

TOOKAD[®] ▼ (padeliporfin) Patient Information Guide

TOOKAD[®] is used to treat low-risk
localized prostate cancer



▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. If you get any side effects, which includes any possible side effects not listed in this leaflet, talk to your doctor, pharmacist or nurse. You can help by reporting any side effects you may get.

Date of approval: <month> <year>

Table of contents	Page
1. What are the aims of this guide? _____	3
2. How is low-risk prostate cancer treated? _____	3
3. What is TOOKAD®? _____	3
4. What are the potential benefits of TOOKAD®? _____	4
5. What are the risks and side effects associated with TOOKAD® therapy? _____	4
• Erectile dysfunction (difficulty in getting or maintaining an erection) _____	5
• Urinary incontinence (leaking urine on coughing, on straining or before you reach the toilet) _	5
• Urinary retention/Urethral stricture _____	6
• Photosensitivity (skin redness and eye damage) _____	6
6. What are the uncertainties about the risks and benefits of TOOKAD® treatment? _____	6
What is known about the long-term effects of TOOKAD®-VTP? _____	6
What happens if you need more treatment after TOOKAD®-VTP? _____	6
Is more information on the potential risks and uncertainties available? _____	6
7. How will you be followed-up after the TOOKAD® procedure? _____	7
Where can you get more information about Vascular-Targeted Photodynamic therapy? _____	7
Reporting of side effects _____	7
Glossary of terms _____	8
NOTES _____	9
Receipt of Patient Information Guide _____	11

1. What are the aims of this guide?

You have been given this guide by your doctor because you have **localised cancer in one lobe** of your prostate. This is considered as low-risk and you are eligible for Vascular-Targeted Photodynamic therapy (VTP) with TOOKAD[®], which is a **focal therapy** i.e. a treatment that focuses on only a part of the prostate. This is just one of the treatment options available for your cancer.

This guide does not state the best treatment for you as you will discuss this with your doctor. It tells you about the possible **benefits, risks and uncertainties** associated with TOOKAD[®]-VTP in order to help you make an **informed decision**. It does not replace the TOOKAD[®] patient information leaflet which will be given to you later, if you go ahead with the TOOKAD[®]-VTP procedure.

2. How is low-risk prostate cancer treated?

Several options exist to manage low-risk prostate cancer. They include:

- **Active surveillance**
 - which involves regular review, intermittent prostate biopsy and treatment only if the disease gets worse
- **Radical prostatectomy**
 - surgical removal of the prostate
- **External beam radiotherapy**
 - radiotherapy where an external source of ionizing radiation is pointed at the prostate
- **Brachytherapy**
 - insertion of radioactive implants into the prostate
- **Other focal therapies** including
 - a. Cryoablation (destruction of the tissue by using extreme cold)
 - b. High-intensity focused ultrasound (HIFU)
 - c. **VTP with TOOKAD[®]** (IV injection of TOOKAD[®] followed by illumination of fibres, inserted in the single lobe of the prostate diagnosed with cancer).

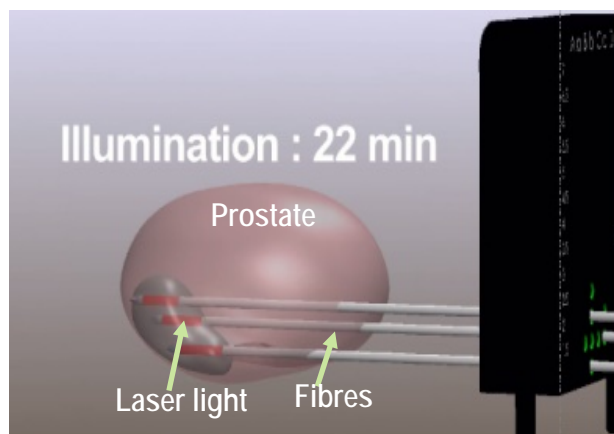
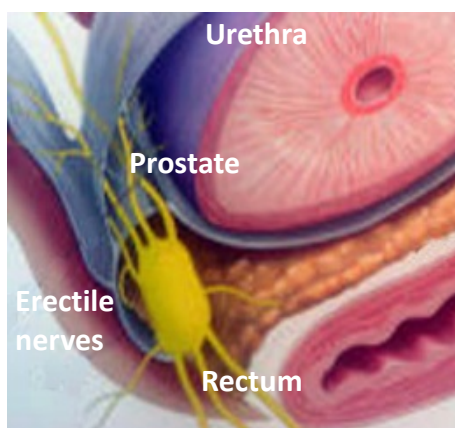
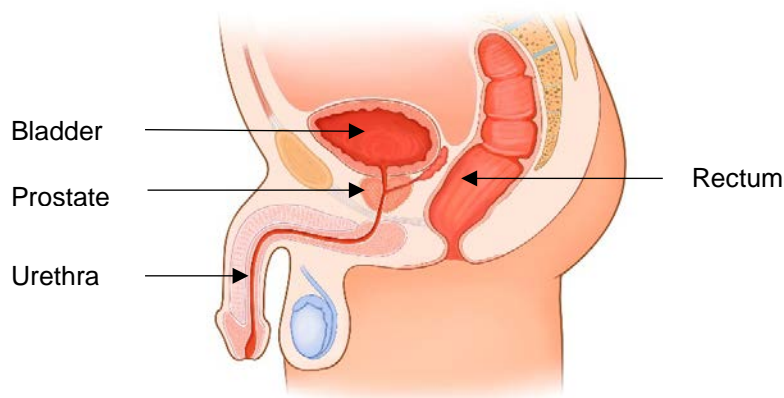
Active surveillance, radical prostatectomy, external beam radiotherapy, and brachytherapy have been studied in long term studies, which have shown that the average long-term survival is 95% after 10 years.

