

# GnRH Agonists: Utilisation analysis

## Drug utilisation sub-committee (DUSC)

*June 2019*

### **Abstract**

#### ***Purpose***

To review the utilisation of gonadotrophin-releasing hormone (GnRH) agonists for the treatment of carcinoma of the prostate, central precocious puberty, breast cancer, endometriosis, and anticipated premature ovarian failure.

#### ***Date of listing on PBS***

Leuprorelin: 1 August 1986  
Goserelin: 1 April 1989  
Nafarelin: 1 October 1994  
Triptorelin: 1 February 2009

#### ***Data Source / methodology***

The analysis used Pharmaceutical Benefits Scheme (PBS) prescription data for prescriptions supplied from 1 January 2014 to 31 December 2018.

#### ***Key Findings***

- The total number of prescriptions dispensed for GnRH agonists is growing. However, due to a price decrease that applied to products containing goserelin and leuprorelin on 1 June 2018, the cost to government in 2018 was less than in 2017.
- Majority of prescriptions (70% in 2018) were supplied to male patients.
- There were 46,739 patients treated with GnRH agonists in 2018, approximately 80% of patients treated in 2018 were male.
- Length of treatment analysis showed approximately 80% of patients identified as being treated for endometriosis are treated for no more than six months.

## Purpose of analysis

To review the utilisation of gonadotrophin-releasing hormone (GnRH) agonists for the treatment of carcinoma of the prostate, central precocious puberty, breast cancer, endometriosis, and anticipated premature ovarian failure.

At its February 2019 meeting DUSC noted the use of GnRH agonists had increased since the change of the restrictions from Authority Required and Authority Required (STREAMLINED) listings to Restricted Benefits (from 1 May 2015 for goserelin and from 1 October 2016 for leuprorelin, triptorelin and nafarelin).

## Background

### Clinical situation

GnRH agonists (goserelin, leuprorelin, triptorelin, nafarelin) are used in the treatment of:

- carcinoma of the prostate,
- central precocious puberty (CPP),
- breast cancer,
- endometriosis, and
- anticipated premature ovarian failure.

Nafarelin and triptorelin are also PBS listed for use in assisted reproduction, these listings are not considered in this review.

### Pharmacology

GnRH agonists are used to lower the amount of sex hormones in the body. In women GnRH agonists (goserelin and nafarelin) reduce the level of oestrogen. In men GnRH agonists (goserelin, triptorelin, and leuprorelin) reduce the level of testosterone.<sup>1</sup>

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<sup>1</sup> Zoladex (goserelin) Consumer Medicine Information, AstraZeneca Pty Ltd, Available from: <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-CMI-04915-3&d=201903011016933>

## Therapeutic Goods Administration (TGA) approved indications

**Table 1: TGA indications for GnRH agonists**

Indication	Goserelin	Goserelin & bicalutamide	Leuprorelin	Leuprorelin & bicalutamide	Triptorelin	Nafarelin
Locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate	✓		✓		✓	
Advanced prostate cancer		✓		✓		
Central precocious puberty			✓			
Breast cancer <sup>a</sup>	✓					
Endometriosis	✓					✓
Uterine fibroids	✓					
Endometrial thinning	✓					
Assisted reproduction	✓					✓

Source: the [Australian Register of Therapeutic Goods](#) .

<sup>a</sup> For advanced breast cancer in premenopausal women, and adjuvant therapy for early breast cancer in pre- and perimenopausal women, who are suitable for hormonal manipulation.

### Contraindications

Although not relevant to the approved indication, leuprorelin acetate is contraindicated in pregnancy due to its embryotoxic effects.<sup>2</sup>

Although not relevant to the approved indication, Lucrin Depot PDS Injection should not be administered to a nursing mother, as it is not known whether leuprorelin acetate is excreted into human milk.<sup>2</sup>

Although not relevant to the approved indication, leuprorelin acetate should not be administered to patients with undiagnosed vaginal bleeding.<sup>2</sup>

Lucrin Depot PDS Injection is contraindicated in patients with known hypersensitivity to leuprorelin acetate or similar nonapeptides or any of the excipients. Isolated cases of anaphylaxis have been reported with the monthly formulation of Lucrin Depot 7.5 mg Injection.<sup>2</sup>

Triptorelin is contraindicated in patients with known hypersensitivity to triptorelin or other GnRH agonist analogues. It is also contraindicated in patients with spinal cord compression secondary to prostate cancer metastases.<sup>3</sup>

Nafarelin should not be administered to patients who are hypersensitive to GnRH, GnRH agonist analogues or any of the excipients in nafarelin, have undiagnosed abnormal vaginal

<sup>2</sup> Leuprorelin PI (Lucrin) <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2009-PI-01299-3>

<sup>3</sup> Triptorelin PI (Decapeptyl) <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2015-PI-01452-1>

bleeding, are pregnant or who may become pregnant while using nafarelin or are breastfeeding.<sup>4</sup>

Bicalutamide is contraindicated in females and children. The combination products containing goserelin with bicalutamide and leuprorelin with bicalutamide are contraindicated in anyone with a known hypersensitivity to bicalutamide or any other constituents of the formulation.<sup>5,6</sup>

Goserelin is contraindicated in patients with known hypersensitivity to GnRH or GnRH agonist analogues.<sup>7</sup>

## Dosage and administration

**Table 2: Dosage and administration of GnRH agonists**

Brand name and sponsor	Product	Dose and frequency of administration
Zoladex Implant AstraZeneca Pty Ltd	goserelin 3.6 mg implant	One 3.6 mg implant of goserelin every 28 days, injected subcutaneously into the anterior abdominal wall.
Zoladex 10.8mg Implant AstraZeneca Pty Ltd	goserelin 10.8 mg implant	One 10.8 mg implant of goserelin every 3 months, injected subcutaneously into the anterior abdominal wall.
ZolaCos CP 3.6/50 AstraZeneca Pty Ltd	goserelin 3.6 mg implant [1 implant] (&) bicalutamide 50 mg tablet [28 tablets]	One 3.6 mg implant of goserelin every 28 days, injected subcutaneously into the anterior abdominal wall. One bicalutamide tablet (50 mg) once a day.
ZolaCos CP 10.8/50(28) ZolaCos CP 10.8/50(84) AstraZeneca Pty Ltd	goserelin 10.8 mg implant [1 implant] (&) bicalutamide 50 mg tablet [28 tablets] goserelin 10.8 mg implant [1 implant] (&) bicalutamide 50 mg tablet [84 tablets]	One 10.8 mg implant of goserelin every 3 months, injected subcutaneously into the anterior abdominal wall. One bicalutamide tablet (50 mg) once a day.
Eligard 1 month PDS Mundipharma Pty Limited	leuprorelin acetate 7.5 mg modified release injection [1 syringe] (&) inert substance diluent [1 syringe],	The recommended dose of Eligard 1 month is one injection every month.
Eligard 3 month PDS	leuprorelin acetate 22.5 mg modified release injection [1	The recommended dose of Eligard 3 month is one injection every three months.

<sup>4</sup> Nafarelin PI (Synarel) <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-05495-3>

<sup>5</sup> Bicalutamide and goserelin composite pack PI (Zolacos CP) <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-06002-3&d=201905021016933>

<sup>6</sup> Bicalutamide and leuprorelin acetate composite pack PI (BI Eligard CP) <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2018-PI-02760-1>

<sup>7</sup> Goserelin PI (Zoladex) <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-04914-3>

<b>Brand name and sponsor</b>	<b>Product</b>	<b>Dose and frequency of administration</b>
Mundipharma Pty Limited	syringe] (&) inert substance diluent [1 syringe]	
Eligard 4 month PDS Mundipharma Pty Limited	leuprorelin acetate 30 mg modified release injection [1 syringe] (&) inert substance diluent [1 syringe]	The recommended dose of Eligard 4 month is one injection every four months.
Eligard 6 month PDS Mundipharma Pty Limited	leuprorelin acetate 45 mg injection: modified release [1] (&) inert substance diluent [1 syringe]	The recommended dose of Eligard 6 month is one injection every six months. The product is injected subcutaneously into areas with adequate amounts of subcutaneous tissue (such as the abdomen) and that do not have excessive pigment, nodules, lesions, or hair.
Lucrin Depot Paediatric 30 mg PDS AbbVie Pty Ltd	leuprorelin acetate 30 mg modified release injection [1 syringe] (&) inert substance diluent [1 syringe]	Administer once every three months (12 weeks) as a single intramuscular injection. Should be discontinued at the appropriate age of onset of puberty at the discretion of the physician. The recommended age at which therapy for CPP should be ceased is at 11 or 12 years of age, for girls and boys respectively.
Lucrin Depot 7.5mg AbbVie Pty Ltd	leuprorelin acetate 7.5 mg injection: modified release [1] (&) inert substance diluent [2 mL syringe]	One intramuscular injection every 4 weeks.
Lucrin Depot 3-Month AbbVie Pty Ltd	leuprorelin acetate 22.5 mg injection: modified release [1] (&) inert substance diluent [2 mL syringe]	One intramuscular injection every 12 weeks.
Lucrin Depot 4-Month AbbVie Pty Ltd	leuprorelin acetate 30 mg injection: modified release [1] (&) inert substance diluent [2 mL syringe]	One intramuscular injection every 16 weeks.
Lucrin Depot 6-Month AbbVie Pty Ltd	leuprorelin acetate 45 mg injection: modified release [1] (&) inert substance diluent [1 syringe]	One intramuscular injection every 24 weeks.
Diphereline 1month formulation Ipsen Pty Ltd	triptorelin 3.75 mg injection [1 vial] (&) inert substance diluent [2 mL ampoule]	One vial administered once a month as a single intramuscular injection
Diphereline 3 month formulation Ipsen Pty Ltd	triptorelin 11.25 mg injection [1 vial] (&) inert substance diluent [2 mL ampoule]	One vial administered every three months as a single intramuscular injection
Diphereline 6 month formulation Ipsen Pty Ltd	triptorelin 22.5 mg injection [1 vial] (&) inert substance diluent [2 mL ampoule]	One vial administered every six months as a single intramuscular injection

