Package leaflet: Information for the patient

ZYNYZ 500 mg concentrate for solution for infusion
retifanlimab

▼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 are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Your doctor will provide you with a patient card. Be sure to keep this card with you while undergoing treatment with ZYNYZ.
- If you have any further questions, ask your doctor or nurse.
- 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 ZYNYZ is and what it is used for

ZYNYZ contains the active substance retifanlimab, a monoclonal antibody (a protein that recognises and attaches to a specific target substance in the body). ZYNYZ helps your immune system fight your cancer.

ZYNYZ is used in adults to treat **Merkel cell carcinoma**, a rare type of **skin cancer**. It is given when the cancer has spread or returned and cannot be treated with surgery or radiation.

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

You must not be given ZYNYZ if you
- are allergic to retifanlimab or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions
Talk to your doctor or nurse before you are given ZYNYZ if you have:
- an autoimmune disease (a condition where the body's immune system attacks its own cells)
- had a solid organ transplant or a bone marrow (stem cell) transplant that used donor stem cells
- lung or breathing problems
- liver or kidney problems
- diabetes

ZYNYZ acts on your immune system. It may cause inflammation in parts of your body. Your risk of these side effects may be higher if you already have an autoimmune disease (a condition where the body attacks its own cells). You may also experience frequent flares of your autoimmune disease, which in the majority of cases are mild.

Tell your doctor immediately if you have any of the following symptoms during treatment or if they get worse:

- **lung inflammation** (pneumonitis) such as breathing difficulties, chest pain or new or worsening cough.
- **bowel inflammation** (colitis) such as frequent diarrhoea often with blood and/or mucus, more bowel movements than usual, stools that are bloody, black or tarry and severe abdominal pain or tenderness.
- **liver inflammation**. Symptoms include persistent nausea or vomiting, loss of appetite, pain on the right side of your stomach, eye and/or skin yellowing, drowsiness, dark-coloured urine, bleeding or bruising more easily than normal.
- **hormone gland problems** (including the pituitary, thyroid and adrenal glands) that may affect how these glands work. Symptoms include fast heartbeat, dizziness, fainting, extreme tiredness, persistent or unusual headaches, weight change, hair loss, feeling cold or constipation.
- **type 1 diabetes or diabetic ketoacidosis**. Symptoms of diabetes include feeling more hungry or thirsty than usual, frequent urination, weight loss, feeling tired or sick. Symptoms of diabetic ketoacidosis include difficulty thinking clearly, sleepiness, stomach pain, fast and deep breathing, breath that smells sweet or fruity, sweet or metallic taste in the mouth or a different odour to urine or sweat.
- **kidney inflammation**. Symptoms include decreased volume of urine, foamy urine, passing blood or traces of blood in the urine that may change its colour, swollen ankles or loss of appetite.
- **skin problems** that can lead to a severe skin reaction known as toxic epidermal necrolysis and Stevens-Johnson syndrome. Symptoms include rash, itching, skin blistering or ulcers in the mouth or in the lining of the nose, throat or genital area.
- **inflammation in other parts of the body** such as eyes (changes in eyesight), joints, muscles, nerves, pancreas (symptoms include abdominal pain, nausea or vomiting), or of the heart muscle.
- **infusion-related reactions** such as chills, shaking, rigor, fever, itching, rash, flushing or swollen face, shortness of breath or wheezing, feeling dizzy or faint.

If you have any of the above-mentioned symptoms during treatment, do not try to treat your symptoms with other medicines on your own. Your doctor may:

- give you other medicines to prevent complications and reduce your symptoms,
- monitor you,
- withhold the next dose of ZYNYZ,
- stop your treatment or
- slow or stop your infusion depending on the severity of the reaction, if you have an infusion-related reaction when you receive ZYNYZ.

Please note that the above listed symptoms are **sometimes delayed** and may occur weeks or months after your last dose.

Complications of solid organ transplant rejection, including graft-versus-host disease, in patients who have received a bone marrow (stem cell) transplant that uses donor stem cells can lead to death. They may occur if you undergo transplantation either before or after treatment with ZYNYZ. Your doctor will monitor you for these complications.

Children and adolescents
ZYNYZ should not be given to children and adolescents under 18 years of age because it has not been studied in this patient group.