TOOKAD[®] has been studied in a clinical study comparing its efficacy and safety to active surveillance.

Your doctor will explain these treatment options to you.

3. What is TOOKAD[®]?

- **TOOKAD[®]** is a medicine that contains a substance called padeliporfin that causes the body's tissues and organs to become **sensitive to light**.
- The medicine is injected intravenously (IV) and then activated by laser light, shone along fibres that have been placed in the prostate.
- This is conducted using a treatment guidance defined for each patient depending of the volume and position of the tumour.
- The treatment is carried out **under general anaesthetic**.



The medicine is injected intravenously for 10 minutes and is immediately activated by laser light, shone for 22 minutes and 15 seconds along fibres that have been placed into the right place in the prostate. The activated medicine causes the death of the cancer cells.

4. What are the potential benefits of TOOKAD®?

In the main clinical trial comparing TOOKAD® with active surveillance (regular monitoring), 197 patients were treated with TOOKAD®-VTP and 207 patients underwent active surveillance. Two years later, out of 80 patients with initial disease in only one lobe of their prostate 52 (65.0%) had a **negative biopsy** (i.e. that did not show cancer) in the lobe treated with TOOKAD®-VTP, **compared with** 11 of 78 patients [14.1%] in the active surveillance group.

Over two years following TOOKAD®-VTP the percentage of patients who had **progression** to a more extensive or more aggressive form of cancer was **half of that seen with active surveillance** (27 of 80 patients [33.8%] compared with 53 of 78 patients [67.9%]).

5. What are the risks and side effects associated with TOOKAD® therapy?

Like all medicines, TOOKAD® can cause side effects, although not everybody gets them. Most side effects, if you do get them, should be short lived but some may last for longer and may not get completely better.

The following information on the **most commonly observed side effects** is based on data from the clinical trial, where 197 patients were treated with TOOKAD[®]-VTP and 207 patients underwent active surveillance (regular monitoring).

- **Erectile dysfunction** (difficulty in getting or maintaining an erection)
 - Patients with prostate cancer may experience problems with sexual function.
 - TOOKAD[®]-VTP may make these worse.
 - If it occurs, erectile dysfunction can be expected soon after the TOOKAD[®]-VTP procedure and tends to gradually improve. However, some degree of erectile dysfunction can remain after 6 months.
 - 60 (30.5%) patients in the TOOKAD[®]-VTP arm experienced erectile dysfunction:
 - 7 (3.6%) patients experienced erectile dysfunction for less than 6 months
 - In 1 of these 7 patients, erectile dysfunction was moderate (need for medication or devices to achieve an erection). This patient recovered with some residual dysfunction.
 - 6 of these patients had mild erectile dysfunction (some difficulty, and potentially the need for medication, to achieve or maintain an erection) and all fully recovered.
 - 19 (9.6%) patients experienced erectile dysfunction for more than 6 months
 - All recovered during the course of the 2-year study.
 - Among these 19 patients, erectile dysfunction was severe in 1 patient (impotence), moderate in 10 patients, and mild in 8 patients.
 - 34 (17.3%) patients experienced erectile dysfunction that had not returned to normal at 2 years
 - Among these 34 patients, erectile dysfunction was moderate in 14 patients and mild in 20 patients.
- **Urinary incontinence** (leaking urine on coughing, on straining or before you reach the toilet)
 - 25 (12.7%) patients in the TOOKAD[®]-VTP experienced urinary incontinence:
 - 13 (6.6%) patients in the TOOKAD[®]-VTP arm experienced urinary incontinence lasting less than 6 months
 - Among these 13 patients, 12 cases started within 2 months after the procedure, and one case started about 4 months after the procedure.
 - 7 cases were moderate (pads were needed) and 6 cases were mild (no need to wear pads).
 - This incontinence may be related, in some cases, to infection, which can occur as a result of the procedure or the need for a urinary catheter.
 - 5 (2.5%) patients in the TOOKAD[®]-VTP arm experienced urinary incontinence for more than 6 months
 - All recovered during the course of the 2-year study.
 - In these 5 patients, urinary incontinence was moderate in 1 patient, and mild in 4 patients.
 - 7 (3.6%) patients in the TOOKAD[®]-VTP arm experienced urinary incontinence that had not returned to normal at 2 years
 - Urinary incontinence was severe (large urine loss) in 1 patient due to previous prostate surgery, which is now not allowed before TOOKAD[®]-VTP.
 - It was moderate in 1 patient, and mild in 5 patients.

