Evidence summary: new medicine

ESNM30: Prostate cancer: triptorelin (Decapeptyl SR)

Published: 13 January 2014

Key points from the evidence

Summary

In 2013, the licensed indications for the luteinising hormone-releasing hormone (LHRH) agonist, triptorelin (Decapeptyl SR), were extended to include 2 new indications for prostate cancer: neoadjuvant treatment before radiotherapy in high-risk localised or locally advanced disease, and adjuvant treatment to radical prostatectomy in locally advanced disease at high risk of progression. These are based on limited clinical data on the use of triptorelin and extrapolation from evidence for other LHRH agonists.

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>• In 2 single-arm randomised controlled trials (n=28 and n=50), compared with baseline, neoadjuvant triptorelin for 2 or 3 months before radiotherapy statistically significantly reduced prostate volume (p&lt;0.001). In 1 study (n=50) it also reduced prostate-specific antigen levels (p&lt;0.001).</td>
<td>• An initial increase in testosterone levels can cause transient worsening of signs and symptoms of prostate cancer in the first weeks.</td>
</tr>
<tr>
<td>• There are no clinical studies of triptorelin as adjuvant treatment to radical prostatectomy.</td>
<td>• LHRH agonists may reduce bone mineral density, increase the risk of depression and cause metabolic changes (glucose intolerance and increased risk of cardiovascular disease).</td>
</tr>
</tbody>
</table>
**Patient factors**

- Intramuscular injection every 4 weeks, 3 months or 6 months.
- An almost complete suppression of testosterone levels can cause hot flushes, erectile dysfunction and decreased libido.

**Resource implications**

- Decapeptyl SR costs £69.00 for the 3 mg formulation (given every 4 weeks), £207.00 for the 11.25 mg formulation (given every 3 months) and £414.00 for the 22.5 mg formulation (given every 6 months).

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**Key points**

Triptorelin is an LHRH (also called gonadotropin-releasing hormone [GnRH]) agonist licensed for use in prostate cancer. In May 2013, the indications for the Decapeptyl SR brand of triptorelin (3 mg, 11.25 mg and 22.5 mg formulations) were extended to include:

- neoadjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer, and
- adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression.

The licence application for neoadjuvant treatment before radiotherapy in patients with high-risk localised or locally advanced prostate cancer was supported by clinical data from 8 studies. Two of these were prospective single-arm studies of triptorelin that investigated change in prostate volume (Samper et al. 2006 and Ozyigit et al. 2003). The other 6 studies were randomised controlled trials of other LHRH agonists, mainly goserelin, which showed benefits in terms of disease progression or survival. The use of LHRH agonists as neoadjuvant treatment before radiotherapy is supported by the NICE clinical guideline on the diagnosis and treatment of prostate cancer, which was updated in January 2014. However, there are no long-term, patient-oriented outcome studies of triptorelin in this population.

Clinical data from 7 studies were submitted in support of the licence application for adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression. None of these trials used triptorelin. Goserelin was used in some trials, but androgen deprivation therapy with anti-androgens or orchidectomy was also used. The UKPAR document states that there is a lack of data to support the benefit of LHRH agonists in
this population. The NICE guideline on the diagnosis and treatment of prostate cancer does not recommend adjuvant hormonal therapy in addition to radical prostatectomy, even to men with margin-positive disease, other than in the context of a clinical trial. However, goserelin (Zoladex) and leuprorelin (Prostap) are licensed for adjuvant use to radical prostatectomy, and the licensed indications for triptorelin (Decapeptyl SR) were extended to be consistent with these.

Local decision makers will need to consider the evidence for triptorelin alongside that for other LHRH agonists. Individual patient factors, and the licensed indications, dosage intervals and costs of the various LHRH agonists available will need to be taken into account in the context of NICE guidance.

