Package leaflet: Information for the user

TOOKAD 183 mg powder for solution for injection
TOOKAD 366 mg powder for solution for injection
padeliporfin

▼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.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- 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 TOOKAD is and what it is used for
2. What you need to know before TOOKAD is used
3. How TOOKAD is used
4. Possible side effects
5. How TOOKAD is stored
6. Contents of the pack and other information

1. What TOOKAD is and what it is used for

TOOKAD is a medicine that contains padeliporfin (as potassium salt). It is used to treat adult men who have low-risk, localised prostate cancer in only one lobe, using a technique called Vascular-Targeted Photodynamic (VTP) therapy. The treatment is carried out under general anaesthetic (medicines that send you to sleep to prevent pain and discomfort).

Hollow needles are used to insert the fibres into the right place in the prostate. Once it has been given, TOOKAD has to be activated by laser light shone along a fibre that targets the light onto the cancer. The activated medicine then causes the death of the cancer cells.

2. What you need to know before TOOKAD is used

TOOKAD must not be used if:
- You are allergic to padeliporfin or any of the other ingredients of this medicine (listed in section 6).
- You have undergone a procedure for treating benign prostatic hypertrophy including Trans-Urethral Resection of the Prostate (TURP).
- You are having or have previously had any treatment for prostate cancer.
- You have been diagnosed with a problem with the liver called cholestasis.
- You are having an exacerbation of rectal inflammatory bowel disease.
- You are not able to have general anaesthesia or invasive procedures.

Warnings and precautions
TOOKAD should only be used by personnel trained in the VTP procedure.

Talk to your doctor or nurse if:
- You feel any irritation of the skin or problems with vision or eye irritation after the VTP procedure.
- You experience difficulties in getting or maintaining an erection.
- You feel any abnormal pain after the VTP procedure.
- You have a history of a narrowing of the urethra or urinary flow problems.
- You experience involuntary passing of urine after the VTP procedure.
- You have had an active inflammatory bowel disease or any condition that may increase the risk of causing abnormal connection between the rectum and the urethra (recto-urethral fistula).
- You have abnormal blood clotting.
- You have a reduced kidney function or if you follow a potassium restricted diet.

To date information beyond two years after VTP procedure is limited and so, at this time, data are currently not available to know whether the benefit of TOOKAD-VTP is long-lasting.

If you do require further treatment, at the moment, there is limited information on whether TOOKAD-VTP affects the efficacy and safety results of other treatments (such as surgery to remove the prostate or radiotherapy).

Photosensitivity
Strong light may cause skin reactions and eye discomfort while TOOKAD is in the blood stream.

For the 48 hours after the procedure you should avoid exposure to direct sunlight (including through windows) and all bright light sources, both indoors and outdoors. This includes sunbeds, bright computer monitor screens (see precautions below), and examination lights from medical equipment.

Sunscreen creams do not protect you against the type of light (near infra-red) that can cause problems after the procedure.

If you feel skin or eye discomfort while in hospital, you must tell your doctor or nurse so the level of lighting can be reduced and extra care can be taken to protect you from artificial and natural light.

First 12 hours after VTP procedure
After the procedure, you should wear protective goggles and will be kept under medical surveillance for at least 6 hours in a room with reduced light.
Your medical team will decide if you can leave hospital on the evening of your treatment. You may need to stay overnight if you have not fully recovered from the general anaesthetic and depending on your condition.
You must remain under reduced light conditions, without exposing your skin and your eyes to daylight. Only use light bulbs with a maximum power of 60 watts (for an incandescent light bulb) or 6 watts (for LED lights), or 12 watts (for fluorescent low-energy lights). You may watch television at a distance of 2 metres and, from 6 hours after the procedure, you may use electronic devices such as smartphones, tablets and computers. In case you need to go out during the day, you must wear protective clothing and high-protection goggles to shield your skin and eyes.

12-48 hours after VTP procedure
You may go outdoors during daylight hours but only in shaded areas or when it is overcast. You should wear dark clothes and take care to protect your hands and face from the sun.

