The three main criteria for initiation of radical treatment in patients showing disease progressions are:
- PSA-DT of less than 2 years,
- re-biopsy of primary tumour to Gleason grade 4 or more
- more than 50 per cent of positive cores showing cancer involvement.

Prostate Cancer UK Best Practice Pathway: ACTIVE SURVEILLANCE

What is the patient’s stage of disease?

Low risk localised
PSA < 10 ng/ml and Gleason score ≤ 6, and clinical stage T1 - T2a
- Offer active surveillance

Intermediate risk localised
PSA 10 - 20 ng/ml, or Gleason score 7, or clinical stage T2b
- Consider active surveillance
- Is Gleason score 3+4
  - Yes: Is Gleason score 3+4
  - No: Not suitable for active surveillance

Does the patient wish to change to alternative treatment options? OR Is there evidence of disease or symptomatic progression?

Low risk localised
PSA < 10 ng/ml and Gleason score ≤ 6, and clinical stage T1 - T2a
- Offer active surveillance

Intermediate risk localised
PSA 10 - 20 ng/ml, or Gleason score 7, or clinical stage T2b
- Consider active surveillance
- Is Gleason score 3+4
  - Yes: Is Gleason score 3+4
  - No: Not suitable for active surveillance

(NICE Active Surveillance Protocol)

Year 1
- 3-month Prostate-Specific Antigen (PSA) check
- 6-month DRE
- 12-month re-biopsy
- Monitor PSA kinetics

Year 2 - 4
- 3 - 6 month PSA check
- 6 - 12 month DRE
- Monitor PSA kinetics

Year 5 and beyond
- 6-month PSA check
- 12-month DRE
- Monitor PSA kinetics

PSA kinetics: include PSA doubling time and velocity

Men offered psychological support

Resume active surveillance as appropriate

Does the patient wish to change to alternative treatment options? OR Is there evidence of disease or symptomatic progression?

Yes
- Consider alternative management/treatment strategies

No
- See Treatment Pathway Commentary for more information on recommendations to move to active treatment

Considerations for alternative management strategies:
- personal preferences, comorbidities and life expectancy
- patient pathology and radiology
- biopsy and grade progression
- clinical progression.

Surgery External Beam Radiotherapy Brachytherapy Hormone therapy Watchful waiting
Recommended for **localised and locally advanced** prostate cancer (M0, N0/1). Suitable for men for whom curative treatment is not an option and are not symptomatic, or those who chose not to undergo treatment.

“*All men with prostate cancer should be given information and advice on likelihood and management of consequences of treatment and late effects, including red flag symptoms, even those men that opt for watchful waiting.*” See **Support Pathway** (General side effect management principles).

Consider for older men and those with medical co-morbidities with a shorter life-expectancy where benefit of radical treatment is unlikely/limited.

Begin watchful waiting

GP management for symptoms and PSA monitoring with predefined monitoring agreed (or defined) by specialist including re-referral criteria.

Evidence of disease progression:
- rapidly rising PSA level
- bone pain

Locally advanced disease (symptomatic or rapid PSA rise)

Urological MDT review

Androgen deprivation therapy to control symptoms

Localised disease (rapid PSA rise)

Urological MDT review

Consider how radical treatments may affect any existing comorbidities and life expectancy
Prostate Cancer UK Best Practice Pathway: Treatment Option: Surgery – RADICAL PROSTATECTOMY

What is the patient’s stage of disease?

Low risk (T1 - 2a): PSA < 10, Gleason 6, with few comorbidities

Intermediate / high risk: T2c - 3a: PSA ≤ 10, Gleason score ≤7

Locally advanced: Any PSA, Any Gleason ≤ 8, N1 T3a - T3b

Active surveillance as optimal treatment unless patient chooses surgery.

Suitable for surgery?

Yes

Consultation with urologist and CNS, to include:
- treatment outcomes – T2c - 3a to be advised that there is a chance secondary treatment in the form of hormone therapy or radiotherapy may be required following surgery
- surgical approaches available
- side effects
- consent.

Gleason 4+3 or 4+4 with PSA > 20 – consider extended lymph node dissection

Pelvic lymph node dissection risks:
- lymph leak
- lymphocele formation
- nerve damage.

Pre-treatment seminar
Nurse led session to discuss;
- side effects
- implications of surgery
- catheter care
- continence and continence products
- pre-surgery baseline sexual function (erectile function)
- pelvic floor exercises / penile rehabilitation.

No

Consider other treatment options (e.g. external beam radiotherapy)

Robotic prostatectomy
Laparoscopic prostatectomy
Open prostatectomy

continues on next page
Prostate Cancer UK Best Practice Pathway: Treatment Option: Surgery – RADICAL PROSTATECTOMY (continued)

- Preoperative Assessment (a/w protocols)
- High risk anaesthetic assessment
- Assess baseline continence and erectile function

Post surgery
- early mobilisation, eating and drinking
- pain relief and anti-emetic medications
- catheter management.

