Package leaflet: Information for the patient

Spexotras® 0.05 mg/ml powder for oral solution
trametinib

Read all of this leaflet carefully before your child starts taking this medicine because it contains important information.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask the doctor, pharmacist or nurse.
- This medicine has been prescribed for your child only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as your child's.
- If your child gets any side effects, talk to the doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.
- The information in this leaflet is for you or your child – but in the leaflet it will just say "your child".

What is in this leaflet

1. What Spexotras is and what it is used for

Spexotras is a medicine that contains the active substance trametinib.

It is used in combination with another medicine (dabrafenib dispersible tablets) in children aged 1 year and older to treat a type of brain tumour called glioma.

Spexotras can be used in patients with:
- low-grade glioma
- high-grade glioma when the patient has received at least one radiation and/or chemotherapy treatment.

Spexotras in combination with dabrafenib dispersible tablets is used to treat patients whose brain tumour has a specific mutation (change) in the so-called BRAF gene. This mutation causes the body to make faulty proteins which in turn may cause the tumour to develop. The doctor will test for this mutation before starting treatment.

In combination with dabrafenib, Spexotras targets these faulty proteins and slows down or stops the development of the tumour. **Also read the leaflet for dabrafenib dispersible tablets.**

2. What you need to know before you give Spexotras

Do not give Spexotras
- **if your child is allergic** to trametinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to the doctor before giving Spexotras. The doctor needs to know if your child:
- has **heart problems** such as heart failure or problems with the way their heart beats.

- has or has had any **lung or breathing problems**, including difficulty in breathing often accompanied by a dry cough, shortness of breath and fatigue.
- has **eye problems** including blockage of the vein draining the eye (retinal vein occlusion) or swelling in the eye which may be caused by fluid leakage (chorioretinopathy).
- has or has had any **liver problems**.
- has or has had any **kidney problems**.
- has or has had any **gastrointestinal problems** such as diverticulitis (inflamed pouches in the colon) or metastases to the gastrointestinal tract.

Before your child starts taking Spexotras, during and after their treatment, the doctor will make checks to avoid complications.

Skin examination
The treatment may cause skin cancer. Usually, these skin changes remain local and can be removed with surgery and the treatment can be continued without interruption The doctor may check your child's skin before and regularly during treatment.

Check your child's skin monthly during the treatment and for 6 months after they stop taking this medicine. **Tell the doctor** as soon as possible if you notice any changes to your child's skin such as a new wart, skin sore or reddish bump that bleeds or does not heal, or a change in the size or colour of a mole.

Tumour lysis syndrome
If your child experiences the following symptoms, **tell the doctor** immediately as this can be a life-threatening condition: nausea, shortness of breath, irregular heartbeat, muscular cramps, seizures, clouding of urine, decrease in urine output and tiredness. These may be caused by a group of metabolic complications that can occur during treatment of cancer that are caused by the breakdown products of dying cancer cells (tumour lysis syndrome or TLS) and can lead to changes in kidney function (see also section 4).

Children younger than 1 year old
Spexotras in combination with dabrafenib dispersible tablets has not been tested in children younger than 1 year old. Therefore, Spexotras is not recommended in this age group.

Patients older than 18 years of age
Information on treating patients older than 18 years of age with glioma is limited, therefore continued treatment into adulthood should be assessed by the doctor.

Other medicines and Spexotras
Before starting treatment, tell the doctor, pharmacist or nurse if your child is taking, has recently taken or might take any other medicines, including medicines used to thin the blood or any other medicines obtained without a prescription.

Pregnancy, breast-feeding and fertility

Pregnancy
- If your child is pregnant, or if you think your child may be pregnant, ask the doctor or nurse for advice before taking this medicine. Spexotras can harm the unborn baby.
- If your child becomes pregnant while taking this medicine, tell the doctor immediately.

Breast-feeding
It is not known whether Spexotras can pass into breast milk. If your child is breast-feeding, or planning to breast-feed, you must tell the doctor. You, your child and the doctor will decide if they will take Spexotras or breast-feed.

Fertility
Spexotras may impair fertility in both males and females.

Taking Spexotras with dabrafenib dispersible tablets: Dabrafenib may reduce sperm count and this may not return to normal levels after stopping treatment with dabrafenib.

Prior to starting treatment with dabrafenib dispersible tablets, talk to the doctor about options to improve your child's chances to have children in the future.