When 48 hours have passed after the procedure, you can resume your normal activities and you can be exposed to direct sunlight.

No patients with light-sensitive conditions such as porphyria, a history of sensitivity to sunlight or a history of photosensitive dermatitis have received TOOKAD in clinical studies. However, the short duration of action of TOOKAD means that the risk of enhanced phototoxicity is expected to be low provided the precautions against light exposure are stricly followed.

There could be an additional risk of eye photosensitivity in patients who have received intra-occular anti-VEGF (medicines used to prevent new blood vessel growth) therapy. If you have received prior VEGF therapy, you should take particular care to protect your eyes from light for 48 hours post TOOKAD injection. Concomitant use of systemic VEGF inhibitors is not recommended with TOOKAD.

See also under "Other medicines and TOOKAD" for photosensitizing medicines.

Difficulties in getting or maintaining an erection
Some difficulties in getting or maintaining an erection is possible soon after the procedure and may last for more than 6 months.

Risk of damage near the prostate gland
Because the fibres that carry the light have to be inserted in such a way that the whole of the lobe of the prostate gland gets exposed, it is possible that some damage may occur outside of the prostate. Normally this is just the fat around the prostate and is not important but nearby organs such as the bladder and rectum may potentially be affected. This is normally avoidable by careful planning but should it occur there is a risk of an abnormal connection forming between the rectum and the bladder or skin. This is very rare.

Problem associated with the urethra
If you have a history of a narrowing of the urethra or urinary flow problems, treatment may increase the risk of poor flow and urinary retention.

Urinary incontinence
Short-term urinary incontinence has been observed and may result from urinary tract infection or from urgency caused by irritation to the urethra from the procedure. The condition gets better on its own or with treatment of the infection.

Active inflammatory bowel disease
If you have had an active inflammatory bowel disease or any condition that may increase the risk of causing abnormal connection between the rectum and the urethra (recto-urethral fistula), the treatment should be given only after careful evaluation.

Abnormal clotting
Patients with abnormal clotting may bleed excessively from the insertion of the needles required to position the fibres that guide the laser light. This may also cause bruising, blood in the urine and/or local pain. Abnormal clotting is not expected to affect how well the treatment works ; however, it is recommended that drugs that affect clotting are stopped prior to and for the immediate period following the VTP procedure.

See also under "Other medicines and TOOKAD" for the effects of anticoagulants and antiplatelet medicines.

Patients on a controlled potassium diet
This medicine contains potassium. In general, the dose of TOOKAD contains less than 1 mmol (39 mg) potassium, i.e. essentially 'potassium free'. However, patients weighing more than 115 kg will receive more than 1 mmol potassium. This should be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet where a rise in serum potassium would be considered detrimental.

Children and adolescents
This medicine should not be given to children and adolescents less than 18 years of age.

Other medicines and TOOKAD
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. Some medicines (in particular any

medicines that are photosensitising or that affect blood clotting) may interact with TOOKAD and should be stopped before using TOOKAD. You may also be required to not take certain medicines for several days after the VTP procedure. Your doctor will also advise what medicines may be substituted where appropriate and when these medicines can be re-started after the VTP procedure.

The following types of medicines may be ones that your doctor will advise you to stop temporarily:

Medicines with a potentially photosensitising effect:
- Certain antibiotics used to treat infection (tetracyclines, sulphonamides, quinolones).
- Certain medicines used to treat psychiatric conditions (phenothiazines).
- Certain medicines used in type II diabetes (hypoglycaemic sulphonamides).
- Certain medicines used for hypertension, oedema, heart failure or renal failure (thiazide diuretics).
- A medicine used to treat fungal infections (griseofulvin).
- A medicine used to treat cardiac arrhythmia (amiodarone).

These medicines should be stopped at least 10 days before the procedure with TOOKAD, and for at least 3 days after the procedure, or replaced by other treatments without photosensitising properties. If it is not possible to stop a photosensitising medicine (such as amiodarone), increased sensitivity may occur, you may need to protect yourself from direct light exposure for a longer period.

