Package Leaflet: Information for the user

Trazimera 150 mg powder for concentrate for solution for infusion
Trazimera 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 Trazimera is and what it is used for

Trazimera 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 Trazimera binds to HER2 it stops the growth of such cells and causes them to die.

Your doctor may prescribe Trazimera 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. Trazimera 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-flououracil and cisplatin.

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

Do not use Trazimera 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 Trazimera 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 Trazimera. 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 Trazimera treatment.

Talk to your doctor, pharmacist or nurse before you are given Trazimera 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 Trazimera.

- you suffer from breathlessness, especially if you are currently using a taxane. Trazimera 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 Trazimera.

- you have ever had any other treatment for cancer.

If you receive Trazimera 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
Trazimera is not recommended for anyone under the age of 18 years.

Other medicines and Trazimera
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 Trazimera to be removed from the body. Therefore you should tell your doctor, pharmacist or nurse that you have had Trazimera 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 Trazimera and for at least 7 months after treatment has ended.

- Your doctor will advise you of the risks and benefits of taking Trazimera 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 Trazimera. 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 Trazimera therapy and for 7 months after the last dose of Trazimera as Trazimera may pass to your baby through your breast milk.

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

Driving and using machines
Trazimera may affect your ability to drive a car or operate machines. If during treatment you experience symptoms, such as dizziness, sleepiness, chills or fever, you should not drive or use machines until these symptoms disappear.

3. How Trazimera 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 Trazimera. Trazimera 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 Trazimera depends on your body weight.

Trazimera intravenous formulation is not for subcutaneous use and should be given as an intravenous infusion only.

Trazimera 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 Trazimera (trastuzumab) and not another trastuzumab-containing product (e.g. trastuzumab emtansine or trastuzumab deruxtecan).

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

If you stop using Trazimera
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 Trazimera 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, Trazimera can cause side effects, although not everybody gets them. Some of these side effects may be serious and may lead to hospitalisation.

During a Trazimera 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, 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 healthcare 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 Trazimera, 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, and 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 or 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 Trazimera has finished, you should see your doctor and tell them that you have previously been treated with Trazimera.

Very common: 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, which occasionally may extend to the rest of the limb
- 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: may affect up to 1 in 10 people

- allergic reactions
- throat infections
- bladder and skin infections
- 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
- asthma
- infection of lungs
- lung disorders
- back pain
- neck pain
- bone pain
- acne
- leg cramps

Uncommon: may affect up to 1 in 100 people

- deafness
- bumpy rash
- wheezing
- inflammation or scarring of the lungs

Rare: may affect up to 1 in 1,000 people

- jaundice
- anaphylactic reactions

Not known: frequency cannot be estimated from the available data

- abnormal or impaired blood clotting
- high potassium levels
- swelling or bleeding at the back of the eyes
- shock
- 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
- 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 Trazimera 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. 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 Trazimera

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).

Store in the original package in order to protect from light.

Unopened vials of Trazimera may be stored up to 30°C for a single period of up to 3 months. Upon removal from refrigerated storage, Trazimera must not be returned to refrigerated storage. Discard at the end of this 3-month period or by the expiry date on the vial, whichever occurs first. Record the "discard by" date in the date field provided on the carton.

Infusion solutions should be used immediately after dilution. Do not use Trazimera if you notice any particulate matter or discoloration 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 Trazimera contains
- The active substance is trastuzumab. One vial contains either:
  - 150 mg trastuzumab that has to be dissolved in 7.2 mL of sterile water for injections, or
  - 420 mg trastuzumab that has to be dissolved in 20 mL of sterile water for injections.

  The resulting solution contains approximately 21 mg/mL trastuzumab.

- The other ingredient(s) are L-histidine hydrochloride monohydrate, L-histidine, sucrose, polysorbate 20 (E 432).

What Trazimera looks like and contents of the pack

Trazimera is a powder for concentrate for solution for 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 cake. Each carton contains 1 vial of powder.

Marketing Authorisation Holder

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Belgium

The following information is intended for medical or healthcare professionals only

Trazimera IV is provided in sterile, preservative-free, non-pyrogenic, single use vials.

In order to prevent medication errors it is important to check the vial labels to ensure that the medicine being prepared and given is Trazimera (trastuzumab) and not another trastuzumab-containing product (e.g. trastuzumab emtansine or trastuzumab deruxtecan).

Always keep this medicine in the closed original pack at a temperature of 2ºC – 8ºC in a refrigerator.

Unopened vials of Trazimera may be stored up to 30°C for a single period of up to 3 months. Upon removal from refrigerated storage, Trazimera must not be returned to refrigerated storage. Discard at the end of this 3-month period or by the expiry date on the vial, whichever occurs first. Record the "discard by" date in the date field provided on the carton.

After aseptic dilution in sodium chloride 9 mg/mL (0.9 %) solution for injection, solutions of Trazimera for intravenous infusion are physically and chemically stable for up to 30 days at 2°C – 8°C, and 24 hours at temperatures not exceeding 30°C.

From a microbiological point of view, the reconstituted solution and Trazimera 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.

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.

<u>Aseptic preparation, handling and storage:</u>

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.
- followed by adequate storage of the prepared solution for intravenous infusion to ensure maintenance of the aseptic conditions.

If preparation is intended to be stored for more than 24 hours prior to use, then the reconstitution and dilution procedure should be performed in a laminar flow hood or biological safety cabinet using standard precautions for the safe handling of intravenous agents.

A vial of Trazimera aseptically reconstituted with water for injections (not supplied) is chemically and physically stable for 48 hours at 2ºC – 8ºC after reconstitution and must not be frozen.

<u>Trazimera 150 mg powder for concentrate for solution for infusion</u>

Appropriate aseptic technique should be used. Each 150 mg vial of Trazimera 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. An overfill of 4% ensures that the labelled dose of 150 mg can be withdrawn from each vial.

<u>Trazimera 420 mg powder for concentrate for solution for infusion</u>

Appropriate aseptic technique should be used. Each 420 mg vial of Trazimera is reconstituted with 20 mL of sterile water for injections (not supplied). Use of other reconstitution solvents should be avoided. This yields a 20.6 mL solution for single-dose use, containing approximately 21 mg/mL

trastuzumab. An overfill of 5% ensures that the labelled dose of 420 mg can be withdrawn from each vial.

Trazimera 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

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

Instructions for Aseptic Reconstitution:

1) Using a sterile syringe, slowly inject the appropriate volume (as noted above) of sterile water for injections in the vial containing the lyophilised Trazimera.
2) Swirl 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 Trazimera results in a colourless to pale brownish-yellow transparent solution and should be essentially free of visible particulates.

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:

$$\textbf{Volume}\ (\text{mL}) = \frac{\textbf{Body weight}\ (\text{kg}) \times \textbf{dose}\ (\textbf{4}\ \text{mg/kg for loading or}\ \textbf{2}\ \text{mg/kg for maintenance})}{\textbf{21}\ (\text{mg/mL, concentration of reconstituted solution})}$$

- 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:

$$\textbf{Volume}\ (\text{mL}) = \frac{\textbf{Body weight}\ (\text{kg}) \times \textbf{dose}\ (\textbf{8}\ \text{mg/kg for loading or}\ \textbf{6}\ \text{mg/kg for maintenance})}{\textbf{21}\ (\text{mg/mL, concentration of reconstituted solution})}$$

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