**Key evidence**


**About this evidence summary**

‘Evidence summaries: new medicines’ provide summaries of key evidence for selected new medicines, or for existing medicines with new indications or formulations, that are considered to be of significance to the NHS. The strengths and weaknesses of the relevant evidence are critically reviewed within this summary to provide useful information for those working on the managed entry of new medicines for the NHS, **but this summary is not NICE guidance.**

**Relevance to NICE guidance programmes**

This evidence summary relates to the use of the luteinising hormone-releasing hormone (LHRH) agonist, triptorelin, for the 2 additional prostate cancer indications added in 2013:

- neoadjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer, and
adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression.

These uses of triptorelin were not considered appropriate for a NICE technology appraisal and are not currently planned into any other work programme.

The NICE clinical guideline on the diagnosis and treatment of prostate cancer was updated in January 2014. This covers the use of androgen deprivation therapy (also known as hormonal therapy), which includes the use of LHRH agonists (see Introduction section).

Introduction

The NICE clinical guideline on the diagnosis and treatment of prostate cancer, which was updated in January 2014, recommends that men with localised disease should be offered active surveillance, or radical treatment with prostatectomy (surgical removal of the prostate) or radiotherapy. For men with intermediate- and high-risk localised prostate cancer, a combination of radical radiotherapy and androgen deprivation therapy (also known as hormonal therapy), rather than radical radiotherapy or androgen deprivation therapy alone, is recommended. Six months of androgen deprivation therapy before, during or after radical external beam radiotherapy is recommended. The guideline recommends considering continuing androgen deprivation therapy for up to 3 years for men with high-risk localised prostate cancer and discussing the benefits and risks of this option with them. Hormonal therapy is also recommended for men with prostate cancer who experience a biochemical relapse after radical (prostatectomy or radiotherapy) treatment if they have symptomatic local disease progression, metastases or a prostate-specific antigen (PSA) doubling time of less than 3 months.

Advanced prostate cancer is defined as locally advanced or metastatic disease (that is, where the cancer has spread beyond the prostatic capsule). For locally advanced disease, the NICE clinical guideline on Prostate cancer: diagnosis and treatment recommends considering pelvic radiotherapy in men with locally advanced prostate cancer who have a higher than 15% risk of pelvic lymph node involvement and who are to receive neoadjuvant hormonal therapy and radical radiotherapy. Adjuvant hormonal therapy in addition to radical prostatectomy is not recommended, even in men with margin-positive disease, other than in the context of a clinical trial.

In metastatic prostate cancer, standard treatments are continuous luteinising hormone-releasing hormone (LHRH) agonist therapy or bilateral orchidectomy (surgical removal of the testes).
LHRH (also called gonadotropin-releasing hormone [GnRH]) agonists licensed for use in prostate cancer are goserelin, leuprorelin, triptorelin, buserelin and histrelin. Other hormonal therapies licensed for use in prostate cancer include degarelix (an LHRH antagonist) and anti-androgens (such as cyproterone acetate, flutamide and bicalutamide).

Product overview

Drug action

Triptorelin is a decapeptide analogue of luteinising hormone-releasing hormone (LHRH, also called gonadotropin-releasing hormone [GnRH]). See summaries of product characteristics: Decapeptyl SR 3 mg (triptorelin acetate), Decapeptyl SR 11.25 mg (triptorelin acetate), and Decapeptyl SR 22.5 mg (triptorelin pamoate).

In men, the first administration of triptorelin stimulates the release of pituitary gonadotropins and leads to a transient increase in testosterone levels ('flare-up'). Prolonged administration leads to a suppression of gonadotropins and a fall in plasma testosterone to 'castrate levels' after approximately 20 days. This is maintained for as long as the drug is administered.

New therapeutic indication

Decapeptyl SR 3 mg (triptorelin acetate), Decapeptyl SR 11.25 mg (triptorelin acetate), and Decapeptyl SR 22.5 mg (triptorelin pamoate) have several indications for prostate cancer.

The original indications were:

- treatment of locally advanced, non-metastatic prostate cancer, as an alternative to surgical castration, and
- treatment of metastatic prostate cancer.