Stratified follow-up
- 6 week post-op PSA test
- follow-up 6 - 8 weeks
- PSA re-testing at 3 months and 6 months
- annual follow-up.

Follow up should include assessment of urinary incontinence and ED with appropriate support and treatment.

PSA remains low or at 0?
No

PSA remains persistent?
Yes

PSA rises 3 times?
Yes

After at least 2 years, NICE guidance advises that for men with a stable PSA, who have had no significant treatment complications, follow-up can be offered outside of hospital by telephone or secure electronic communications (unless they are taking part in a clinical trial that requires formal clinic-based follow-up). Direct access to the urological cancer MDT should be offered and explained.

Try to locate the recurrent cancer and refer to Clinical Oncologist for local control with adjuvant radiotherapy.

Refer to Clinical Oncologist for salvage radical radiotherapy to the prostatic bed if they have +/- lymph nodes and no known metastases.

Patients with high volume nodal disease and multiple adverse tumour characteristics: early adjuvant hormone therapy.
Prostate Cancer UK Best Practice Pathway: EXTERNAL BEAM RADIOTHERAPY (EBRT)

Is the patient suitable for radiotherapy?

Consultation with Oncologist and CNS, to include:
• potential treatment outcomes
• length of treatment and patient attendance
• side effects
• consent.
See Support Pathway for more information on pelvic radiotherapy side effects (section 3.4)

What is the patient’s stage of disease?

Localised T1 - 3a, Gleason < 8, any PSA

Low or intermediate/high risk?

Low risk (T1 - 2a): hypo-fractionated high-dose IMRT
60 gy in 20 fractions over 4 weeks

In case of recurrence, men exposed to 78 gy will not have the option of additional radiotherapy

T2b and T2c - 3a: IMRT
78 gy in 37 fractions over 7 - 8 weeks

External beam radiotherapy to a dose of 76 – 78 gy, combined with brachytherapy (high-dose rate).
Radiotherapy should be given in combination with long-term androgen deprivation therapy (2 – 3 years).

Optimal treatment for locally advanced disease: combination external beam radiotherapy and brachytherapy.

Optimal treatment administration.

Locally advanced

Offer medical castration (luteinising-hormone-releasing hormone [LHRH] agonist) as androgen deprivation therapy. Include co-administration of an antiandrogen to LHRHa to prevent testosterone flare – 1 week before and 3 weeks after the first injection. Administer for 4 weeks.

 combined with Radical Radiotherapy (EBRT) – NICE Guidelines 2014

External beam radiotherapy to a dose of 76 – 78 gy, combined with brachytherapy (high-dose rate).
Radiotherapy should be given in combination with long-term androgen deprivation therapy (2 – 3 years).

Optimal treatment for locally advanced disease:

Patient struggling with side-effects of androgen deprivation therapy?

Intermittent treatment (strategy to minimise side effects of testosterone loss):
• highly motivated patients with a major PSA response after induction period
• stop – PSA level < 4 ng/ml after 6 - 7 months of treatment
• resume – PSA level is > 10-20 ng/ml.

continues on next page
On the day of treatment with Radiographer:
- fluid intake checked
- bladder scan to ensure full bladder
- check bowel activity / bowel preparation
- positioning (Radiographer).

Assessment prior to next fraction administered to check fitness and side effects

Is the patient medically fit enough to continue with radiotherapy?
Are the side effects of treatment well controlled?
Does the patient wish to continue to the next fraction of radiotherapy?

Yes
Proceed to next fraction or complete treatment

No
Consultation with Oncologist to explore alternative treatment options or referral back to Urologist

Mid-treatment review with Radiographer or CNS (weekly)

PSA test one week before Oncology review
Post treatment consultation with Oncologist

Is there a sign of biochemical recurrence?
(2 - 3 years androgen deprivation therapy – PSA rise within this timeframe is likelihood of castrate resistance)

Yes
Definition of biochemical relapse: The 2005 ASTRO consensus definition (PSA greater than current nadir + 2 ng/ml: Roach, 2006), has a sensitivity of 74 per cent and specificity of 71 per cent for any clinical failure.

Staging investigation is undertaken to identify whether cancer is still present locally within the prostate or has metastasised.

Localised/ locally advanced

Metastatic

Is the patient symptomatic?

Yes
For physically fit patients, radical prostatectomy can provide a curative salvage therapy for biochemical relapse after radiotherapy.

No
Monitor for symptoms

Short-term side effects (6 - 8 weeks) including: diarrhoea, rectal pain, unusual urinary frequency.

Late effects can occur months to years after radiotherapy, may include: urinary problems (weak flow), bowel problems, erectile dysfunction, hip and bone pain/ weakness.
See Support Pathway (section 3.4).