Other medicines and ZYNYZ
Tell your doctor or nurse if you are using, have recently used or might use any other medicines. This applies in particular to medicines that suppress your immune system, such as corticosteroids, which may disrupt the effect of ZYNYZ. Once you are treated with ZYNYZ, your doctor may prescribe corticosteroids to reduce side effects that you may have during treatment. This will not impact the effect of the medicine.

Contraception
Women who could become pregnant must use effective contraception during treatment and for minimum 4 months after the last ZYNYZ dose.

Pregnancy
You must not be given ZYNYZ if you are pregnant unless your doctor specifically recommends it. ZYNYZ can cause harmful effects or death to your unborn baby. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine.

Breast-feeding
It is not known if ZYNYZ passes into breast milk. A risk to the breast-feeding newborns/infants cannot be excluded. Ask your doctor for advice if you are breast-feeding.

Driving and using machines
ZYNYZ may have a minor influence on the ability to drive and use machines. If you feel tired, do not drive or use machines until you feel better.

ZYNYZ contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose unit, that is to say essentially 'sodium-free.' However, before ZYNYZ is given to you, it is mixed with a solution that may contain sodium. Talk to your doctor if you are on a low-salt diet.

ZYNYZ contains polysorbate 80
This medicine contains 2 mg of polysorbate 80 (E433) in each 20 mL of concentrate which is equivalent to 0.1 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How ZYNYZ is given

ZYNYZ will be given to you in a hospital or clinic, supervised by a doctor experienced in cancer treatment.

The recommended dose of ZYNYZ is 500 mg every 4 weeks.

Your doctor will give you ZYNYZ as a drip into a vein (intravenous infusion) which will last about 30 minutes.

Your doctor will decide how many treatments you need.

If you miss an appointment to receive ZYNYZ
It is very important that you do not miss a dose of this medicine. Contact your doctor or hospital immediately to reschedule your appointment.

If you stop receiving ZYNYZ
Stopping your treatment may stop the effect of the medicine. Do not stop treatment with ZYNYZ without the agreement of your doctor.

Patient card
Important information from this package leaflet can be found in the patient card you have been given by your doctor. It is important that you keep this patient card and show it to your partner or caregivers.

If you have any further questions about your treatment, ask your doctor or nurse.

4. Possible side effects

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

ZYNYZ can have serious side effects, which can sometimes become life-threatening and can lead to death. These side effects may happen at any time during treatment, or even after your treatment has ended. You may get more than one side effect at the same time (See section 2, "Warnings and precautions" for symptoms).

Tell your doctor immediately if you have any of the following **serious side effects**:

Common (may affect up to 1 in 10 people):
- lung inflammation *(pneumonitis)*
- bowel inflammation *(colitis)*
- liver inflammation *(hepatitis)*
- liver cell injury *(hepatocellular injury)*
- sudden kidney damage *(acute kidney failure)*
- kidney failure *(renal failure)*
- infusion-related reactions that can cause symptoms such as chills, shaking or fever, itching or rash, flushing or swollen face, being short of breath or wheezing, feeling dizzy or nausea.

Uncommon (may affect up to 1 in 100 people)
- inflammation of the pituitary gland in the base of the brain *(hypophysitis)*
- acid in the blood produced from diabetes *(diabetic ketoacidosis)*
- damage to nerves causing numbness and weakness *(polyneuropathy)*
- pinched nerve caused by damage to the root of the nerve(s) in the spine *(radiculopathy)*
- nerve damage to voice box which is used for breathing, swallowing and talking *(vocal cord paralysis)*
- inflammation of the eyes *(uveitis)*
- inflammation of the cornea or the clear tissue on the front of the eye *(keratitis)*
- inflammation of the covering of the heart which often causes sharp chest pain *(pericarditis)*
- inflammation of the heart muscle *(myocarditis)*
- inflammation of the pancreas *(pancreatitis)*

Other side effects may occur with the following frequencies:

Very common (may affect more than 1 in 10 people):
- decrease in the number of red blood cells *(anaemia)*
- decreased appetite
- diarrhoea
- nausea
- constipation
- rash
- itching of the skin *(pruritus)*
- joint pain *(arthralgia)*
- tiredness *(fatigue)*
- fever *(pyrexia)*

Common (may affect up to 1 in 10 people):
- underactive thyroid gland *(hypothyroidism)*
- overactive thyroid gland *(hyperthyroidism)*
- abnormal sensation such as tingling or numbness of the hands or feet *(paraesthesia)*