In November 2011, the indications were extended to include:

- adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.

In May 2013, indications were further extended to include:
neoadjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer, and

adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression.

This evidence summary covers these last 2 indications.

Course and cost

Triptorelin (Decapeptyl SR) is available in 3 formulations for prostate cancer:

- Decapeptyl SR 3 mg for intramuscular injection every 4 weeks (28 days)
- Decapeptyl SR 11.25 mg for intramuscular injection every 3 months, and
- Decapeptyl SR 22.5 mg for intramuscular injection every 6 months.

Triptorelin (Decapeptyl SR) is supplied as a powder and solvent for suspension for injection. It must be reconstituted using an aseptic technique and only using the ampoule of mannitol solution 0.8% for injection that is provided as the suspension vehicle with the 3 mg and 11.25 mg formulation or the ampoule of 'water for injections' that is provided with the 22.5 mg formulation. No dosage adjustment is necessary for older people. See summaries of product characteristics: Decapeptyl SR 3 mg (triptorelin acetate), Decapeptyl SR 11.25 mg (triptorelin acetate), and Decapeptyl SR 22.5 mg (triptorelin pamoate).

The cost of Decapeptyl SR is £69.00 for the 3 mg formulation, £207.00 for the 11.25 mg formulation and £414.00 for the 22.5 mg formulation (costs taken from MIMS December 2013 and excluding VAT).

Evidence review

As outlined in the summaries of product characteristics for Decapeptyl SR 3 mg (triptorelin acetate), Decapeptyl SR 11.25 mg (triptorelin acetate) and Decapeptyl SR 22.5 mg (triptorelin pamoate), the efficacy and safety of triptorelin in locally advanced or metastatic prostate cancer (the original licensed indication) was determined in clinical studies involving 645 patients. In these studies, triptorelin reduced testosterone to 'castrate levels' at least as rapidly as surgical
pulpectomy and was as effective as surgical castration in the long-term palliative treatment of locally advanced or metastatic prostate cancer.

The extension of the licence in November 2011 to include adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer was supported by a phase III randomised controlled trial that included 970 patients with locally advanced prostate cancer (Bolla et al. 2009). In this trial, triptorelin was administered to 62% of patients and goserelin to 30%; the other patients received other types of luteinising hormone-releasing hormone (LHRH) agonist or switched to triptorelin during treatment. The combination of radiotherapy plus 6-month treatment with an LHRH agonist was inferior to radiotherapy plus 3-year treatment with an LHRH agonist for prostate cancer-specific survival and overall survival. The 5-year all-cause mortality rate was 15.2% for the long-term group and 19.0% for the short-term group (hazard ratio 1.42, 95.71% confidence interval 1.09 to 1.85). However, overall quality of life did not differ statistically significantly between the 2 groups.

Evidence to support the most recent licence extensions (in May 2013) is given in the UKPAR document for Decapeptyl SR 22.5 mg (Annex 2) and is reviewed here. The reason given for these licence extensions is to further define the target population and align with current clinical practice and uro-oncology clinical guidelines.

For adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression, the summaries of product characteristics state that: 'The use of a LHRH agonist may be considered after radical prostatectomy in selected patients considered at high risk of disease progression. There are no disease-free survival data or survival data with triptorelin in this setting'.

Clinical data from 7 studies were submitted in support of this licence extension. None of these trials used triptorelin. Some used goserelin, but androgen deprivation therapy with anti-androgens or orchidectomy was also used.

For neoadjuvant treatment before radiotherapy in patients with high-risk localised or locally advanced prostate cancer, the summaries of product characteristics state that: 'Neoadjuvant triptorelin prior to radiotherapy has been shown to significantly reduce prostate volume'.

The UKPAR document states that this licence extension is supported by clinical data from 8 studies, 2 of which were prospective single-arm studies of triptorelin that investigated the
change in prostate volume (Samper et al. 2006 and Ozyigit et al. 2003). The other 6 studies were randomised controlled trials of other LHRH agonists, mainly goserelin, which showed benefits in terms of disease progression or survival.