Contraception

- If your child could become pregnant, they must use a reliable method of birth control (contraception) while they are taking Spexotras and for at least 16 weeks after they stop taking it.
- Birth control containing hormones (such as pills, injections or patches) may not work as well while taking Spexotras in combination with dabrafenib dispersible tablets. An alternative effective method of birth control should be used to avoid the risk of pregnancy while taking this combination of medicines. Ask the doctor or nurse for advice.

Driving and using machines
Spexotras can have side effects that may affect your child's ability to drive, ride a bike/scooter, use machines, or take part in other activities that need alertness. If your child has problems with vision or feels tired or weak, or their energy levels are low, they should avoid such activities.

Descriptions of these effects can be found in section 4. Read all the information in this leaflet for guidance.

Discuss with the doctor, pharmacist or nurse if you are unsure about anything. Your child's disease, symptoms and treatment situation may also affect their ability to take part in such activities.

Spexotras contains a cyclodextrin
This medicine contains 100 mg of a cyclodextrin in each ml of Spexotras oral solution.

Spexotras contains methyl parahydroxybenzoate
May cause allergic reactions (possibly delayed).

Spexotras contains sodium
This medicine contains 1.98 mg sodium (main component of cooking/table salt) in each ml of Spexotras oral solution. This is equivalent to 4% of the recommended maximum daily dietary intake of sodium for an adult at the highest recommended trametinib dose.

Spexotras contains potassium
This medicine contains potassium, less than 1 mmol (39 mg) per maximum daily dose, i.e. essentially 'potassium-free'.

3. How to give Spexotras

Always give this medicine to your child exactly as the doctor, pharmacist or nurse has told you. Check with the doctor, pharmacist or nurse if you are not sure.

How much to give
The doctor will decide on the correct dose of Spexotras based on your child's body weight.

The doctor may decide that your child should be given a lower dose if they get side effects.

How to give it
Please read the Instructions for Use at the end of this leaflet for details on how to give the oral solution. The oral solution will be prepared for you by your pharmacist.

- Give **Spexotras once** a **day**. Giving Spexotras at the same time each day will help you to remember when to give the medicine. Give Spexotras with **either** the morning dose **or** the evening dose of dabrafenib dispersible tablets. The dabrafenib doses should be given about 12 hours apart.
- Give Spexotras on an empty stomach, at least one hour before or two hours after a meal, this means that:
  - after taking Spexotras, your child must wait **at least 1 hour** before eating.
  - after eating, your child must wait **at least 2 hours** before taking Spexotras.
  - if necessary, breast-feeding and/or baby formula may be given on demand.

If you give more Spexotras than you should
If you give too much Spexotras, **contact the doctor, pharmacist or nurse for advice**. If possible, show them the Spexotras pack and this leaflet.

If you forget to give Spexotras
If the missed dose is less than 12 hours late, give it as soon as you remember.
If the missed dose is 12 hours or more than 12 hours late, skip that dose. Give the next dose at the usual time and carry on giving Spexotras at regular times as usual.
Do not give a double dose to make up for a forgotten dose.

If your child vomits after taking Spexotras
If your child vomits after taking Spexotras, do not give another dose until the next scheduled dose.

If you stop giving Spexotras
Give Spexotras for as long as the doctor recommends. Do not stop unless the doctor advises you to.

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

4. Possible side effects

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

Stop giving this medicine and seek urgent medical attention if your child has any of the following symptoms:
- coughing up of blood, passing blood in urine, vomit containing blood or that looks like “coffee grounds”, red or black stools that look like tar. These may be signs of bleeding.
- fever (temperature 38°C or above).
- chest pain or shortness of breath, sometimes with fever or cough. These may be signs of pneumonitis or inflamed lungs (interstitial lung disease).
- blurred vision, loss of vision or other vision changes. These may be signs of retinal detachment.
- eye redness, eye pain, increased sensitivity to light. These may be signs of uveitis.
- unexplained muscle pain, muscle cramps or muscle weakness, dark urine. These may be signs of rhabdomyolysis.
- strong abdominal pain. This may be a sign of pancreatitis.
- fever, swollen lymph glands, bruising or skin rash at the same time. These may be signs of a condition where the immune system makes too many infection-fighting cells that may cause various symptoms (haemophagocytic lymphohistiocytosis).
- nausea, shortness of breath, irregular heartbeat, muscular cramps, seizures, clouding of urine, decrease in urine output and tiredness. These may be signs of a condition resulting from a rapid breakdown of cancer cells which in some people may be fatal (tumour lysis syndrome or TLS).