Brand name and sponsor	Product	Dose and frequency of administration
Synarel Pfizer Australia Pty Ltd	nafarelin 200 microgram/actuation nasal spray	One spray (200 µg of nafarelin free base) to one nostril in the morning and one spray into the other nostril in the evening (400 µg/day).  The dose may be increased to 800 µg daily. The 800 µg dose is administered as one spray into each nostril in the morning (a total of two sprays) and again in the evening.  The recommended duration of therapy is six months.

Source: Product information for goserelin, leuprorelin, nafarelin, and triptorelin

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from [the TGA \(Product Information\)](#) and [the TGA \(Consumer Medicines Information\)](#).

### PBS listing details (as at 1 March 2019)

The current PBS listings as at 1 March 2019 can be found in Appendix A.

#### Restrictions

All listings included in the analysis are on the General Schedule as Restricted Benefits. The dates that medicines changed restriction levels are summarised in the 'Changes to listings' section below.

**Table 3: PBS restrictions for GnRH agonists**

Indication	Goserelin	Goserelin & bicalutamide	Leuprorelin	Leuprorelin & bicalutamide	Triptorelin	Nafarelin
Locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate	✓		✓		✓	
Metastatic (stage D) carcinoma of the prostate		✓		✓		
Central precocious puberty			✓			
Breast cancer	✓					
Endometriosis	✓					✓
Anticipated premature ovarian failure	✓					

Source: the [PBS website](#).

For details of the current PBS listing refer to the [PBS website](#).

### **Date of listing on PBS**

Leuprorelin: 1 August 1986  
Goserelin: 1 April 1989  
Nafarelin: 1 October 1994  
Triptorelin: 1 Feb 2009

### **Changes to listing**

Goserelin became a Restricted Benefit on 1 May 2015. Leuprorelin, triptorelin and nafarelin became Restricted Benefits on 1 October 2016. Prior to these dates some items were Authority Required and others were Authority Required (STREAMLINED).

**Table 4: Changes to the PBS listings of GnRH agonists**

<b>Drug name</b>	<b>Restriction change</b>	<b>Date</b>
Leuprorelin	Listed for advanced cancer of the prostate	1 August 1986
Goserelin	Listed for advanced cancer of the prostate	1 April 1989
Goserelin	Listed for treatment of premenopausal women with advanced breast cancer	1 August 1993
Goserelin	Listed for short-term treatment (up to 6 months) of visually proven endometriosis.	1 December 1994
Nafarelin	Listed for initial treatment (up to 6 months) of visually proven endometriosis.	1 October 1994
Nafarelin	Listed for subsequent treatment (up to 6 months) of visually proven endometriosis, where 2 years or more have elapsed since the end of the previous course and where a recent bone density assessment has been made.	1 May 2000
Goserelin	Listed for locally advanced (equivalent to stage c) or metastatic (equivalent to stage d) carcinoma of the prostate.	1 February 2004
Goserelin	Listed for hormone-dependent locally advanced (equivalent to stage III) or metastatic (equivalent to stage IV) breast cancer in pre-menopausal women.	1 February 2004
Leuprorelin	Listed for locally advanced (equivalent to stage c) or metastatic (equivalent to stage d) carcinoma of the prostate.	1 February 2004
Goserelin	Listed for locally advanced (equivalent to stage c) or metastatic (equivalent to stage d) carcinoma of the prostate.	1 February 2004
Leuprorelin	Suspension for subcutaneous injection (modified release), 45 mg injection set (6 monthly) listed for locally advanced (equivalent to stage c) or metastatic (equivalent to stage d) carcinoma of the prostate.	1 December 2005
Leuprorelin	Lucrin Depot 7.5 mg, 3 Month and 4 Month listed for locally advanced (equivalent to stage c) or metastatic (equivalent to stage d) carcinoma of the prostate.	1 February 2006
Triptorelin	One month and three month formulations listed for locally advanced (equivalent to stage C) or metastatic (equivalent to stage D) carcinoma of the prostate as Authority Required listings.	1 February 2009
Goserelin	Authority Required listing for hormone-dependent breast cancer as an alternative to adjuvant chemotherapy in peri- or pre-menopausal women.	1 March 2010
Goserelin	Listing for 10.8 mg implant for prostate cancer changed to Streamlined Authority.	1 March 2010

Drug name	Restriction change	Date
Leuprorelin	Listings for leuprorelin changed to Streamlined Authority.	1 April 2010
Triptorelin	Six month formulation listed for locally advanced (equivalent to stage C) or metastatic (equivalent to stage D) carcinoma of the prostate as a Streamlined Authority.	1 November 2010
Goserelin	Listings for 3.6 mg implant for breast cancer, carcinoma of the prostate and endometriosis became restricted benefits.	1 May 2015
Goserelin	Listing for 10.8 mg implant for carcinoma of the prostate became restricted benefit.	1 May 2015
Leuprorelin	Authority Required listing for central precocious puberty, patients must be under 8 years of age (girls) or 9 years of age (boys). Listing for continuing therapy was listed as a Streamlined Authority.	1 May 2015
Goserelin	Breast cancer restriction simplified, was listed for hormone receptor positive breast cancer in stage III or stage IV, or hormone receptor positive breast cancer as an alternative to adjuvant chemotherapy. Listed for hormone receptor positive breast cancer as a Restricted Benefit.	1 October 2015
Leuprorelin	Authority Required listing for central precocious puberty altered, patients must now be aged 10 years or younger (girls) or 11 years or younger (boys) rather than under 8 years of age (girls) or 9 years of age (boys); added grandfather listing. Listing for continuing therapy remains a Streamlined Authority.	1 December 2015
Leuprorelin	Streamlined Authority listing of Lucrin 6 month depot for locally advanced (stage c) or metastatic (stage d) carcinoma of the prostate.	1 March 2016
Nafarelin	Listings for endometriosis became restricted benefits.	1 October 2016
Leuprorelin	Listings for carcinoma of the prostate and CPP became restricted benefits.	1 October 2016
Triptorelin	Locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate became restricted benefits.	1 October 2016
Leuprorelin and bicalutamide	Listed for carcinoma of the prostate as a Restricted Benefit.	1 December 2016
Goserelin	Listed for anticipated premature ovarian failure as a Restricted Benefit.	1 December 2017

Current PBS listing details are available from the [PBS website](#).

### **Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)**

At its December 2014 special meeting, the PBAC recommended that goserelin be listed as a restricted benefit.<sup>8</sup>

At its March 2016 meeting, the PBAC recommended amending the current PBS listings for intramuscular injection leuprorelin (Lucrin) for the treatment of locally advanced (stage C)

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<sup>8</sup> Goserelin (Zoladex) Public Summary Document March 2017 <http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2017-03/files/goserelin-psd-march-2017.pdf>

or metastatic (stage D) carcinoma of the prostate and CPP, from Authority Required and Authority Required (STREAMLINED) to Restricted Benefit, for consistency with goserelin.

The PBAC noted that the goserelin PBS listing was altered from Authority Required to Restricted Benefit on 1 May 2015 as part of the Post Market Review of Authority Required PBS listings for the following indications: carcinoma of the prostate, endometriosis and breast cancer. The PBAC considered that as leuprorelin is in the same class as goserelin (GnRH agonist), changing its listing from Authority Required (STREAMLINED) to Restricted Benefit would ensure consistency between the two drugs.

As requested by the sponsor, the PBAC recommended amending the current PBS listings for intramuscular injection leuprorelin (Lucrin) for the treatment of locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate, and CPP, from Authority Required to Restricted Benefit. The PBAC noted this amendment would ensure consistency with the restriction level for goserelin. As a flow on from this recommendation for leuprorelin, the PBAC also recommended that triptorelin for the treatment of locally advanced (stage C) or metastatic (stage D) carcinoma of the prostate and the nasal spray presentations of nafarelin for endometriosis be amended from Authority Required to Restricted Benefit.