Continue to monitor with PSA measurements after 6 and 12 months
Prostate Cancer UK Best Practice Pathway: BRACHYThERAPY

What is the patient’s stage of disease?

- **Low risk localised**
  - PSA < 10 ng/ml and Gleason score ≤ 6, and clinical stage T1 - T2a

- **Intermediate risk localised**
  - PSA 10 - 20 ng/ml, or Gleason score 7, or clinical stage T2b

- **High risk localised**
  - PSA > 20 ng/ml, or Gleason score 8-10, or clinical stage ≥ T2c

- **Locally advanced**
  - T3+, NX, N1

Is the prostate now adequately sized?

- **Yes**
  - Consider 3 - 6 months of hormone therapy to shrink prostate to acceptable size before proceeding to pre-operative assessment
  - Start low-dose rate brachytherapy

- **No**
  - Large prostate (> 75cc)? IPSS > 12? History of prostate outflow surgery? Poor urinary stream?
    - **Yes**
      - Unsuitable for brachytherapy, explore alternative treatments: active surveillance or external beam radiotherapy or surgery
    - **No**
      - Is Gleason score 3+4
        - **Yes**
          - Do not offer brachytherapy alone to men with high-risk localised prostate cancer
        - **No**
          - Start low-dose rate brachytherapy

Does Gleason score 3+4 continue on next page
Prostate Cancer UK Best Practice Pathway: BRACHYTHERAPY (continued)

Stratified follow-up
- Initial follow-up 4 - 6 weeks
- PSA testing and subsequent follow-up (for men not on androgen deprivation therapy):
  - Year 1: every 3 months
  - Years 2 - 5: every 6 months
  - Years 6+: every 12 months
  - Men on androgen deprivation therapy will have their PSA levels suppressed for up to 3 years
- Ensure effective short-term side-effect support
- Ensure support for late-effects

Is there a sign of biochemical recurrence?
(2 - 3 years androgen deprivation therapy – PSA rise within this timeframe is likelihood of castrate resistance)

Definition of biochemical relapse: The 2005 ASTRO consensus definition (PSA greater than current nadir + 2 ng/ml: Roach, 2006), has a sensitivity of 74 per cent and specificity of 71 per cent for any clinical failure.

Staging investigation is undertaken to identify whether cancer is still present locally within the prostate or has metastasised.

Continue to monitor with PSA measurements after 6 and 12 months

Localised/locally advanced

Is the patient symptomatic?

Yes

For physically fit patients, radical prostatectomy can provide a curative salvage therapy for biochemical relapse after radiotherapy.

No

Monitor for symptoms

Metastatic

Go directly to M1 pathway

Late effects can occur months to years after radiotherapy, may include: urinary problems (weak flow), bowel problems, erectile dysfunction, hip and bone pain/weakness. Please see Support Pathway (section 3.4).
Prostate Cancer UK Best Practice Pathway: HORMONE THERAPY – (First Line)
Locally Advanced and Metastatic Prostate Cancer

What is the patient’s stage of disease?

Locally advanced (N1 M0)
Offer medical castration (luteinising-hormone-releasing hormone [LHRH] agonist) as androgen deprivation therapy. Include co-administration of an anti androgen to LHRHa to prevent testosterone ‘flare’ – 1 week before and 3 weeks after the first injection. Administer for 4 weeks.

Metastatic prostate cancer (M1)
Offer medical or surgical castration (luteinising-hormone-releasing hormone [LHRH] agonist) as androgen deprivation therapy. Include co-administration of an anti androgen to LHRHa to prevent testosterone ‘flare’ – 1 week before and 3 weeks after the first injection. Administer for 4 weeks.

Consider radical prostatectomy (RP) with patients high-risk localised disease and a life expectancy of > 10 years.

Consider Degarelix for advanced hormone-dependent prostate cancer in patients with spinal metastases who present with signs or symptoms of spinal cord compression – no anti-androgen needed.

Intermittent treatment (strategy to minimise side effects of testosterone loss):
- highly motivated patients with a major PSA response after induction period
- stop – PSA level < 4 ng/ml after 6 - 7 months of treatment
- resume – PSA level is > 10-20 ng/ml.

Patient struggling with side-effects of androgen deprivation therapy?

Is the patient able to tolerate radical treatment?

Yes
Consultation with Oncologist and CNS, to include:
- potential combination treatment outcomes
- length of treatment and patient attendance
- side effects
- consent.

No

Main side effect profile, mainly due to testosterone loss:
- hot flushes
- changes to sex life
- weight gain strength and muscle loss
- loss of body hair
- bone thinning
- mood changes
- risk of heart disease, stroke and diabetes.
Please see Support Pathway (section 3.6).