Samper et al. (2006)

- **Design:** prospective, single-arm study to investigate change in prostate volume after 2 months of neoadjuvant triptorelin therapy before radiotherapy.

- **Population:** 28 patients (average age 68 years) with localised histologically confirmed prostate adenocarcinoma referred for conformal 3-dimensional radical radiotherapy. Nineteen patients were at high risk, defined as having a T3 or Gleason score greater than 7 or a prostate-specific antigen (PSA) level greater than 20 ng/ml.

- **Intervention:** intramuscular triptorelin 11.25 mg every 3 months in combination with flutamide 250 mg 3 times a day as neoadjuvant treatment for 2 months before radiotherapy. Patients at low risk received no further hormone treatment. Patients at medium risk were treated until the end of radiotherapy. Patients at high risk were treated for up to 2 years.

- **Outcomes and results:** prostate volume was calculated before and after 2 months of neoadjuvant hormone therapy, based on transrectal ultrasound. After 2 months, mean prostate volume was reduced by 24% (from 50.65±31.96 cm³ [range 18.7 to 137 cm³] to 38.97±22.8 cm³ [range 14.9 to 114 cm³]; p<0.001). There were also statistically significant reductions in radiotherapy planning volumes and in radiation doses administered to normal surrounding tissues (bladder and rectum).

Ozyigit et al. (2003)

- **Design:** prospective, single-arm study to investigate change in prostate volume after 3 months of neoadjuvant triptorelin therapy before radiotherapy.

- **Population:** 50 patients (median age 68 years) with histologically confirmed prostate adenocarcinoma, stage T1–T3bN0M0. Forty patients were at high risk, defined as having stage T2b to T3b or a Gleason score of at least 7 or a PSA level of 10 ng/ml or greater.

- **Intervention and comparison:** 47 patients received intramuscular triptorelin 3.75 mg every month in combination with cyproterone acetate 300 mg every 2 weeks as neoadjuvant treatment for 12 weeks before radiotherapy. Three patients received goserelin instead of
triptorelin. Patients at low risk received no further hormone treatment. Patients at high risk received a further 24 weeks of adjuvant hormone treatment.

- Outcomes and results: prostate volume was based on transrectal ultrasound. Before neoadjuvant hormone treatment, median prostate volume was 38 cm$^3$ (range 15–105 cm$^3$). After 12 weeks' treatment (before radiotherapy), median prostate volume was 28 cm$^3$ (range 14.5–65 cm$^3$), which was a statistically significant reduction (p<0.001). PSA levels were also statistically significantly reduced from a median of 15 ng/ml to 1.05 ng/ml (p<0.001).

**Clinical effectiveness**

**Neoadjuvant treatment before radiotherapy in patients with high-risk localised or locally advanced prostate cancer**

The studies by Samper et al. (2006) and Ozyigit et al. (2003) show that neoadjuvant triptorelin before radiotherapy significantly reduces prostate volume (and PSA levels in Ozyigit et al. 2003).

However, there are no comparative studies of triptorelin as neoadjuvant treatment before radiotherapy or studies with patient-oriented outcomes, such as survival rates or effects on quality of life. In the UKPAR document, 6 additional trials using other LHRH agonists are used to support this licence extension. In several of these trials, neoadjuvant goserelin or leuprorelin before radiotherapy demonstrated clinical benefits on overall survival or prostate cancer-specific survival compared with radiotherapy alone (Roach et al. 2008, Denham et al. 2011, Jones et al. 2011).

**Adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression**

None of the trials used to support this licence extension used triptorelin. Goserelin was used in some trials, but androgen deprivation therapy with anti-androgens or orchidectomy was also used. The UKPAR document states that there is a lack of data to support the benefit of LHRH agonists as adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression. In a trial by Messing et al. (2006), long-term adjuvant treatment with goserelin or bilateral orchidectomy did demonstrate clinical benefits on overall survival or prostate cancer-specific survival in men undergoing radical prostatectomy. However, this trial has limitations (see Likely place in therapy section).
Safety

As with other LHRH agonists or after surgical castration, the most common adverse effects of triptorelin are a result of its expected pharmacological effects: an initial increase in testosterone levels, followed by almost complete suppression of testosterone. These adverse effects include hot flushes, erectile dysfunction and decreased libido. See summaries of product characteristics: Decapeptyl SR 3 mg (triptorelin acetate), Decapeptyl SR 11.25 mg (triptorelin acetate), and Decapeptyl SR 22.5 mg (triptorelin pamoate).

LHRH agonists may cause a reduction in bone mineral density, and caution is needed in men with established osteoporosis or with risk factors for osteoporosis. Rarely, treatment with LHRH agonists may reveal the presence of a previously unknown gonadotroph cell pituitary adenoma. There is an increased risk of depression (which may be severe) in patients receiving treatment with LHRH agonists, and the summaries of product characteristics state that patients with known depression should be monitored closely during therapy.

Because triptorelin causes a transient increase in serum testosterone levels, transient worsening of signs and symptoms of prostate cancer may occasionally develop during the first weeks of treatment. In these cases, additional administration of a suitable anti-androgen may be needed. As with other LHRH agonists, isolated cases of spinal cord compression or urethral obstruction have been observed, and careful monitoring is indicated during the first weeks of treatment (Summaries of product characteristics: Decapeptyl SR 3 mg, Decapeptyl SR 11.25 mg, and Decapeptyl SR 22.5 mg).

Metabolic changes, such as glucose intolerance, or an increased risk of cardiovascular disease have been seen during androgen deprivation therapy, and the summaries of product characteristics state that patients at high risk should be carefully assessed before starting treatment and their glucose, cholesterol and blood pressure adequately monitored during androgen deprivation therapy.

Evidence strengths and limitations

The most important limitation with the evidence to support the new indications for triptorelin in prostate cancer is the lack of patient-oriented outcome data. The UKPAR document states that no benefits in terms of disease progression or survival can be concluded from the available data on triptorelin.
For the new indication of neoadjuvant treatment before radiotherapy in patients with high-risk localised or locally advanced prostate cancer, studies with triptorelin show only reductions in prostate volume and PSA levels (Samper et al. 2006 and Ozyigit et al. 2003). These outcomes are clinically relevant because there is a consequent reduction in radiotherapy planning volume and, as a result, an increased radiation dose can be delivered to the affected tissues without increasing damage to surrounding normal tissues. However, no studies show directly that neoadjuvant use of triptorelin improves survival or quality of life, although such evidence is available for other LHRH agonists.

For the new indication of adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression, there are no studies at all with triptorelin and the UKPAR document states that there is a lack of data to support the benefit of LHRH agonists in this population.

Context

Treatment alternatives

Several hormonal therapies are licensed for use in prostate cancer. The luteinising hormone-releasing hormone (LHRH; also called gonadotropin-releasing hormone [GnRH]) agonists specifically licensed for neoadjuvant treatment before radiotherapy in patients with high-risk localised or locally advanced prostate cancer, or for adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression are:

- goserelin (Zoladex 3.6 mg implant and Zoladex LA 10.8 mg)
- leuprorelin (Prostap 3 DCS and Prostap SR DCS)
- triptorelin (Decapeptyl SR 3 mg, Decapeptyl SR 11.25 mg, Decapeptyl SR 22.5 mg).

Another triptorelin product (Gonapeptyl depot 3.75 mg) is available, but it is licensed for the narrower indication of hormone-dependent locally advanced or metastatic prostate cancer. Other LHRH agonists licensed for use in prostate cancer, but not for these specific indications, are buserelin (Suprefact nasal spray and Suprefact injection) and histrelin (Vantas 50 mg implant). Other hormonal therapies licensed for use in prostate cancer include the LHRH antagonist, degarelix (Firmagon 80 mg injection and Firmagon 120 mg injection), and anti-androgens, such
as cyproterone acetate, flutamide and bicalutamide (generic or Casodex 50 mg tablet and Casodex 150 mg tablet).