- increased blood level of liver enzymes, including alanine aminotransferase, aspartate aminotransferase
- increased blood levels of bilirubin
- increased blood levels of creatinine
- increased blood levels of thyroid stimulating hormone
- increased level of amylase, an enzyme that breaks down starch
- increased levels of lipase, an enzyme that breaks down fats

Uncommon (may affect up to 1 in 100 people):
- decreased secretion of hormones produced by the adrenal glands *(adrenal insufficiency)*
- thyroid gland inflammation *(thyroiditis)*
- inflammation of the bile ducts *(cholangitis)*
- increased blood levels of bilirubin causing yellowing of the eyes and skin *(hyperbilirubinaemia)*
- joint inflammation *(arthritis)*
- muscle inflammation *(myositis)*
- inflammation of the tissue between the muscle and skin which may cause skin swelling *(eosinophilic fasciitis)*
- inflammation of the muscles causing pain or stiffness *(polymyalgia rheumatica)*
- decreased blood levels of thyroid stimulating hormone

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 below:

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store ZYNYZ

ZYNYZ will be given to you in a hospital or clinic and the healthcare professionals will be responsible for its storage.

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

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

Once prepared, the infusion may be stored for up to 24 hours at 2 °C to 8 °C or 8 hours at 20 °C to 25 °C, from time of preparation until the end of infusion.

Do not store any unused medicine for reuse. Any unused medicine or waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What ZYNYZ contains

- The active substance is retifanlimab.
  One mL of concentrate for solution for infusion contains 25 mg of retifanlimab.
  One vial of 20 mL of concentrate contains 500 mg of retifanlimab.
- The other ingredients are sodium acetate trihydrate (E262), acetic acid (glacial) (E260), sucrose, polysorbate 80 (E433), water for injections. See section 2 “ZYNYZ contains sodium" and “ZYNYZ contains polysorbate 80”.

What ZYNYZ looks like and contents of the pack
ZYNYZ is a clear to slightly opalescent, colourless to pale yellow concentrate for solution for infusion (sterile concentrate).

It is available in a pack containing 1 glass vial of 20 mL of concentrate.

Marketing Authorisation Holder
Incyte Biosciences UK Ltd
First Floor Q1, The Square
Randalls Way, Leatherhead
KT22 7TW, UK

Manufacturer
Incyte Biosciences Distribution B.V.
Paasheuvelweg 25
1105 BP Amsterdam
Netherlands

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Other sources of information

Detailed information on this medicine is available on the Medicines and Healthcare products Regulatory Agency web site: www.gov.uk/mhra

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The following information is intended for healthcare professionals only:

Preparation and administration

- Parenteral medicinal products should be inspected visually for particulate matter and discoloration prior to administration. Retifanlimab is a clear to slightly opalescent, colourless to pale yellow solution, free of visible particles. Discard the vial if the solution is cloudy, discoloured or visible particles are observed.
- Do not shake the vial.
- Withdraw 20 mL (500 mg) of retifanlimab concentrate from the vial and transfer into an intravenous infusion bag containing sodium chloride 9 mg/mL (0.9%) solution for injection or glucose 50 mg/mL (5%) solution for injection to prepare a diluted solution with a final concentration between 1.4 mg/mL to 10 mg/mL. Use polyvinylchloride (PVC) and di-2-ethylhexyl phthalate (DEHP), polyolefin copolymer, polyolefin with polyamide, or ethylene vinyl acetate infusion bags.
- Mix the diluted solution by gentle inversion. Do not shake the infusion bag.
- From a microbiological point of view, the diluted solution, once prepared, should be used immediately. If not used immediately, chemical and physical in-use stability has been demonstrated:
  - For 8 hours at room temperature (20 °C to 25 °C) (including infusion time).

OR

- For 24 hours under refrigeration at (2 °C to 8 °C). If refrigerated, allow the diluted solution to come to room temperature prior to administration. The diluted solution must be administered within 4 hours (including infusion time) once it is removed from the refrigerator. Do not freeze.

- Discard if the diluted solution is discoloured or contains extraneous particulate matter other than trace amounts of translucent to white particles.
- Administer the retifanlimab solution by intravenous infusion over 30 minutes using a sterile, non-pyrogenic, low-protein binding polyethersulfone, polyvinylidene fluoride, or cellulose acetate 0.2 micron to 5 micron in-line or add-on filter or 15 micron mesh in-line or add-on filter.
- Do not coadminister other medicinal products through the same infusion line.

Disposal

- Retifanlimab is for single use only; discard any unused portion left in the vial.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.