Anticoagulants (medicines that prevent the blood from clotting)
These medicines (e.g. acenocoumarol, warfarin) should be stopped at least 10 days before the VTP procedure with TOOKAD.

Antiplatelet agents (medicines that decrease platelet aggregation (stickiness) in the blood and reduce clotting)
These medicines (e.g. acetylsalicylic acid) should be stopped at least 10 days before the VTP procedure with TOOKAD and re-started at least 3 days after the procedure.

Other medicines that may interact with TOOKAD
The use of medicines such as repaglinide, atorvastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin, bosentan, glyburide should be avoided on the day of TOOKAD administration and for at least 24 hours after administration.

Contraception
You or your partner or both should use an effective form of birth control to prevent your partner getting pregnant for 90 days after the VTP procedure. Check with your doctor about the birth control methods to use and how long to use them for. If your partner becomes pregnant within three months of your treatment, you must immediately tell your doctor.

Pregnancy and breast-feeding
TOOKAD is not indicated for the treatment of women.

Driving and using machines
TOOKAD has no influence on the ability to drive or use machines. However, as the procedure includes general anaesthesia, you should not perform complex tasks like driving or using machines until 24 hours after a general anaesthetic is used.

3. How TOOKAD is used

TOOKAD is restricted to hospital use only. It should only be used by personnel trained in the VTP procedure.

Dose
The recommended dose of TOOKAD is one single dose of 3.66 mg per kg of body weight, injected into a vein. The injection lasts 10 minutes.
For instructions to healthcare professionals on reconstitution of TOOKAD before injection, see "Reconstitution of the TOOKAD powder for solution for injection".

Only the lobe that contains the cancer will be treated. Additional VTP procedures of the prostate are not recommended.

VTP procedure
The day before and at the beginning of the VTP procedure, a rectal preparation is performed in order to clean the rectum. Your doctor may prescribe antibiotics to prevent infection and alpha-blockers (medicines given to prevent difficulties in urinating). You will be given a general anaesthetic to send you to sleep before the VTP procedure. Fibres to carry the laser light are inserted into the prostate gland by using hollow needles. TOOKAD is activated immediately after injection by shining light through the fibres from a connected laser device.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
In addition, inserting needles into the prostate gland and inserting a urinary catheter for the procedure may be associated with further side effects.

Possible side effects can occur with TOOKAD and VTP procedure.

If you get any of the side effects below, **tell your doctor immediately**:
- Urinary retention (not able to pass urine). In the few days after the VTP procedure some patients may have difficulties (poor stream due to urethral narrowing) or inability to pass urine. This may necessitate inserting a catheter inside your bladder through the penis and the catheter will remain in place for a few days or weeks to drain the urine.
- Fever, pain and swelling in the area of the operation might occur after the procedure. These may be signs of infection in the urinary tract, the prostate or the genital system. In this case, you should contact your doctor as you may need further blood or urine analysis and antibiotics treatment. These infections are usually easily treated.

In addition to the side effects listed previously, other side effects can occur.

Very common side effects (may affect more than 1 in 10 people)
- Problems with or pain on passing urine (including pain or discomfort on passing urine, bladder pain, the need to pass urine urgently or more frequently or at night; involuntary passing of urine),
- Sexual problems (including difficulty in getting or maintaining an erection, ejaculation failure, loss of desire or pain on intercourse),
- Blood in the urine (haematuria),
- Perineal injury including bruising in the skin, bruising near where the needles are put into the prostate, pain and tenderness,
- Genital pain and discomfort (inflammation of the testicles or the epididymis, pain due to inflammation or fibrosis of the prostate).

