

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}

| Drug | Goserelin | | Leuprorelin acetate | | Triptorelin | | | |
|-----------------------------|---------------------------------|--|---|---|--|--|--|---|
| Brand and dose | Zoladex® 3.6mg ¹³ | Zoladex LA® 10.8mg ¹⁴ | Prostap® SR DCS 3.75 mg ¹⁵ | Prostap® 3 DCS 11.25 mg ¹⁶ | Decapeptyl® SR 3 mg ³ | Gonapeptyl Depot® 3.75 mg ⁴ | Decapeptyl® SR 11.25 mg ² | Decapeptyl® SR 22.5 mg ¹ |
| Indications* | 1,2,3,4,5 | 1,2,3,4,5 | 1,2,3,4,5 | 1,2,3,4,5 | 1,3,4,5,6 | 7 | 1,3,4,5,6 | 1,3,4,5,6 |
| Administration interval | 4-weekly | 12 weekly | Monthly | 3- monthly | 4-weekly | 4-weekly | 3-monthly | 6-monthly |
| Form | Implant in prefilled syringe | Implant in prefilled syringe | Powder and Solvent in prefilled syringe | Powder and Solvent in Prefilled syringe | Powder for suspension with diluent | Powder and solvent in prefilled syringes | Powder for suspension with diluent | Powder for suspension with diluent |
| Needle safety device | Yes | Yes | Yes | Yes | No | No | No | No |
| Needle size | 16 gauge | 14 gauge | 23 gauge | 23 gauge | 20 gauge | 21 gauge | 20 gauge | 20 gauge |
| Injection route | S/C | S/C | S/C or I/M | S/C | I/M | S/C or I/M | I/M | I/M |
| NHS list price ⁸ | £65.00 | £235.00 | £75.24 | £225.72 | £69.00 | £81.69 | £207.00 | £414.00 |
| Drug cost per year | £845.00 | £1018.33 | £902.88 | £902.88 | £897.00 | £1061.97 | £828.00 | £828.00 |

*** 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.^{6,7}
- Switch existing patients to **triptorelin SR 22.5mg** if appropriate.^{6,7}

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 backpain 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.

Reference:

1. Summary of Product Characteristics. Decapeptyl® SR 22.5mg. Ipsen Ltd. Last updated 06/05/2016. Accessed on 26/10/2016 via <https://www.medicines.org.uk/emc/medicine/24154>
2. Summary of Product Characteristics. Decapeptyl® SR 11.25mg. Ipsen Ltd. Last updated 06/05/2016. Accessed on 26/10/2016 via <http://www.medicines.org.uk/emc/medicine/13851/SPC/Decapeptyl+SR+11.25mg>
3. Summary of Product Characteristics. Decapeptyl® SR 3mg Ipsen Ltd. Last updated 06/05/2016. Accessed on 26/10/2016 via <http://www.medicines.org.uk/emc/medicine/868>
4. Summary of Product Characteristics. Gonapeptyl Depot® 3.75mg. Ferring Pharmaceuticals Ltd. Last updated 29/09/2015. Accessed on 26/10/2016 via <http://www.medicines.org.uk/emc/medicine/12870>
5. London New Drugs Group APC/DTC Briefing Document. Triptorelin and GnRH Analogues Review. Feb 2007 (updated Nov 2007). <http://www.medicinesresources.nhs.uk/upload/documents/News/2008%20-%20March/17/Triptorelin1107.pdf>
6. Oxfordshire Clinical Commissioning Group. Prescribing Points Volume 25 Issue 3. April 2014. Available via <http://www.oxfordshireccg.nhs.uk/wp-content/uploads/2014/04/Prescribing-Points-April-2014-RK2.pdf>
7. Oxfordshire Clinical Commissioning Group. Prescribing Points Volume 22.05. April 2013. Available via <http://www.oxfordshireccg.nhs.uk/wp-content/uploads/2013/08/Prescribing-Points-Vol-22-05-Strontium-IFR-Gonadotrophins-and-Temazepam-Costs.pdf>
8. Drug tariff. NHSBSA prescription services. October 2016. Available via http://www.nhsbsa.nhs.uk/PrescriptionServices/Documents/PPD%20Drug%20Tariff/October_2016.pdf
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.
10. National Institute for Health and Care Excellence. Clinical Guideline 175. Prostate cancer: diagnosis and treatment. NICE, 2014. Available via <http://www.nice.org.uk/guidance/CG175>
11. NICE Evidence Summary. Prostate cancer: triptorelin (Decapeptyl® SR). New medicine [ESNM30]. Jan 2014. Accessed on 26/10/2016 via <https://www.nice.org.uk/advice/esnm30/chapter/Key-points-from-the-evidence>
12. PrescQIPP. Bulletin 88. Luteinising hormone-releasing hormone (LHRH) agonists in prostate cancer. April 2015.
13. Summary of Product Characteristics. Zoladex® 3.6mg implant. AstraZeneca UK Ltd. Last updated 22/06/2015. Accessed on 26/10/2016 via <http://www.medicines.org.uk/emc/medicine/7855>
14. Summary of Product Characteristics. Zoladex LA® 10.8mg implant. AstraZeneca UK Ltd. Last updated 22/06/2015. Accessed on 26/10/2016 via <http://www.medicines.org.uk/emc/medicine/8146>
15. Summary of Product Characteristics. Prostav® SR DCS 3.75 mg. Takeda UK Ltd. Last updated 05/04/2016. Accessed on 26/10/2016 via <http://www.medicines.org.uk/emc/medicine/24679>
16. Summary of Product Characteristics. Prostav® 3 DCS 11.25 mg. Takeda UK Ltd. Last updated 05/04/2016. Accessed on 26/10/2016 via <http://www.medicines.org.uk/emc/medicine/24680>