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Prostate Cancer UK Best Practice Pathway: HORMONE THERAPY – (First Line)
Locally Advanced and Metastatic Prostate Cancer (continued)

What is the patient’s stage of disease?

Locally advanced (N1 M0)
- Combine medical castration with radical radiotherapy (EBRT) – NICE Guidelines 2014
  - External beam radiotherapy to a dose of 76–78 gy, combined with brachytherapy (high-dose rate). Radiotherapy should be given in combination with long-term androgen deprivation therapy (2 - 3 years).
  - Consider Bicalutamide after RP or external beam radiotherapy – on its own or with other hormonal treatments such as goserelin, buserelin, triptorelin or leuprorelin.

Has the patient’s cancer progressed?
- Definition of biochemical relapse: The 2005 ASTRO consensus definition (PSA greater than current nadir + 2 ng/ml: Roach, 2006), has a sensitivity of 74 per cent and specificity of 71 per cent for any clinical failure.

Consultation with Oncologist to explore alternative treatment options including abiraterone (if metastatic) and enzalutamide.

Metastatic prostate cancer (M1)
- Newly diagnosed M1 with 12 weeks androgen deprivation therapy?
  - Yes
    - Is the patient suitable for chemotherapy?
      - Yes
        - Combine medical castration with chemotherapy (docetaxel) to all patients whose first presentation is M1 disease and who are fit enough for chemotherapy.
      - No
        - Offer medical castration alone to patients unfit for, or unwilling to consider, castration combined with chemotherapy.
  - No
    - Has the patient’s cancer progressed?
      - Yes
        - Has the patient’s cancer progressed further and in what way?
          - Yes
            - In patients with measurable disease, progression is the appearance of new soft tissue metastases or a clear increase in size of existing metastases (usually at least a 20 cent increase in size). If bone metastases = at least 2 new metastases on a bone scan confirmed by appearance of at least 2 more on another scan performed at least 6 weeks later.
          - No
            - Continue to monitor with PSA measurements after 6 and 12 months.
      - No
        - Rising PSA after 3 years or the appearance of new metastases with castrate levels of testosterone.
Prostate Cancer UK Best Practice Pathway: Treatment Option: HORMONE THERAPY (Second Line)

What is the patient’s stage of disease?

Any N and M0: rising PSA levels in the absence of metastases or symptoms and despite androgen-deprivation therapy.

Consultation with Medical Oncologist and CNS, to include:
• treatment options
• side effects
• consent.

Bone scan to rule out the presence of metastases or micrometastases.

Combined Anti-Androgen Blockage (CAB)

External beam radiotherapy (if not previously received) and consider high-dose rate brachytherapy in combination.

If bone pain provide Radium 223. Please see the Support Pathway (section 3.7).

M1: metastases and symptoms

Docetaxel (if no prior docetaxel) – before or after abiraterone or before or after enzalutamide – based on patient choice only as no evidence is available for sequencing.

Main side effects of abiraterone:
• tiredness
• anaemia
• diarrhoea
• fluid retention
• rise in blood pressure
• bone thinning.

Please see the Support Pathway (section 3.8).

Enzalutamide or abiraterone

Docetaxel

Abiraterone or enzalutamide

Main side effects of enzalutamide:
• tiredness
• hot flushes
• headache
• memory impairment
• rise in blood pressure.

Palliative care

Regularly monitor blood pressure

Monitor liver function every 2 weeks for first 3 months, then monthly.
Prostate Cancer UK Best Practice Pathway: CHEMOTHERAPY

What is the patient's stage of disease?

Metastatic
T3(a/b)/4, N0/1, M1

Consultation with Medical Oncologist and CNS, to include:
- treatment options
- side effects
- consent.

Hormone sensitive with < 12 weeks androgen deprivation therapy?

Is the patient suitable for chemotherapy?

No
Offer medical castration alone to patients unfit for, or unwilling to consider, castration combined with chemotherapy.

Yes

Castrate-resistant?

Yes
Offer medical castration (androgen deprivation therapy) combined with chemotherapy (docetaxel) to all patients whose first presentation is M1 disease and who are fit enough for chemotherapy. Docetaxel is administered as a 1-hour infusion once every 3 weeks for 6 cycles. The recommended dose is 75 mg/m², with twice daily oral administration of prednisone or prednisolone at a dose of 5 mg.

No

Has the patient's cancer progressed?

Yes
Initial = rising PSA or the appearance of new metastases with castrate levels of testosterone.

Abiraterone or enzalutamide

Abiraterone or enzalutamide

Enzalutamide or abiraterone

Docetaxel (if no prior docetaxel) – before or after abiraterone or before or after enzalutamide – based on patient choice only as no evidence is available for sequencing

Docetaxel

Abiraterone or enzalutamide

Cabazitaxel

Palliative care, which can include radiotherapy

See Support Pathway (section 3.8) for men with advanced metastatic prostate cancer

Optimal treatment.