For further details refer to the [Public Summary Document](#) from the March 2016 PBAC meeting.

## Methods

PBS prescription data for products containing goserelin, leuprorelin, nafarelin and triptorelin dispensed from 1 January 2014 to 31 December 2018 were extracted from the DHS PBS prescription database. These data were used to determine the number of prescriptions supplied and the number of incident and prevalent patients. They were also used to analyse patient demographics and length of treatment.

As this analysis used date of supply prescription data, there may be small differences compared with publicly available Department of Human Services (DHS) Medicare date of processing data.<sup>9</sup> The publicly available DHS Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included.

### Determination of gender

Of the 93,102 patients in the five year data set, 16 were excluded because their gender was not recorded on any prescription or could not be reliably determined from the data. Patients who were recorded as being both male and female in the claims records may be due to a Medicare number belonging to a different family member on the same Medicare card being recorded against a prescription. The analysis dataset included 21,204 patients who were determined to be female and 71,882 who were determined to be male.

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<sup>9</sup> PBS statistics. Australian Government Department of Human Services Medicare. Canberra. Available from <<http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>>.

### Determination of indication

In female patients, GnRH agonists are used to treat endometriosis, premenopausal breast cancer and premature ovarian failure. A small number of female patients are supplied leuprorelin for CPP. The number of prescriptions supplied, the number of incident and prevalent patients and patient demographics were analysed using all prescriptions supplied to the 21,204 patients who were determined to be female. These prescriptions included small numbers of leuprorelin and triptorelin prescriptions.

The length of treatment for breast cancer and endometriosis was analysed in a subset of the patients determined to be female. As goserelin is a Restricted Benefit Listing with multiple indications, to identify patients who may have been treated for breast cancer, additional prescriptions were extracted for chemotherapy medicines used to treat breast cancer. Patients were included in the breast cancer cohort if they were treated with a chemotherapy used to treat breast cancer between 1 January 2013 and 31 December 2018, and were prescribed a GnRH agonist by an oncologist. A list of chemotherapy medicines and prescriber types used to categorise patients as having breast cancer can be found in Appendix B.

Patients were included in the endometriosis cohort if they were not treated with chemotherapy medicine relevant to the treatment of breast cancer, were not prescribed a GnRH agonist by an oncologist, and were prescribed GnRH agonists by a gynaecologist or obstetrician more times than a GP.

In male patients, GnRH agonists are used to treat prostate cancer. A small number of male patients are supplied leuprorelin for CPP. All prescriptions supplied to the 71,882 patients who were determined to be male were analysed together.

### Length of treatment analyses

The Kaplan Meier method was used to determine the length of treatment for different indications and medicines. As the GnRH agonists are supplied as implants which are effective from between one and six months and have different resupply times, the standard coverage days (SCD) was calculated as the median for each PBS item code in each analysis. Breaks in therapy and censoring were determined using  $3 \times \text{SCD}$  for the previously supplied medicine. Patients were censored if they were considered to be continuing on treatment, i.e. if they had a supply of a medicine within  $3 \times \text{SCD}$  from the end date for the analysis period. Length of treatment without accounting for breaks uses the patient's entire time on treatment. Length of treatment accounting for breaks counts the patient's time on treatment with the breaks removed.

For the 5,959 patients in the breast cancer cohort, the Kaplan Meier method was used to determine the length of treatment for the 5,898 patients who received goserelin and did not receive another GnRH agonist.

The Kaplan Meier method was used to determine the length of treatment for the whole endometriosis cohort (8,068 patients), patients who received goserelin and did not receive

another GnRH agonist (4,920 patients), and patients who received nafarelin and did not receive another GnRH agonist (2,850 patients).

The Kaplan Meier method was used to determine the length of treatment for 71,882 male patients for prostate cancer.

#### Limitations in identifying treatment indications from the PBS data

In early breast cancer, goserelin may be used as an alternative to combination chemotherapy or as adjuvant therapy post combination chemotherapy.<sup>7</sup> As the identification of breast cancer patients relies on them also receiving a supply of a chemotherapy medicine for breast cancer, the breast cancer cohort includes patients treated with goserelin as adjuvant treatment, but may not include some patients who may have received goserelin as an alternative to chemotherapy. The length of treatment may be different between these groups of patients.

Hormonal contraceptives may or may not be used to regulate hormones in patients with endometriosis and uterine fibroids. It was not attempted in this analysis to use oral and other hormonal contraceptives to determine a patient's indication as patients may also access hormonal contraceptives as private prescriptions outside of the PBS.

## Results

### Analysis of drug utilisation

#### Overall utilisation

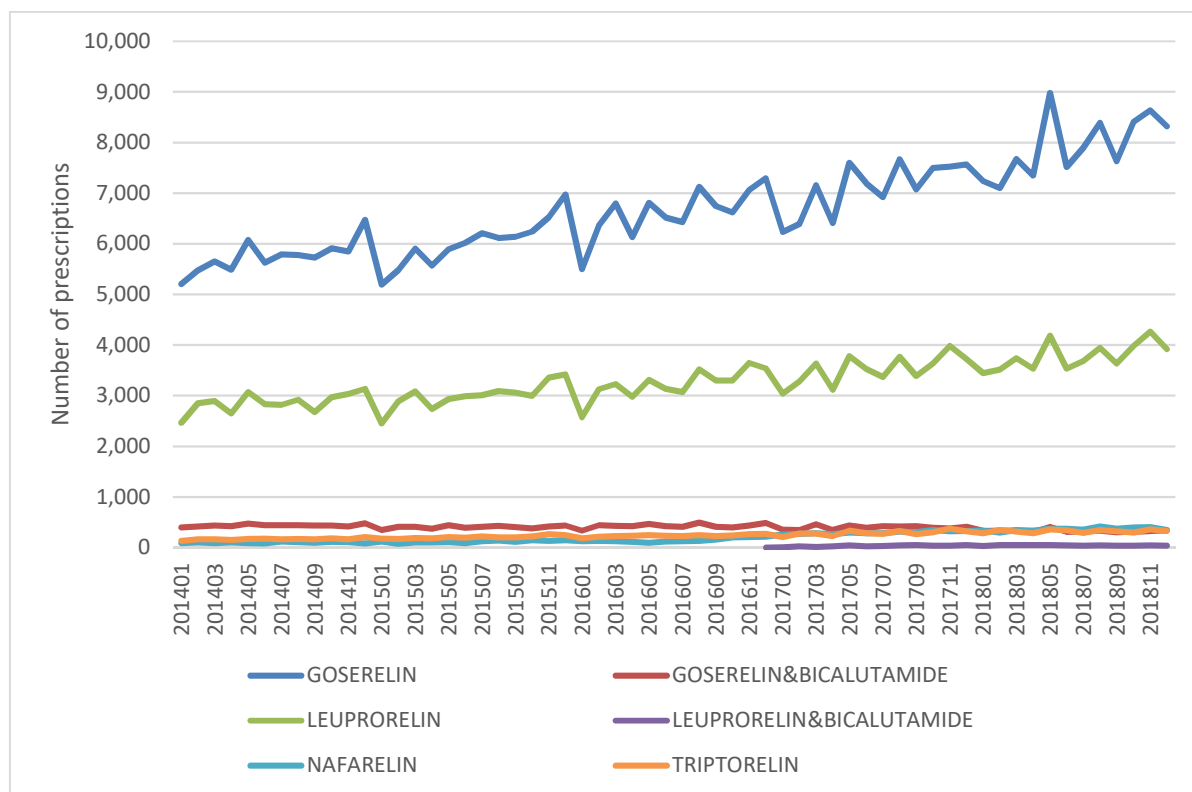


Figure 1: Prescriptions by medicine and month of supply

Table 5: Prescriptions by medicine and year

	Goserelin	Goserelin & bicalutamide	Leuprorelin	Leuprorelin & bicalutamide	Nafarelin	Triptorelin
2014	69,049	5,243	34,324		1,166	2,009
2015	72,255	4,849	36,024		1,391	2,481
2016	79,396	5,157	38,730	≤5	1,743	2,821
2017	85,238	4,771	42,257	376	3,576	3,470
2018	95,138	3,962	45,373	512	4,349	3,886
Total	401,076	23,982	196,708	889	12,225	14,667

Overall, goserelin is the most used GnRH agonist. Its use is approximately two times higher than the second most used GnRH agonist, leuprorelin. Use of the combination items for metastatic prostate cancer, which are supplied as an implant or injection of goserelin or leuprorelin, and tablets of bicalutamide which are taken daily, remained at similar levels over time. The use of leuprorelin with bicalutamide is very low. The use of nafarelin is small

in the context of the GnRH agonist market, but its use increased by one and a half times between 2016 and 2018 after it became a Restricted Benefit listing from October 2016. The use of triptorelin is also small relative to the overall GnRH agonist market and is growing at a lower rate than nafarelin.