See the summaries of product characteristics and Likely place in therapy section for details of the indications.

### Costs of treatment alternatives

<table>
<thead>
<tr>
<th>Drug</th>
<th>1-month treatment&lt;sup&gt;a&lt;/sup&gt;</th>
<th>3-month treatment&lt;sup&gt;a&lt;/sup&gt;</th>
<th>6-month treatment&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goserelin</td>
<td>Zoladex 3.6 mg implant £65.00&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Zoladex LA 10.8 mg £235.00&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-</td>
</tr>
<tr>
<td>Leuprorelin</td>
<td>Prostap SR DCS 3.75 mg £75.24&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Prostap 3 DCS 11.25 mg £225.72&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-</td>
</tr>
<tr>
<td>Triptorelin</td>
<td>Decapeptyl SR 3 mg £69.00&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Decapeptyl SR 11.25 mg £207.00&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Decapeptyl SR 22.5 mg £414.00&lt;sup&gt;c&lt;/sup&gt;</td>
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</tbody>
</table>

<sup>a</sup> Doses and dosage intervals taken from the relevant summary of product characteristics. These do not imply therapeutic equivalence, and the specific indications for prostate cancer vary.

<sup>b</sup> Costs are excluding VAT; taken from Drug Tariff November 2013.

<sup>c</sup> Costs are excluding VAT; taken from MIMS November 2013.

### Estimated impact for the NHS

### Likely place in therapy

The reason given in the UKPAR document for the most recent licence extensions for triptorelin (Decapeptyl SR 3 mg, Decapeptyl SR 11.25 mg, Decapeptyl SR 22.5 mg) in prostate cancer is to further define the target population and align with current clinical practice and uro-oncology clinical guidelines.

For neoadjuvant treatment before radiotherapy in patients with high-risk localised or locally advanced prostate cancer, the summaries of product characteristics for triptorelin state that:
'Neoadjuvant triptorelin prior to radiotherapy has been shown to significantly reduce prostate volume.'

Although this indication is not supported by direct evidence that triptorelin produces benefits in terms of disease progression or survival in this population, trials of neoadjuvant goserelin or leuprorelin before radiotherapy have demonstrated such clinical benefits (Roach et al. 2008; Denham et al. 2011; Jones et al. 2011). The UKPAR document states that the results of these other studies can be used to support this indication because it is widely accepted that the efficacy of luteinising hormone-releasing hormone (LHRH) analogues in prostate cancer depends on the reduction of testosterone to 'castrate levels', and triptorelin has shown this.

Goserelin (Zoladex 3.6 mg implant and Zoladex LA 10.8 mg) also has an indication for neoadjuvant treatment before radiotherapy in patients with high-risk localised or locally advanced prostate cancer. However, leuprorelin (Prostap 3 DCS and Prostap SR DCS) does not.

This indication is also consistent with the NICE clinical guideline on the diagnosis and treatment of prostate cancer, which was updated in January 2014. For men with intermediate- and high-risk localised prostate cancer, the guideline recommends a combination of radical radiotherapy and androgen deprivation therapy (also known as hormonal therapy), rather than radical radiotherapy or androgen deprivation therapy alone. Six months of androgen deprivation therapy before, during or after radical external beam radiotherapy is recommended. The guideline recommends considering continuing androgen deprivation therapy for up to 3 years for men with high-risk localised prostate cancer and discussing the benefits and risks of this option with them.

For adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression, the summaries of product characteristics for triptorelin state that: 'The use of a LHRH agonist may be considered after radical prostatectomy in selected patients considered at high risk of disease progression. There are no disease-free survival data or survival data with triptorelin in this setting'.