- reddish patches on the trunk that are circular or target-shaped, with or without central blisters, skin peeling, ulcers of the mouth, throat, nose, genitals and eyes. These may be signs of serious skin rashes, which can be life-threatening, and can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome), widespread rash, fever and enlarged lymph nodes (DRESS).

Other possible side effects

Very common *(may affect more than 1 in 10 people)*
- Headache
- Dizziness
- Cough
- Diarrhoea, feeling sick (nausea), being sick (vomiting), constipation, stomach ache
- Skin problems such as rash, acne-like rash, dry or itching skin, redness of skin
- Wart-like growths (skin papilloma)
- Nail bed infection
- Pain in arms or legs or joints
- Lack of energy or feeling weak or tired
- Increase in weight
- Upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis)
- Increase of liver enzymes seen in blood tests
- Decreased level of white blood cells (neutropenia, leukopenia)
- Decreased level of red blood cells (anaemia)

Common *(may affect up to 1 in 10 people)*
- Frequent urination with pain or burning sensation (urinary tract infection)
- Skin effects including infection of the skin (cellulitis), inflammation of hair follicles in the skin, inflamed flaky skin (dermatitis exfoliative generalised), thickening of the outer layer of the skin (hyperkeratosis)
- Decreased appetite
- Low blood pressure (hypotension)
- High blood pressure (hypertension)
- Shortness of breath
- Sore mouth or mouth ulcers, inflammation of mucosa
- Inflammation of the fatty layer under the skin (panniculitis)
- Unusual loss of hair or thinning
- Red, painful hands and feet (hand-foot syndrome)
- Muscle spasms
- Chills
- Allergic reaction (hypersensitivity)
- Dehydration
- Eyesight problems including blurred vision
- Decreased heart rate (bradycardia)
- Tiredness, chest discomfort, light headedness, palpitations (ejection fraction decreased)
- Tissue swelling (oedema)
- Muscle pain (myalgia)
- Tiredness, chills, sore throat, joint or muscles aching (influenza-like illness)
- Abnormal test results related to creatine phosphokinase, an enzyme found mainly in heart, brain and skeletal muscle
- Increase in blood sugar level
- Low levels of sodium or phosphate in the blood
- Decreased level of blood platelets (cells that help blood to clot)
- Increased sensitivity of the skin to sun

Uncommon *(may affect up to 1 in 100 people)*
- Irregular heartbeat (atrioventricular block)
- Inflammation of the intestines (colitis)
- Cracking of skin
- Night sweats
- Excessive sweating
- Raised, painful, red to dark reddish-purple skin patches or sores that appear mainly on the arms, legs, face and neck, with a fever (signs of acute febrile neutrophilic dermatosis)

In addition to the side effects described above, the following side effects have so far only been reported in adult patients, but may also occur in children:
- problem with the nerves that can produce pain, loss of sensation or tingling in hands and feet and/or muscle weakness (peripheral neuropathy)
- dry mouth
- kidney failure
- benign skin tumour (acrochordon)
- inflammatory disease mainly affecting the skin, lung, eyes and lymph nodes (sarcoidosis)
- inflammation of the kidneys
- a hole (perforation) in the stomach or intestines
- inflammation of the heart muscle which can result in breathlessness, fever, palpitations and chest pain

Reporting of side effects
If your child gets any side effects, talk to the doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: 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 Spexotras

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

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

Before reconstitution: Store in a refrigerator (2°C – 8°C).

After reconstitution: Store below 25ºC. Do not freeze. Discard any unused solution 35 days after reconstitution.

Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Spexotras contains
- The active substance is trametinib. One bottle contains trametinib dimethyl sulfoxide equivalent to 4.7 mg of trametinib. Each ml of the reconstituted solution contains 0.05 mg of trametinib.
- The other ingredients are: sulfobutylbetadex sodium (see section 2), sucralose (E 955), citric acid monohydrate (E 330), disodium phosphate (E 339) (see section 2), potassium sorbate

(E 202) (see section 2), methyl parahydroxybenzoate (E 218) (see section 2), and strawberry flavour.

What Spexotras looks like and contents of the pack
Spexotras 0.05 mg/ml powder for oral solution is a white or almost white powder.

Spexotras is supplied in an amber glass bottle of 180 ml with a child-resistant screw cap closure, containing 12 g of powder. Each carton contains one bottle, one press-in bottle adapter and one 20 ml re-usable oral dosing syringe with 0.5 ml graduation marks.