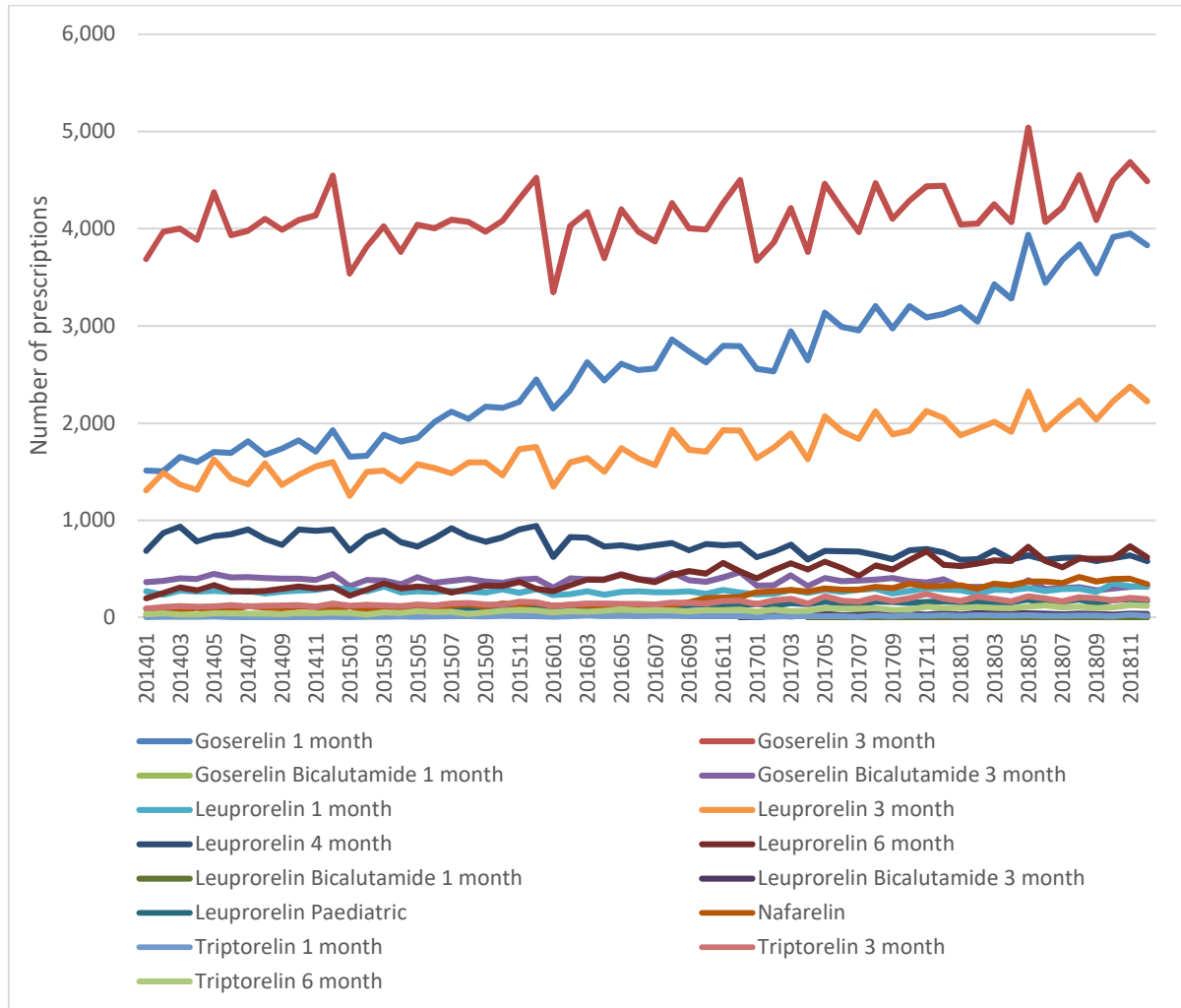


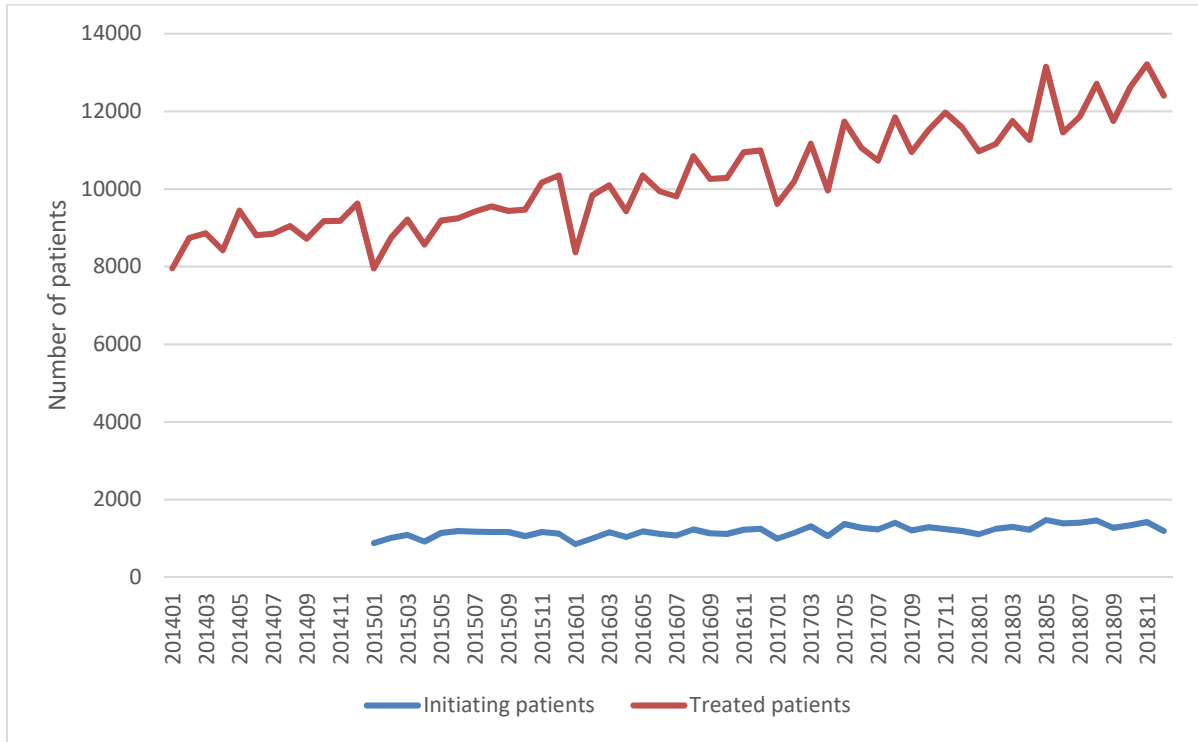
Figure 2: Prescriptions by product and month of supply

**Table 6: Prescriptions by product and year of supply**

	2014	2015	2016	2017	2018	Total
Goserelin 1 month	20,358	24,036	31,088	35,361	43,088	153,931
Goserelin 3 month	48,691	48,219	48,308	49,877	52,050	247,145
Goserelin Bicalutamide 1 month	372	342	336	248	210	1,508
Goserelin Bicalutamide 3 month	4,871	4,507	4,821	4,523	3,752	22,474
Leuprorelin 1 month	3,263	3,316	3,098	3,279	3,524	16,480
Leuprorelin 3 month	17,490	18,415	20,253	22,845	25,203	104,206
Leuprorelin 4 month	10,143	9,949	8,928	8,011	7,371	44,402
Leuprorelin 6 month	3,428	3,668	4,993	6,312	7,267	25,668
Leuprorelin Bicalutamide 1 month				21	24	45
Leuprorelin Bicalutamide 3 month			≤5	355	488	844
Leuprorelin Paediatric		676	1,458	1,810	2,008	5,952
Nafarelin	1,166	1,391	1,743	3,576	4,349	12,225
Triptorelin 1 month	87	154	195	199	253	888
Triptorelin 3 month	1,431	1,643	1,758	2,234	2,315	9,381
Triptorelin 6 month	491	684	868	1,037	1,318	4,398
<b>Total</b>	<b>111,791</b>	<b>117,000</b>	<b>127,848</b>	<b>139,688</b>	<b>153,220</b>	<b>649,547</b>

Overall the greatest increase in prescriptions has come from 3.6 mg subcutaneous implant of goserelin which is administered once every four weeks. The use of 10.8 mg goserelin (3 month) is higher than 3.6 mg goserelin. The product information recommends the 10.8 mg implant be used in male patients for prostate cancer and is not indicated for use in female patients or children. The 3.6 mg implant may be used in male patients for prostate cancer and in female patients for endometriosis, hormone receptor positive breast cancer and anticipated premature ovarian failure. The increase in prescriptions for goserelin is likely due to a combination of factors, including the change in restriction level to Restricted Benefits on 1 May 2015, the listing for hormone receptor positive breast cancer on 1 October 2015, and the listing for anticipated premature ovarian failure on 1 December 2017.