Common side effects (may affect up to 1 in 10 people)
- Anorectal discomfort (discomfort near the anus and just inside the anus), haemorrhoids (piles), proctalgia (pain in the anal region),
- Problems with bowels (including diarrhoea or occasional soiling),

- General and musculoskeletal pain (muscle/bony pain, pain in the end of the limbs, back pain or bleeding into the joints),
- Haematospermia (presence of blood in the ejaculate),
- High blood pressure,
- Increases in blood lipids, lactate dehydrogenase increased, white blood cell increased, creatine phosphokinase increased, potassium decreased, prostatic specific antigen (PSA) increased,
- Skin reaction, erythema (reddening), rash, dryness, pruritus, depigmentation,
- Abnormal blood tests related to coagulation,
- Discomfort in the abdominal region,
- Fatigue (tiredness).

Uncommon side effects (may affect up to 1 in 100 people)
- Dizziness, fall,
- Headache,
- Sensory disturbance, formication (sensation like crawling insects on or under the skin),
- Eye irritation, photophobia (intolerance to light),
- Dyspnoea exertional (excessive shortness of breath during or after exercise),
- Mood disorder,
- Weight decreased.

Reporting of side effects
If you get any side effects, talk to your doctor or 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, 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 TOOKAD is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist.

The following information is intended for the specialist only.

Keep this medicine out of the sight and reach of children.

Do not use after the expiry date which is stated on the shield 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 outer carton in order to protect it from light.

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

6. Contents of the pack and other information

What TOOKAD contains
- The active substance is padeliporfin.
  Each vial of TOOKAD 183 mg contains 183 mg of padeliporfin (as potassium salt).
  Each vial of TOOKAD 366 mg contains 366 mg of padeliporfin (as potassium salt).
  1 mL of reconstituted solution contains 9.15 mg of padeliporfin.

- The other ingredient is mannitol.

What TOOKAD looks like and contents of the pack
TOOKAD is a dark powder.

Each carton of TOOKAD 183 mg powder for solution for injection contains an amber glass vial with a blue cap.
Each carton of TOOKAD 366 mg powder for solution for injection contains an amber glass vial with a white cap.

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Steba Biotech S.A.
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Luxembourg

Manufacturer
Praxis Pharmaceutical S.A.
C/ Hermanos Lumiere 5
Parque Tecnologico de Álava (Miñano)
Vitoria-Gasteiz
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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.

The following information is intended for healthcare professionals only:

Reconstitution of the TOOKAD powder for solution for injection
The solution must be prepared in a dimmed-light environment due to the photosensitizing properties of the medicine.

1. Reconstitute the solution by adding:
   - for TOOKAD 183 mg: **20 mL** of a 5 % glucose solution in the vial containing the powder;
   - for TOOKAD 366 mg: **40 mL** of a 5 % glucose solution in the vial containing the powder.
2. Swirl the vial gently for 2 minutes. The final solution concentration is 9.15 mg/mL.
3. Allow the vial to rest in a vertical position for 3 minutes without further shaking or moving.
4. Transfer the contents of the vial into an opaque syringe.
5. Allow the opaque syringe to rest in a vertical position for 3 minutes to ensure any foam disappears.
6. Place a 0.22 µm injection filter on the syringe.
7. Connect an opaque tube to the filter.

The reconstituted solution for infusion is dark.

Illumination for photoactivation of TOOKAD
TOOKAD is locally activated immediately after injection by laser light at 753 nm delivered via interstitial optical fibres from a laser device at a power of 150 mW/cm of fibre, delivering an energy of 200 J/cm over 22 minutes 15 seconds.
Planning of optical fibre positioning should be performed at the beginning of the procedure using the treatment guidance software. During the procedure, the optical fibres are selected and positioned transperineally into the prostate gland under ultrasound guidance to achieve a Light Density Index (LDI) ≥ 1 in the targeted tissue.

Storage conditions
Store in a refrigerator (2°C-8°C).
Keep the vial in the outer carton in order to protect from light.

After reconstitution with a 5 % glucose solution in its vial, the chemical and physical stability of TOOKAD has been demonstrated for 8 hours at 15°C-25°C and at 5°C ± 3°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.