Marketing Authorisation Holder
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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The following information is intended for pharmacists only:

Reconstitution instructions (for the pharmacist only):

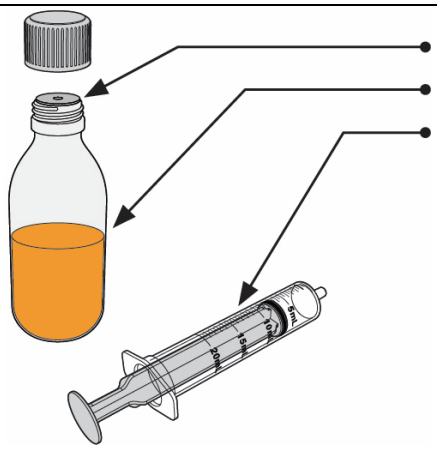
1. Wash and dry your hands.
2. Check the powder expiry date on the bottle.
3. Tap the bottle to loosen the powder.
4. Remove the cap and add 90 ml distilled or purified water to the powder in the bottle.
5. Attach the cap and invert the bottle repeatedly for up to 5 minutes, until fully dissolved. You may also gently shake.
6. Separate the bottle adapter from the oral syringe. Remove the bottle cap and insert the bottle adapter into the bottle neck. Push hard until the bottle adapter is fully inserted. The bottle adapter should be fully flush with the bottle neck.
7. Write the date of preparation on the carton. The solution expires 35 days after preparation.
8. Inform the recipient of the dose and the date the solution was prepared on.

INSTRUCTIONS FOR USE

Ask your healthcare professional or pharmacist to show you how to use Spexotras correctly. Always use Spexotras exactly as your healthcare professional or pharmacist tells you to.

If you have any questions about how to use Spexotras, contact your healthcare professional or pharmacist.

SECTION A ADMINISTRATION VIA ORAL SYRINGE

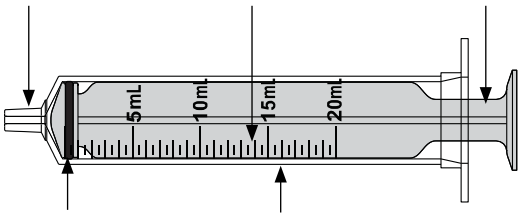


To administer Spexotras, you will need:
Bottle adapter (already inserted into the bottle neck)
Solution in bottle
Oral syringe

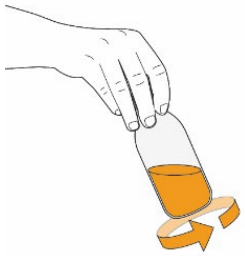
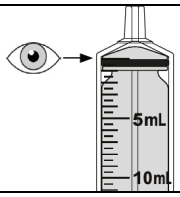
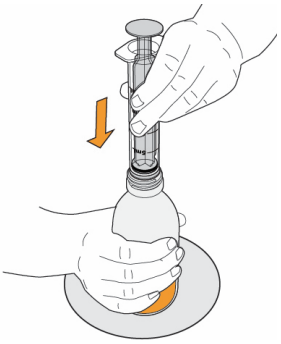
In case of spillage or contact of the Spexotras solution with the skin or eyes, follow the information in the "SPILLAGE CLEANING" section.

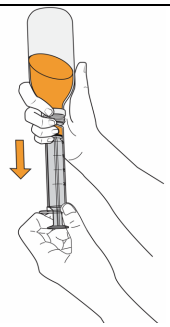
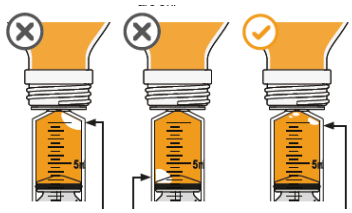
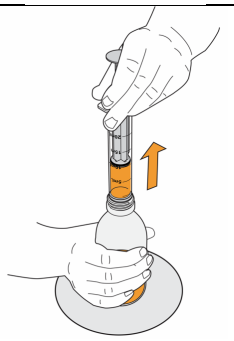
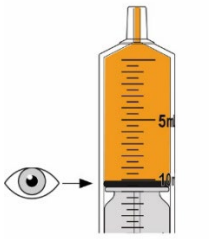
Wash and dry your hands before administering Spexotras.

Resuable oral syringe parts:



1 Check the solution preparation date on the carton. **Do not** administer Spexotras if more than 35 days have passed after solution preparation. **Note:** The printed expiry date on the right side of the bottle label does **NOT** apply to the solution. This printed expiry date applies only to the powder before it is reconstituted into a solution by your pharmacist.	