This licence extension is not supported by any clinical data from studies with triptorelin. There are some clinical data with goserelin or androgen deprivation therapy with anti-androgens or orchidectomy. However, the UKPAR document suggests that there is a lack of data to support the use of LHRH analogues in general as adjuvant treatment to prostatectomy in this population. A trial by Messing et al. (2006), which found long-term adjuvant treatment with goserelin or bilateral orchidectomy was beneficial in this population may not be fully generalisable to current
clinical practice. Prostate-specific antigen (PSA) levels were not considered when making the
decision to start treatment in the observation arm of this trial. The trial has also been criticised
because of its small sample size and an imbalance between treatment groups.

Some other LHRH agonists, goserelin (Zoladex 3.6 mg implant and Zoladex LA 10.8 mg) and
leuprorelin (Prostap 3 DCS and Prostap SR DCS), are also indicated for adjuvant treatment to
radical prostatectomy. However, as with triptorelin, the summaries of product characteristics point
out the limitations of the evidence. The goserelin summary of product characteristics states:
'After prostatectomy, in patients found to have extra-prostatic tumour spread, adjuvant Zoladex
may improve disease-free survival periods, but there is no significant survival improvement
unless patients have evidence of nodal involvement at time of surgery. Patients with
pathologically staged locally advanced disease should have additional risk factors such as PSA
of at least 10 ng/mL or a Gleason score of at least 7 before adjuvant Zoladex should be
considered'. For leuprorelin, the summary of product characteristics states: 'The use of a LHRH
agonist may be considered after prostatectomy in selected patients considered at high risk of
disease progression. There are no disease-free survival data or survival data with leuprorelin
acetate in this setting'.

The use of LHRH agonists for adjuvant treatment in addition to radical prostatectomy is not
recommended by the NICE clinical guideline on the diagnosis and treatment of prostate cancer,
even in men with margin-positive disease, other than in the context of a clinical trial.

Triptorelin (Decapeptyl SR) is available in 3 formulations for intramuscular injection every
4 weeks, every 3 months, or every 6 months. Another triptorelin product (Gonapeptyl depot
3.75 mg) is available as a 1-monthly preparation, but is licensed for the narrower indication of
hormone-dependent locally advanced or metastatic prostate cancer.

The alternative LHRH agonists, goserelinit and leuprorelin are both available in 1-monthly and
3-monthly, but not 6-monthly, preparations. Goserelin is licensed for both neoadjuvant treatment
before radiotherapy in patients with high-risk localised or locally advanced prostate cancer, and
as adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer
at high risk of disease progression. Leuprorelin is licensed for adjuvant treatment to radical
prostatectomy in patients with locally advanced prostate cancer at high risk of disease
progression, but not neoadjuvant treatment before radiotherapy in patients with high-risk
localised or locally advanced prostate cancer.
The LHRH agonist, histrelin, is available as a 12-monthly implant (Vantas 50 mg implant) and is licensed for the palliative treatment of advanced prostate cancer. Buserelin is also available for the treatment of advanced hormone-dependent prostatic carcinoma as an injection (Suprefact injection) for use subcutaneously at 8-hourly intervals for 7 days and a nasal spray (Suprefact nasal spray) given 6 times a day from day 8.

Local decision makers will need to consider the evidence for triptorelin alongside that for other LHRH agonists. Individual patient factors, the licensed indications, dosage intervals and costs of the various LHRH agonists will need to be considered in the context of NICE guidance.

**Estimated usage**

It is not possible to provide estimated usage based on the available data.

**References**

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Ipsen Limited (2013) Decapeptyl SR 3 mg, Decapeptyl SR 11.25 mg and Decapeptyl SR 22.5 mg summaries of product characteristics [online; accessed 4 October 2013]


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Sanofi (2013) Suprefact nasal spray and Suprefact injection summaries of product characteristics [online; accessed 4 October 2013]

Takeda UK Limited (2013) Prostap 3 DCS and Prostap SR DCS summaries of product characteristics [online; accessed 4 October 2013]
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For information about the process used to develop this evidence summary, see Evidence summaries: new medicines – integrated process statement.

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