Gonadotropin-releasing hormone (GnRH) analogues in Prostate Cancer

Triptorelin (Decapeptyl® and Gonapeptyl®), leuprorelin (Prostap®) and goserelin (Zoladex®) are gonadotrophin releasing hormone (GnRH) analogues that are licensed for monthly, 3-monthly or 6-monthly treatment for a number of indications including prostate cancer, endometriosis, uterine fibroids, and central precocious puberty (CPP).\(^1\)\(^-\)\(^4\) For the treatment of endometriosis, as a class GnRH analogues are considered to have comparable efficacy.\(^5\) In Oxfordshire, triptorelin is the only recommended GnRH analogue for Central precocious puberty (CPP) as part of Shared Cared arrangement. This guideline focuses on GnRH analogues in prostate cancer.

In Oxfordshire, the recommended first-line GnRH analogue for the treatment of prostate cancer is triptorelin SR 22.5mg, which is a 6-monthly preparation and has the advantage of saving on both GP and patient consultation time.\(^6\)\(^,\)\(^7\) It is the cheapest long acting GnRH analogues available and an additional discount is available for GPs purchasing directly via the manufacturer.\(^8\) Uro-oncologists at the OUH recommend triptorelin as an option for suitable patients.\(^6\)\(^,\)\(^7\) Existing patients on goserelin or leuprorelin may be switched to triptorelin if appropriate, without concern for any potential testosterone flare response, as even in patients where a GnRH analogue has been ceased intentionally (particularly those on long term therapy); an extended period of time usually passes prior to noting rising testosterone levels.\(^6\)\(^,\)\(^7\)\(^,\)\(^9\) The first dose should be a monthly preparation (Decapeptyl® SR 3mg) to ensure the drug is tolerated and 6-monthly preparation should only be used for patients on long term treatment.\(^6\)\(^,\)\(^7\)

There is limited comparative data of different GnRH analogues, while available evidence suggests that GnRH analogues are similar in effectiveness to surgical castration and that no one GnRH analogue is superior to another in terms of adverse effects.\(^5\)\(^,\)\(^10\)\(^-\)\(^12\) The table below shows comparison of doses, frequency of administration and costs of GnRH analogues for the treatment of prostate cancer.\(^1\)\(^-\)\(^4\)\(^,\)\(^12\)\(^-\)\(^16\)

- Triptorelin is administered via a smaller sized needle (20 gauge) compared with goserelin LA 10.8mg (14 gauge), therefore minimising discomfort to patients.\(^12\)
- Drugs which raise prolactin levels, e.g. antipsychotics should not be prescribed concomitantly as they reduce GnRH receptors in the pituitary. The SPC advises caution with triptorelin and it is recommended that the patient’s hormonal status be supervised.\(^1\)\(^,\)\(^3\)\(^,\)\(^12\)
- Subcutaneously administered GnRH analogues (goserelin or leuprorelin) may be preferable in anti-coagulated patients, rather than triptorelin.\(^1\)\(^-\)\(^4\)\(^,\)\(^13\)\(^-\)\(^16\)
<table>
<thead>
<tr>
<th>Drug</th>
<th>Goserelin</th>
<th>Leuprorelin acetate</th>
<th>Triptorelin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand and dose</strong></td>
<td>Zoladex® 3.6mg</td>
<td>Zoladex LA® 10.8mg</td>
<td>Prostap® SR DCS 3.75 mg</td>
</tr>
<tr>
<td><strong>Indications</strong></td>
<td>1,2,3,4,5</td>
<td>1,2,3,4,5</td>
<td>1,2,3,4,5</td>
</tr>
<tr>
<td><strong>Administration interval</strong></td>
<td>4-weekly</td>
<td>12 weekly</td>
<td>Monthly</td>
</tr>
<tr>
<td><strong>Form</strong></td>
<td>Implant in prefilled syringe</td>
<td>Implant in prefilled syringe</td>
<td>Powder and Solvent in prefilled syringe</td>
</tr>
<tr>
<td><strong>Needle safety device</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Needle size</strong></td>
<td>16 gauge</td>
<td>14 gauge</td>
<td>23 gauge</td>
</tr>
<tr>
<td><strong>Injection route</strong></td>
<td>S/C</td>
<td>S/C or I/M</td>
<td>S/C</td>
</tr>
<tr>
<td><strong>NHS list price</strong></td>
<td>£65.00</td>
<td>£235.00</td>
<td>£75.24</td>
</tr>
<tr>
<td><strong>Drug cost per year</strong></td>
<td>£845.00</td>
<td>£1018.33</td>
<td>£902.88</td>
</tr>
</tbody>
</table>

**Indications:**
1. Metastatic prostate cancer.
2. Locally advanced prostate cancer, as an alternative to surgical castration.
3. As an adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.
4. As neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.
5. As an adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression.
6. Locally advanced, non-metastatic prostate cancer, as an alternative to surgical castration.
7. Treatment of hormone dependent locally advanced or metastatic prostate cancer.

**Action Points:**
- 6-monthly triptorelin SR 22.5mg should be used as first line GnRH analogue in the treatment of prostate cancer. The first dose should be a monthly preparation to ensure tolerance.
- Switch existing patients to triptorelin SR 22.5mg if appropriate.

**Degarelix (Firmagon®)** may be initiated by specialists in line with NICE TA404, Degarelix for treating advanced hormone-dependent prostate cancer.

Criteria for initiation:
- Only for men presenting with newly-diagnosed prostate cancer with spine metastases and back pain requiring more than simple analgesia or patients with associated neurological deficit (spinal cord or nerve root compression clinically or on MRI imaging).
- In these cases specialists will prescribe the 2 initial degarelix injections (240mg total) in the hospital and the patient will receive them in the clinic as this will provide faster suppression of testosterone and should relieve symptoms more quickly. Patients will not be prescribed bicalutamide 50mg.
- The GP will then be asked to prescribe and administer subsequent injections (80mg) on a monthly basis.

Estimated use for 9 – 12 patients per year in Oxfordshire.

Approved by APCO November 2016, updated July 2017
Reference:
9. Personal communication. Mr Ben Challacombe, Consultant Urological Surgeon and Hon Senior Lecturer Surgical Tutor for Guys & St Thomas Hospitals and colleagues. 14th April 2013.

Approved by APCO November 2016, updated July 2017