2 Gently swirl the bottle for 30 seconds to mix the solution. If foam appears, allow the bottle to stand until the foam disappears.	
3 Remove the child-resistant cap by pushing down on the cap and turning it anti-clockwise.	
4 Check if there is a bottle adapter already inserted in the bottle neck. If not inserted, contact your pharmacist.	
5 Push the plunger down into the oral syringe as far as it will go to remove all the air inside.	
6 Place the bottle on a flat surface and hold it upright. Insert the tip of the oral syringe into the opening of the bottle adapter. Make sure the oral syringe is securely attached. **IMPORTANT:** Due to air pressure, the plunger may move by itself when you measure your dose during Step 7. Hold the plunger to prevent it moving.	

7 Carefully turn the bottle upside down and pull the plunger to measure out your dose. With the tip facing up, the **top** of the black stopper must line up with your prescribed dose. If large air bubbles appear in the syringe, as shown in the pictures, push the medicine back into the bottle and withdraw your dose again. Keep doing this until there are no large air bubbles present. Small air bubbles are acceptable.	  Large air bubble Small air bubbles
8 Continue to hold the plunger in place, turn the bottle back around and place it onto a flat surface. Remove the oral syringe from the bottle by gently pulling straight up.	
9 Double check the **top** of the black stopper is at your prescribed dose. If not, repeat Steps 6 to 8. If you are administering via oral syringe, continue to Step 10. If you are administering via a feeding tube, go to “SECTION B”.	
10 Place the end of the oral syringe inside the mouth with the tip touching the inside of either cheek. Slowly push the plunger all the way down to give the full dose. **WARNING:** Administering Spexotras to the throat or pushing the plunger too fast may cause choking.	

11 Check there is no Spexotras left in the oral syringe. If there is any solution left in the oral syringe, administer it. **Note:** If your dose is larger than the oral syringe's capacity, repeat administration until the total volume is delivered.	
12 Place the cap back on the bottle and turn it clockwise to close it. Make sure the cap is securely attached onto the bottle. **Do not** remove the bottle adapter.	
13 Clean the oral syringe in accordance with the instructions in "SECTION C", then store the solution and oral syringe in accordance with the instructions in the "STORAGE" section.	

SECTION B ADMINISTRATION VIA A FEEDING TUBE
Please follow this section **only** if you are going to administer Spexotras via a feeding tube. To administer via a feeding tube, read the following information then move to Step 1. • The solution is suitable for administration via a feeding tube. • Use a Nasogastric (NG) or Gastric (G) feeding tube with a **minimum** size of 4 French gauge. • Always use the 20 ml oral syringe provided in this pack to administer Spexotras. • You may need an ENFIT adapter (not included in pack) to connect the 20 ml oral syringe to the feeding tube.
1 Flush the feeding tube according to the manufacturer's instructions immediately before administering Spexotras.
2 Follow Steps 1 to 9 in "SECTION A", then move to Step 3 in this section.
3 Connect the 20 ml oral syringe containing Spexotras to the feeding tube. You may need an ENFIT adapter to connect the oral syringe to the feeding tube.

4 Apply steady pressure to dispense the solution into the feeding tube.
5 Check there is no Spexotras left in the oral syringe. If there is any solution left in the oral syringe, administer it.
6 Flush the feeding tube again according to the manufacturer's instructions.
7 Go to "SECTION C" for cleaning.

SECTION C CLEANING

To prevent Spexotras coming into contact with other kitchen items, always clean the oral syringe separately from other kitchen items.

To clean the oral syringe:

1. Fill a glass with warm, soapy water.
2. Place the oral syringe into the glass with the warm, soapy water.
3. Pull water into the oral syringe and empty again 4 to 5 times.
4. Separate the plunger from the barrel.
5. Rinse the glass, plunger and barrel under warm tap water.
6. Leave the plunger and barrel on a dry surface to air dry before next use.

SPILLAGE CLEANING

If Spexotras gets on your skin, wash the area well with soap and water. If Spexotras gets in your eyes, rinse your eyes with water.

Follow these steps if you spill any Spexotras solution:

1. Put on plastic gloves.
2. Soak up the solution completely using an absorbent material, such as paper towels.
3. Place the absorbent material into a sealable plastic bag.
4. Wipe all surfaces exposed to the solution with an alcohol wipe.
5. Place the gloves and wipes into the same plastic bag and seal.
6. Ask the pharmacist how to throw away the plastic bag.
7. Wash your hands well with soap and water.

STORAGE
Keep your Spexotras solution and oral syringe out of the sight and reach of children. Store the solution upright, in the carton provided with the cap tightly closed. Store below 25°C. **Do not** freeze. Store your oral syringe in the carton provided alongside your Spexotras solution.