- **Urinary retention/Urethral stricture**

- Urinary retention (not being able to pass all or some of your urine) may be observed as a result of the swelling of the prostate after the TOOKAD®-VTP procedure.
- In the main clinical study, 15 (7.6%) patients had urinary retention
 - 2 of these were severe (intervention indicated) and 12 were moderate (medication indicated)
 - for both these groups of patients, temporary urinary catheter was required.
 - 1 case was mild (able to void / no medication needed).
 - All patients got better by 43 days.
- In addition, 2 (1.0%) patients developed a urethral stricture (an abnormal narrowing of the tube that carries urine out of the body from the bladder).
 - They required urethral dilatation (surgery to enlarge the tube that carries urine from the bladder outside the body).

- **Photosensitivity (skin redness and eye damage)**

- TOOKAD® is a photosensitiser, i.e. it makes your skin and eyes react to light.
- Therefore, you will need to protect yourself from light for 48 hours after the TOOKAD®-VTP procedure.
- To date, there has not been an issue with photosensitivity as patients have been able to successfully follow the light protection instructions.

6. What are the uncertainties about the risks and benefits of TOOKAD® treatment?

What is known about the long-term effects of TOOKAD®-VTP?

- At the moment, there is very little information beyond two years after the TOOKAD®-VTP procedure.
- Patients in the study did not normally have a prostate biopsy beyond two years, so **it is not known whether the benefit of TOOKAD®-VTP is long-lasting** i.e. we do know that it delays the time until another treatment for prostate cancer is needed but not whether it can get rid of prostate cancer long term.
- It is too early to say whether TOOKAD®-VTP could be the only treatment for your prostate cancer that you might need.
- We do not know whether other side effects might develop later due to the tissue damage (necrosis and fibrosis) caused by TOOKAD®-VTP.
- **It is not known** whether, if any prostate cancer cells remain after the procedure, TOOKAD®-VTP may have made them **become more aggressive**.

What happens if you need more treatment after TOOKAD®-VTP?

If you do need more treatment for your prostate cancer after TOOKAD®-VTP (such as surgery to remove the prostate or radiotherapy), we do not know whether this treatment will be as successful as if you just had it in the first place i.e. treatment with TOOKAD®-VTP might make additional treatments for your prostate cancer more difficult to do properly, less likely to work or have more side effects.

Is more information on the potential risks and uncertainties available?

Information is being collected from patients who have had the TOOKAD®-VTP procedure to work out the long-term risks and benefits, but we do not have the answer at the moment.

7. How will you be followed-up after the TOOKAD® procedure?

If you have TOOKAD®-VTP therapy you will be followed up to check that the treatment has worked like this:

- Prostate Specific Antigen (PSA) measurement every 3 months for the first 2 years post VTP and then every 6 months;
- Digital Rectal Examination (DRE) at least once a year, or more often if decided by your doctor;
- Prostate biopsies at 2 to 4 years and at 7 years. You may need a biopsy outside of these times if your doctor is concerned that, based on your PSA or DRE, your cancer may have returned.
- Magnetic Resonance Imaging (MRI) may also be used to check whether you have remained cancer-free and this may also indicate the need for a biopsy.

Where can you get more information about Vascular-Targeted Photodynamic therapy?

Your doctor will advise you what additional information is available on the efficacy and safety of TOOKAD®-VTP.

This guide aims to provide accurate information; however, its contents may occasionally differ from the advice given to you by your doctor.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. You can also report side effects directly via the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

Glossary of terms

Term	Meaning
Vascular-Targeted Photodynamic therapy (VTP)	Therapy using a photosensitizer and laser light to occlude blood vessels around the targeted zone of the prostate to be treated
Active Surveillance	Regular review, intermittent prostate biopsy and treatment of the prostate only if the disease gets worse
Radical prostatectomy	Surgical removal of the prostate
External beam	Commonest form of radiotherapy where an external source of ionizing radiation is pointed at the prostate
Brachytherapy	Insertion of radioactive implants into the prostate
Focal therapy	Treatment aiming at treating only the part of the prostate containing the cancer
Cryoablation	Destruction of the tissue by using extreme cold
High-intensity focused ultrasound (HIFU)	Destruction of the tissue by using focused ultrasound waves
Erectile dysfunction	Difficulty in getting or maintaining an erection
Urinary incontinence	Leaking urine on coughing, on straining or before you reach the toilet
Urinary retention	Not being able to pass all or some of your urine
Urethral stricture	Abnormal narrowing of the tube that carries urine out of the body from the bladder
Urethral dilatation	Surgery to enlarge the tube that carries urine from the bladder outside the body
Photosensitivity	Sensitivity to light that can cause skin redness and eye damage

Receipt of Patient Information Guide

I confirm that I have received the TOOKAD® Patient Information Guide and had an opportunity to ask questions about TOOKAD® VTP and other treatments for my prostate cancer.

Signed:

Name:

Dated: