for medical or healthcare professionals only

Always keep this medicine in the closed original pack at a temperature of 2°C - 8°C in a refrigerator.

Appropriate aseptic technique should be used for reconstitution and dilution procedures. Care must be taken to ensure the sterility of prepared solutions. Since the medicinal product does not contain any anti-microbial preservative or bacteriostatic agents, aseptic technique must be observed.

A vial of KANJINTI aseptically reconstituted with sterile water for injections (not supplied) is chemically and physically stable for 48 hours at 2°C - 8°C after reconstitution and must not be frozen.

After aseptic dilution in polyvinylchloride, polyethylene or polypropylene bags containing sodium chloride 9 mg/mL (0.9%) solution for injection, chemical and physical stability of KANJINTI has been demonstrated for up to 30 days at 2°C - 8°C, and subsequently for 24 hours at temperatures not exceeding 30°C.

From a microbiological point of view, the reconstituted solution and KANJINTI infusion solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user, and would not normally be longer than 24 hours at 2°C - 8°C, unless reconstitution and dilution have taken place under controlled and validated aseptic conditions.

Aseptic preparation, handling and storage:

Aseptic handling must be ensured when preparing the infusion. Preparation should be:
- performed under aseptic conditions by trained personnel in accordance with good practice rules especially with respect to the aseptic preparation of parenteral products.
- prepared in a laminar flow hood or biological safety cabinet using standard precautions for the safe handling of intravenous agents.
- followed by adequate storage of the prepared solution for intravenous infusion to ensure maintenance of the aseptic conditions.

KANJINTI 150 mg powder for concentrate for solution for infusion

Each 150 mg vial of KANJINTI is reconstituted with 7.2 mL of sterile water for injections (not supplied). Use of other reconstitution solvents should be avoided. This yields a 7.4 mL solution for single-dose use, containing approximately 21 mg/mL trastuzumab. A volume overage of 4% ensures that the labelled dose of 150 mg can be withdrawn from each vial.

KANJINTI 420 mg powder for concentrate for solution for infusion

Each 420 mg vial of KANJINTI is reconstituted with 20 mL of sterile water for injections (not supplied). Use of other reconstitution solvents should be avoided. This yields a 21 mL solution for single-dose use, containing approximately 21 mg/mL trastuzumab. A volume overage of 5% ensures that the labelled dose of 420 mg can be withdrawn from each vial.

KANJINTI vial		Volume of sterile water for injections		Final concentration
150 mg vial	+	7.2 mL	=	21 mg/mL
420 mg vial	+	20 mL	=	21 mg/mL

Instructions for aseptic reconstitution

KANJINTI should be carefully handled during reconstitution. Causing excessive foaming during reconstitution or shaking the reconstituted solution may result in problems with the amount of KANJINTI that can be withdrawn from the vial.

1) Using a sterile syringe, slowly inject the appropriate volume (as noted above) of sterile water for injections in the vial containing the lyophilised KANJINTI, directing the stream into the lyophilised cake.

2) Swirl the vial gently to aid reconstitution. DO NOT SHAKE.

Slight foaming of the product upon reconstitution is not unusual. Allow the vial to stand undisturbed for approximately 5 minutes. The reconstituted KANJINTI results in a colourless to pale yellow transparent solution and should be essentially free of visible particulates.

Instructions for aseptic dilution of the reconstituted solution

Determine the volume of the solution required:
- based on a loading dose of 4 mg trastuzumab/kg body weight, or a subsequent weekly dose of 2 mg trastuzumab/kg body weight:

Volume (mL) = **Body weight** (kg) × **dose** (**4** mg/kg for loading or **2** mg/kg for maintenance)
21 (mg/mL, concentration of reconstituted solution)

- based on a loading dose of 8 mg trastuzumab/kg body weight, or a subsequent 3-weekly dose of 6 mg trastuzumab/kg body weight:

Volume (mL) = **Body weight** (kg) × **dose** (**8** mg/kg for loading or **6** mg/kg for maintenance)
21 (mg/mL, concentration of reconstituted solution)

The appropriate amount of solution should be withdrawn from the vial and added to a polyvinylchloride, polyethylene or polypropylene infusion bag containing 250 mL of sodium chloride 9 mg/mL (0.9%) solution for injection. Do not use with glucose-containing solutions. The bag should be gently inverted to mix the solution in order to avoid foaming. Parenteral solutions should be inspected visually for particulates and discolouration prior to administration.