Use of the paediatric leuprorelin product for CPP had grown since its first listing in 2015, with 2,008 prescriptions dispensed in 2018.

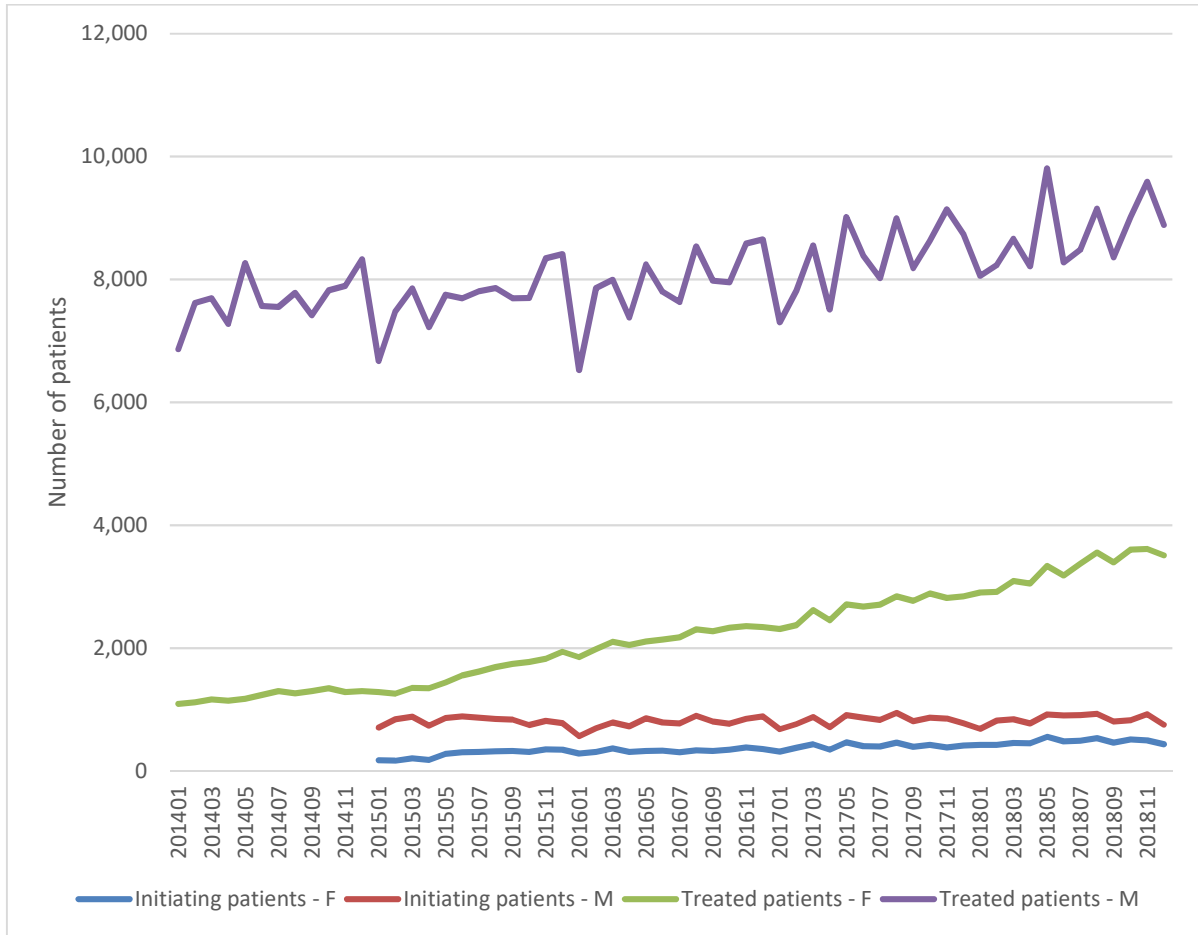


**Figure 3: Initiating and prevalent treated patients supplied goserelin, leuprorelin, triptorelin or nafarelin by month of supply**

Figure 3 above shows the number of initiating patients has been relatively stable since 2015. A total of 15,859 patients first initiated treatment in 2018. The number of prevalent treated patients is gradually growing over time. There were 46,739 total patients treated in 2018, compared to 40,123 in 2016.

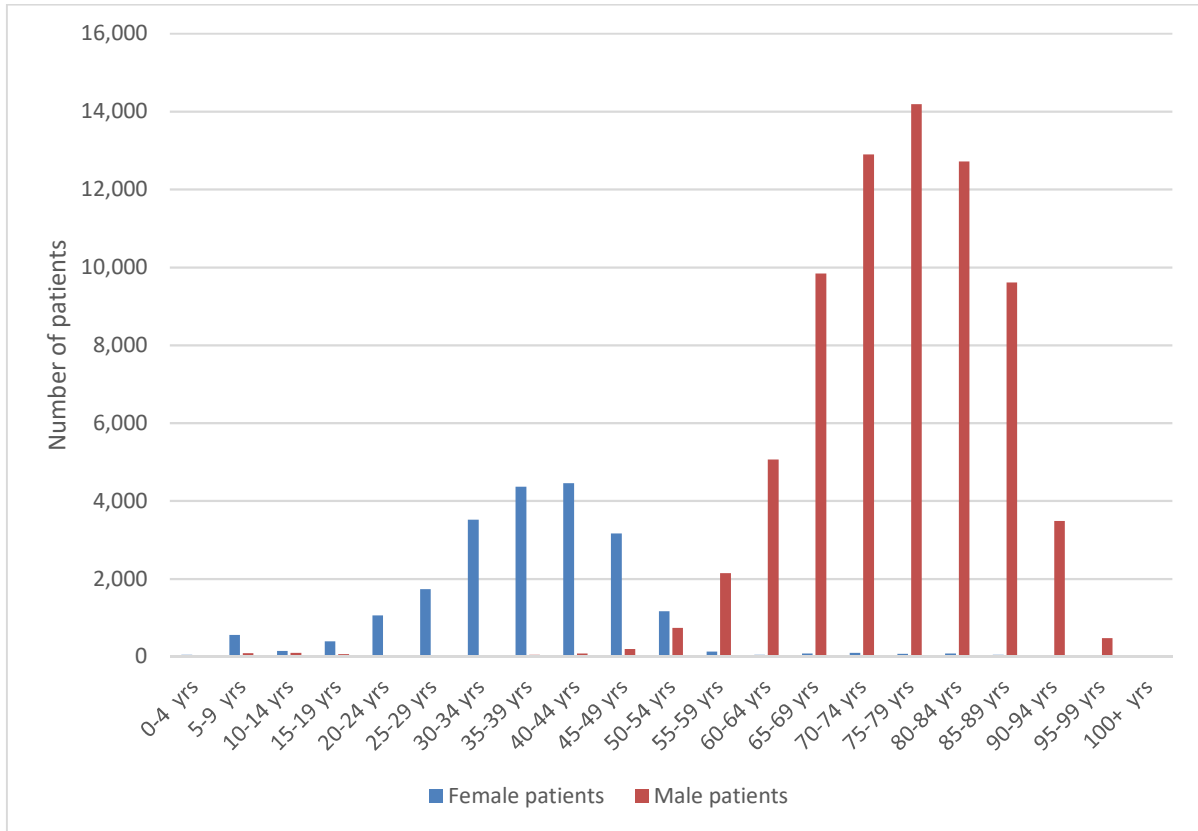
**Table 7: Initiating and prevalent treated patients supplied goserelin, leuprorelin, triptorelin or nafarelin by year of supply**

Year	Initiating patients	Treated patients
2014		36,004
2015	13,109	37,570
2016	13,400	40,123
2017	14,730	43,631
2018	15,859	46,739



**Figure 4: Initiating and prevalent treated patients supplied goserelin, leuprorelin, triptorelin or nafarelin by gender and month of supply**

Figure 4 above shows the number of male patients who first initiate on treatment per month is higher than the number of female patients. In 2018 approximately 1.8 times more men first initiated on therapy than women. The total number of male patients who are treated is also higher than the number of female patients, in 2018 approximately four times more men (37,330) were treated with GnRH agonists than women (9,403).



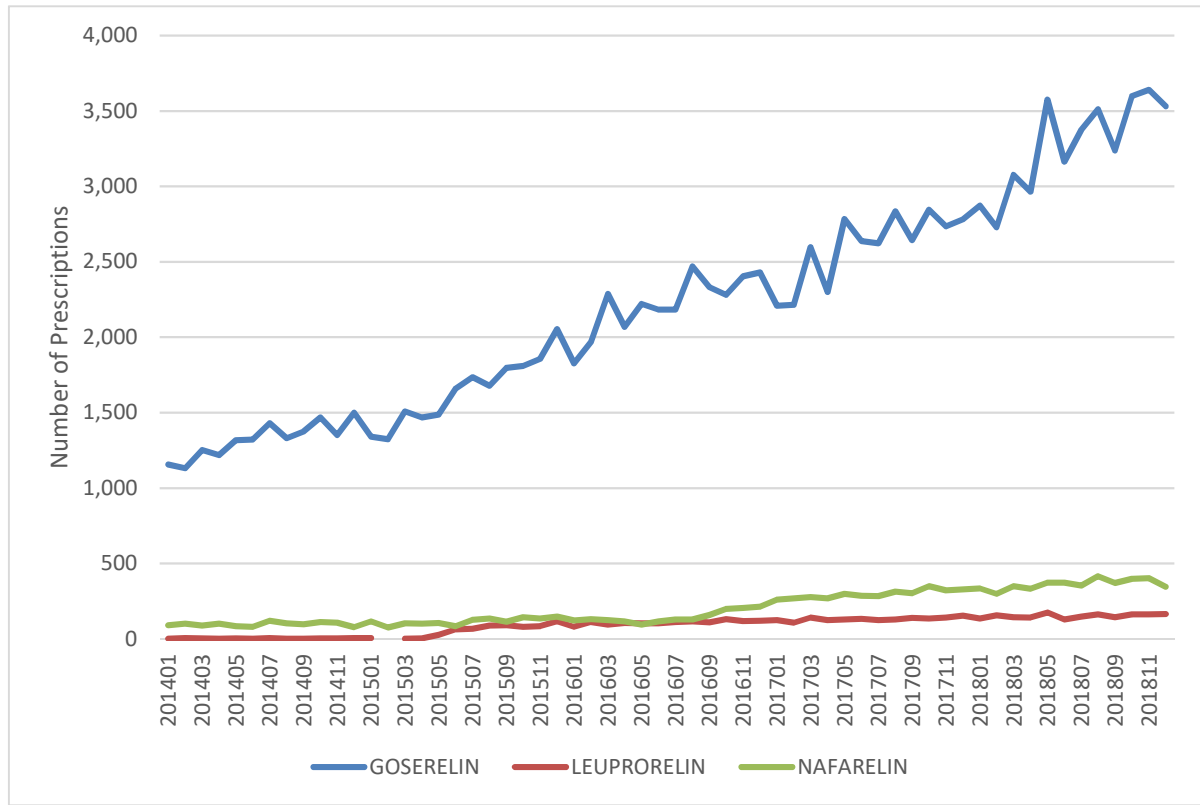
**Figure 5: Gender and age of patients first initiating on GnRH agonist therapy**

Of 93,102 patients in the complete five year dataset, 21,204 were determined to be female, 71,882 were determined to be male, and 16 were excluded because their gender could not be determined. Eleven patients are excluded in Figure 5 because their age was not recorded for their initial prescription. The number of patients in each age group can be found in Appendix C.

The use of GnRH agonists by age and gender shows that male patients generally first initiate treatment after the age of 55, which correlates with the expected onset of prostate cancer. Conversely, there are very small numbers of women treated with GnRH agonists after the age of 55. GnRH agonists block hormones and are used to treat endometriosis, the symptoms of which tend to lessen after menopause, and breast cancer in premenopausal women.

The use of GnRH agonists for CPP is higher in females than males; 102 male patients and 609 female patients initiated before the age of 10.

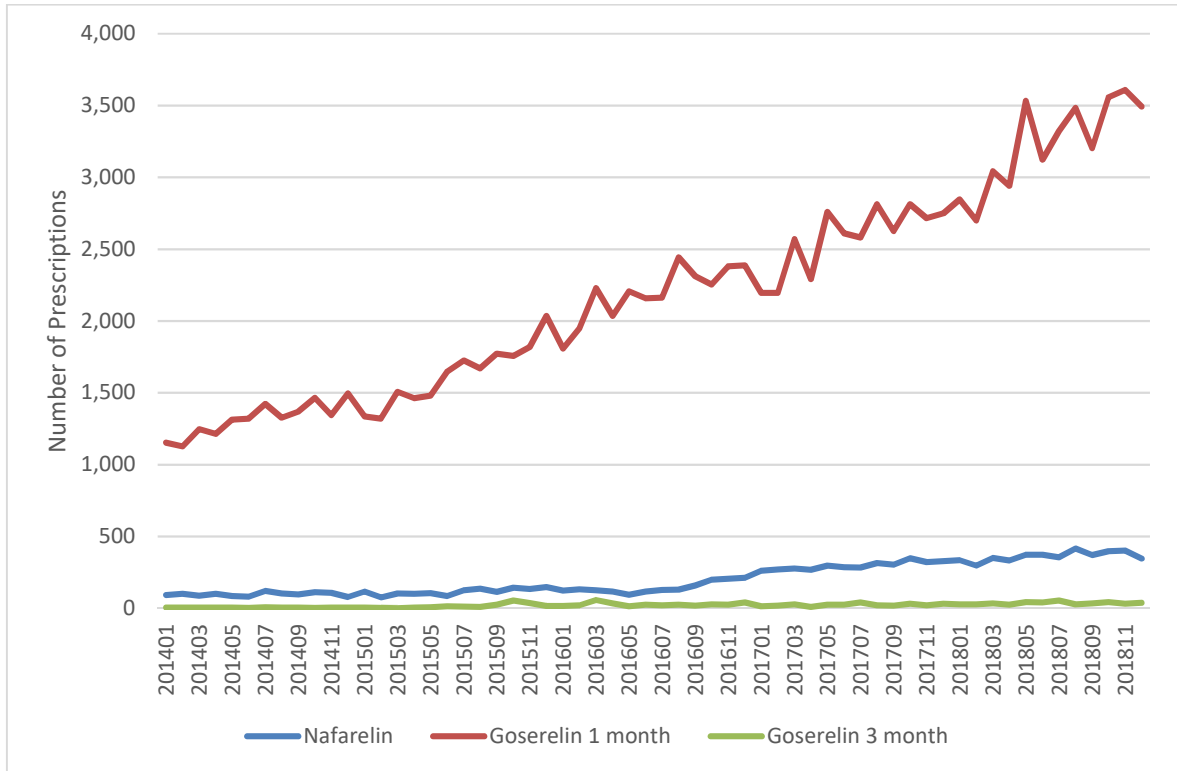
**Utilisation of GnRH agonists in female patients**



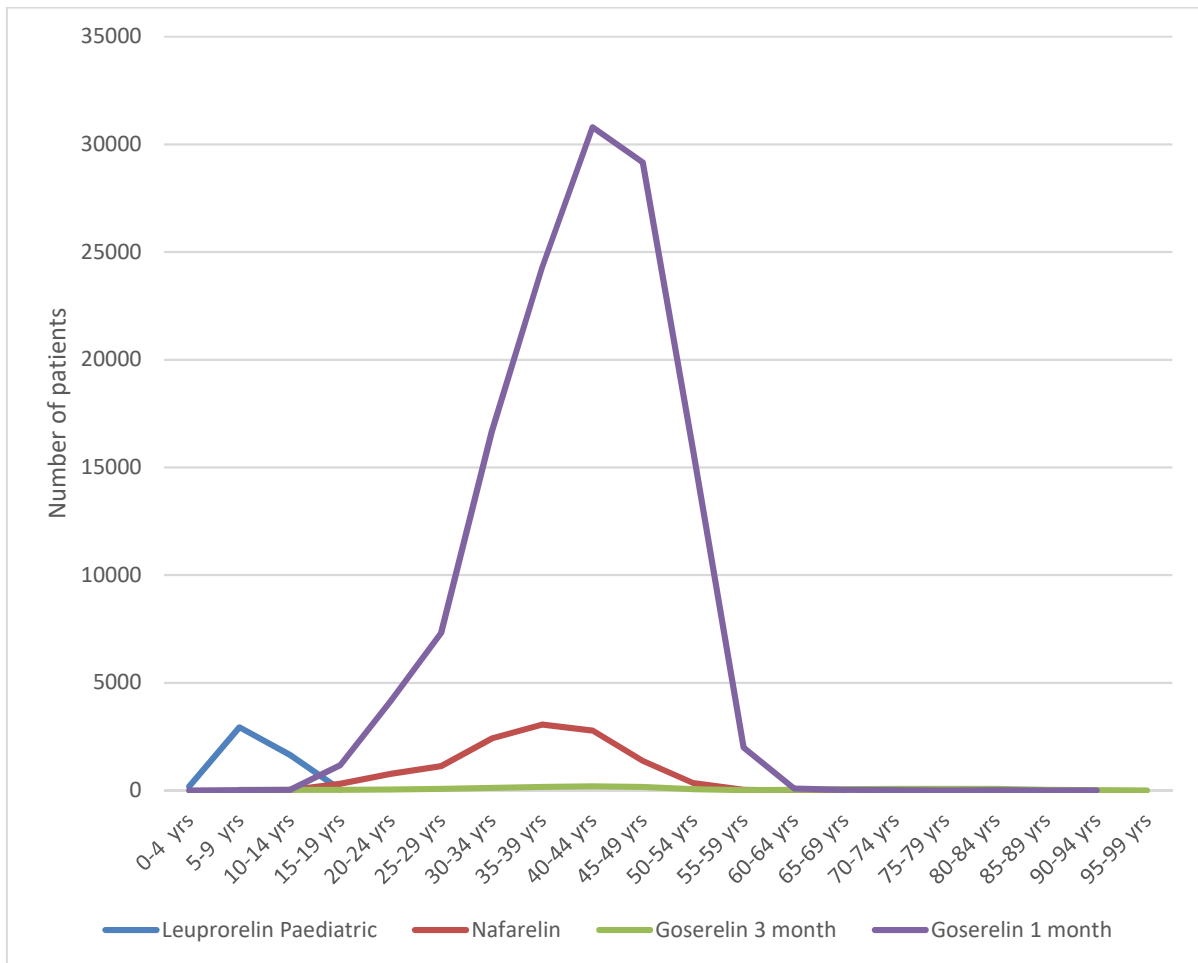
**Figure 6: Prescriptions for female patients by medicine and month of supply**

Figure 6 shows that in female patients the most commonly used GnRH agonist is goserelin, and Figure 7 shows the most common product supplied to female patients is the 3.6 mg (1 month) implant.

Some prescriptions of triptorelin (139 over five years) and goserelin and bicalutamide (282 over five years) that were supplied to female patients are not shown in Figure 6 or 7 due to small prescription numbers. These supplies may have been recorded as being supplied to females due to miscoding, or may reflect outside of the PBS restrictions.



**Figure 7: Prescriptions for female patients by product and month of supply**



**Figure 8: Prescriptions for female patients in 2018 by product and age**

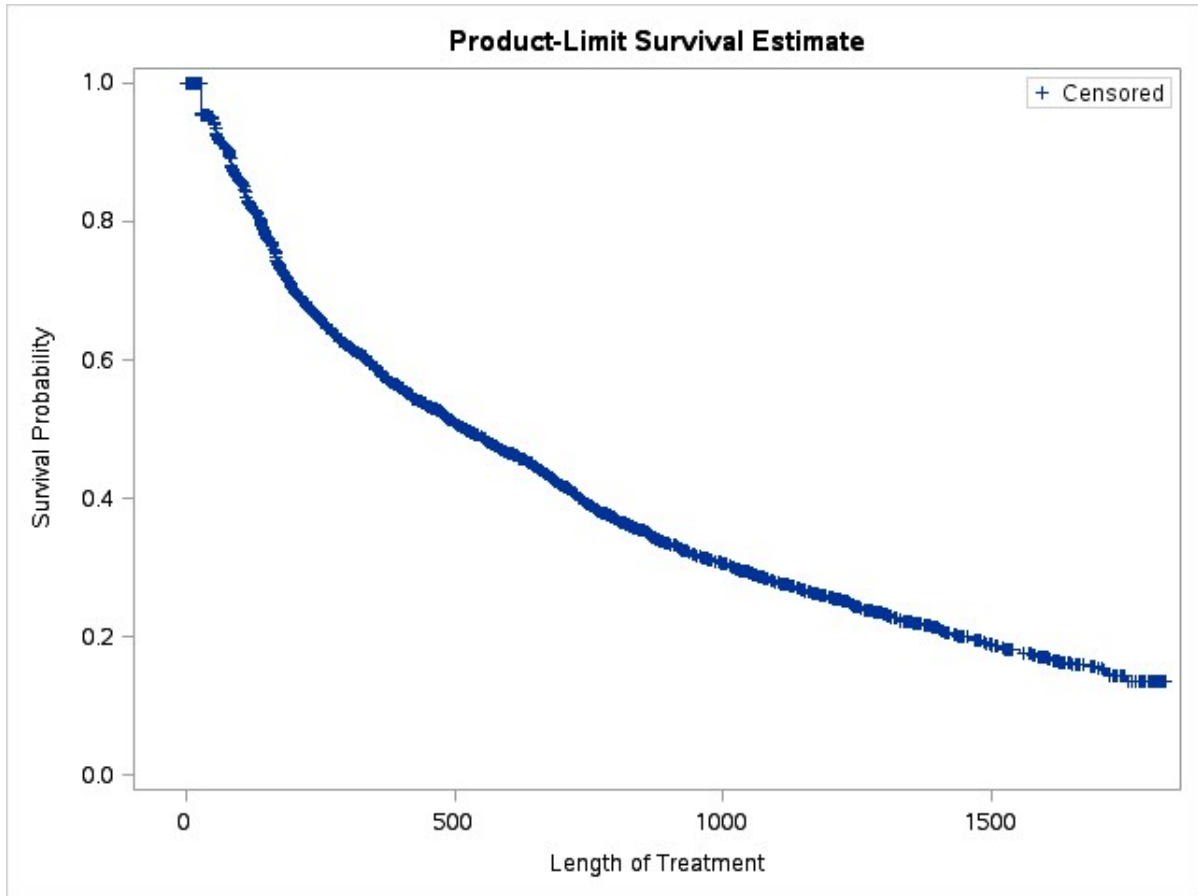
Figure 8 shows that women aged 15 to 59 have predominantly been supplied the 1 month implant of goserelin and nafarelin, and that goserelin is used more than nafarelin. Leuprorelin Paediatric has mainly been used to treat young female patients.

***Duration of GnRH agonist treatment in female patients***

**Breast cancer**

The analyses below examine the length of treatment for 5,898 female patients who were supplied goserelin and also a chemotherapy which may be used for breast cancer, and who were treated by an oncologist.

The median length of treatment of GnRH agonists in breast cancer was less than 10 months, and less than eight months not including breaks.



**Figure 9: Length of treatment with goserelin in days for female breast cancer patients not accounting for breaks**

**Table 8: Length of treatment in days for female breast cancer patients not accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
5898	452	290	1,103	1,372	1,454	1,574	1,692	1,803	1,824

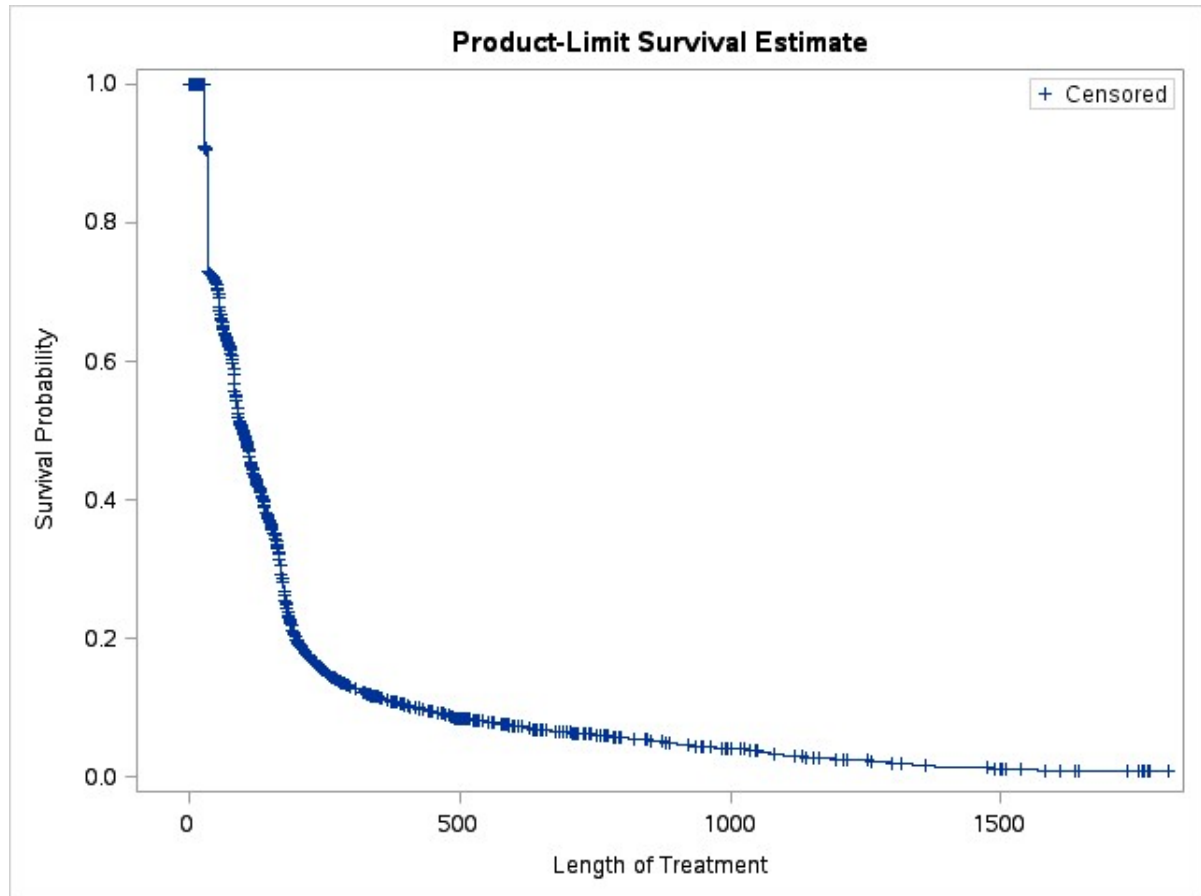
**Table 9: Length of treatment in days for female breast cancer patients accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
5898	376	226	909	1,179	1,272	1,378	1,526	1,732	1,824

### Endometriosis

The analyses below examine the length of treatment for 8,068 female patients categorised as being supplied a GnRH agonist for endometriosis, i.e. did not receive chemotherapy for breast cancer, and their most common prescriber of GnRH agonists was a gynaecologist or obstetrician. This cohort may include patients treated for premature ovarian failure after

1 December 2017, or prior to this date outside of the PBS restrictions, and outside the PBS restrictions for uterine fibroids.



**Figure 10: Length of treatment for female endometriosis patients in days not accounting for breaks**

The median length of treatment for endometriosis patients was approximately three months. The PBS restriction for goserelin allows for only one course of not more than 6 month’s treatment. The PBS restriction for nafarelin allows for up to 6 months of initial treatment and for up to 6 months of subsequent treatment. Approximately 80% of patients stop treatment by six months after first initiation.

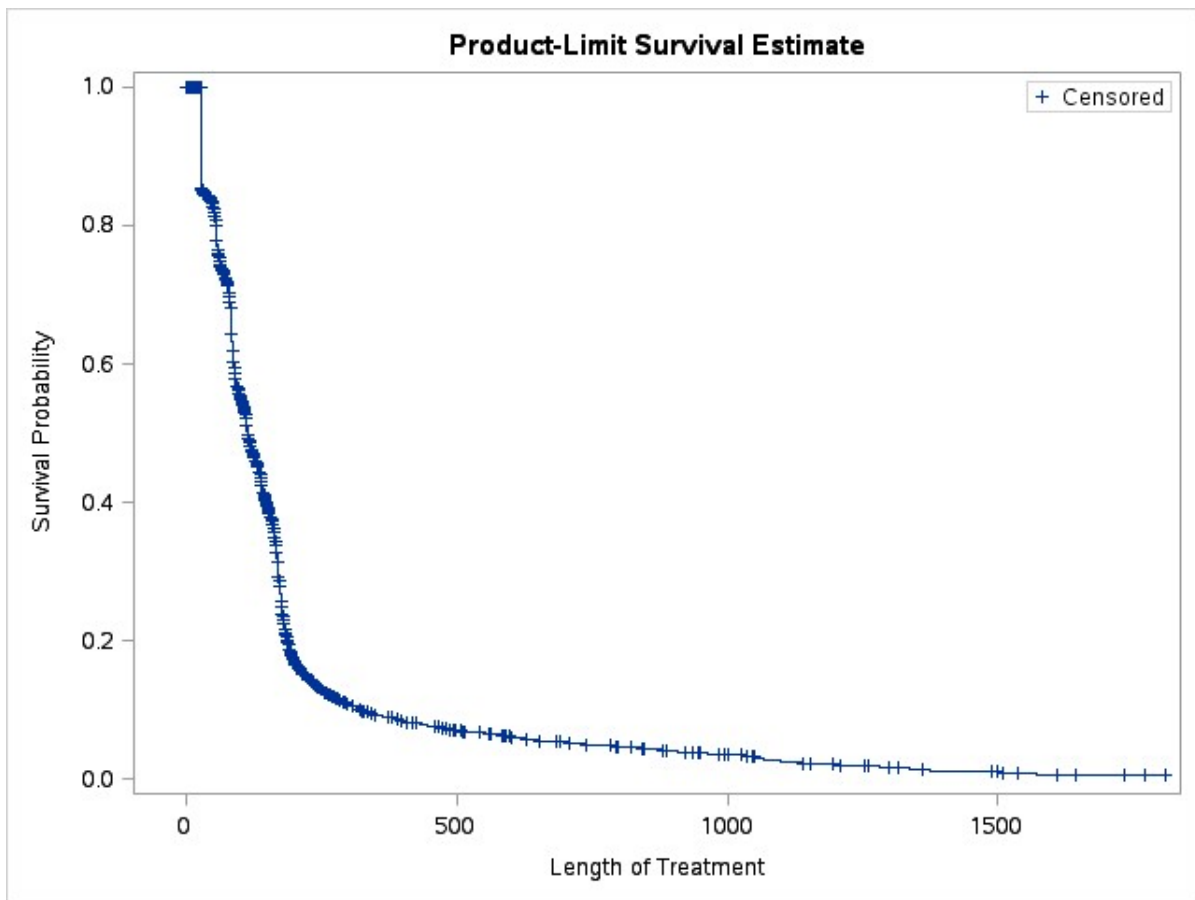
**Table 10: Length of treatment in days for female endometriosis patients not accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
8,068	145	87	263	490	590	711	891	1132	1,809

**Table 11: Length of treatment in days for female endometriosis patients accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
8,068	106	83	193	238	255	287	342	480	1,809

The analyses below examine the length of treatment for patients in the endometriosis cohort who were exclusively treated with either goserelin or nafarelin. Of the 8,068 patients in the cohort, 4,920 were treated with goserelin and did not receive other GnRH agonists, and 2,850 were treated with nafarelin and did not receive other GnRH agonists.



**Figure 11: Length of treatment with goserelin for female endometriosis patients in days not accounting for breaks**

**Table 12: Length of treatment in days with goserelin for female endometriosis patients not accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
4,920	147	102	231.5	406	497	630	876	1,098	1,809

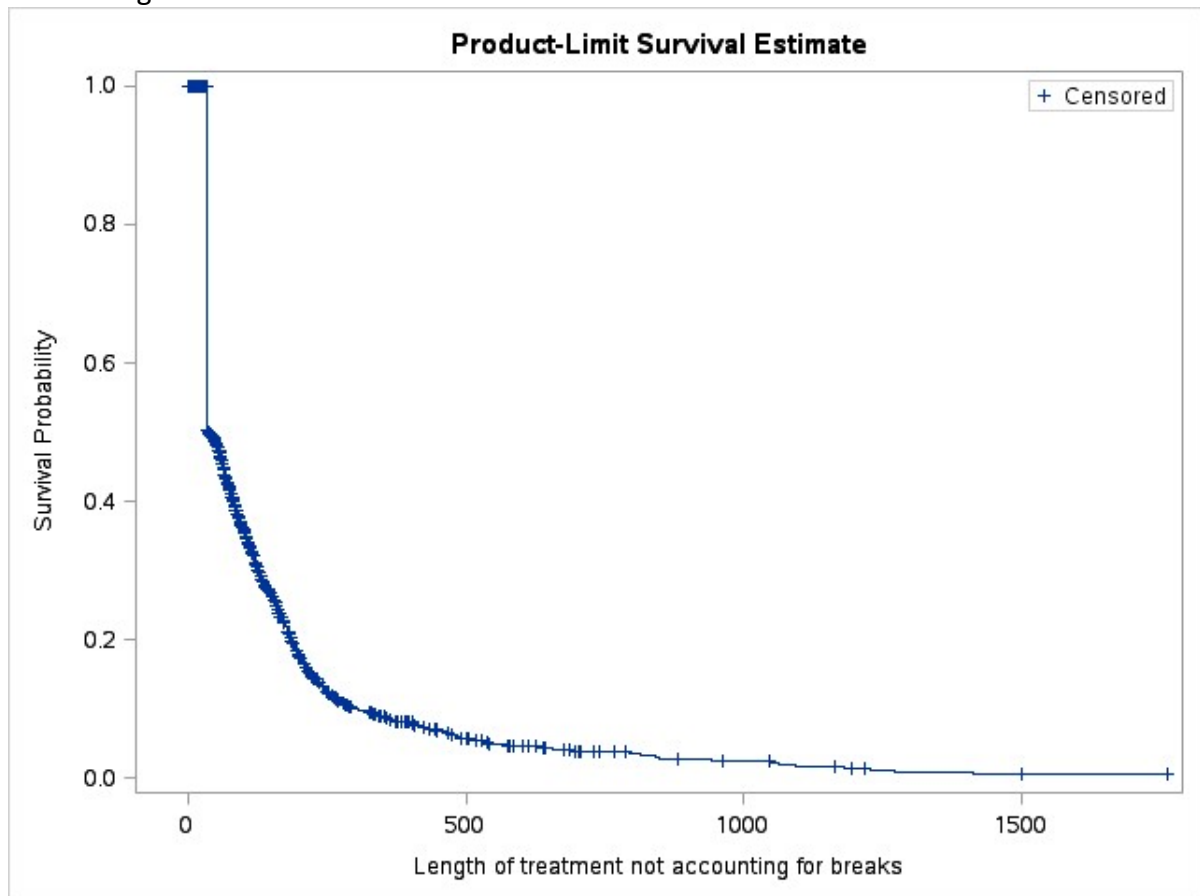
**Table 13: Length of treatment in days with goserelin for female endometriosis patients accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
4,920	112	91	189	224	236	257	294	364	1,809

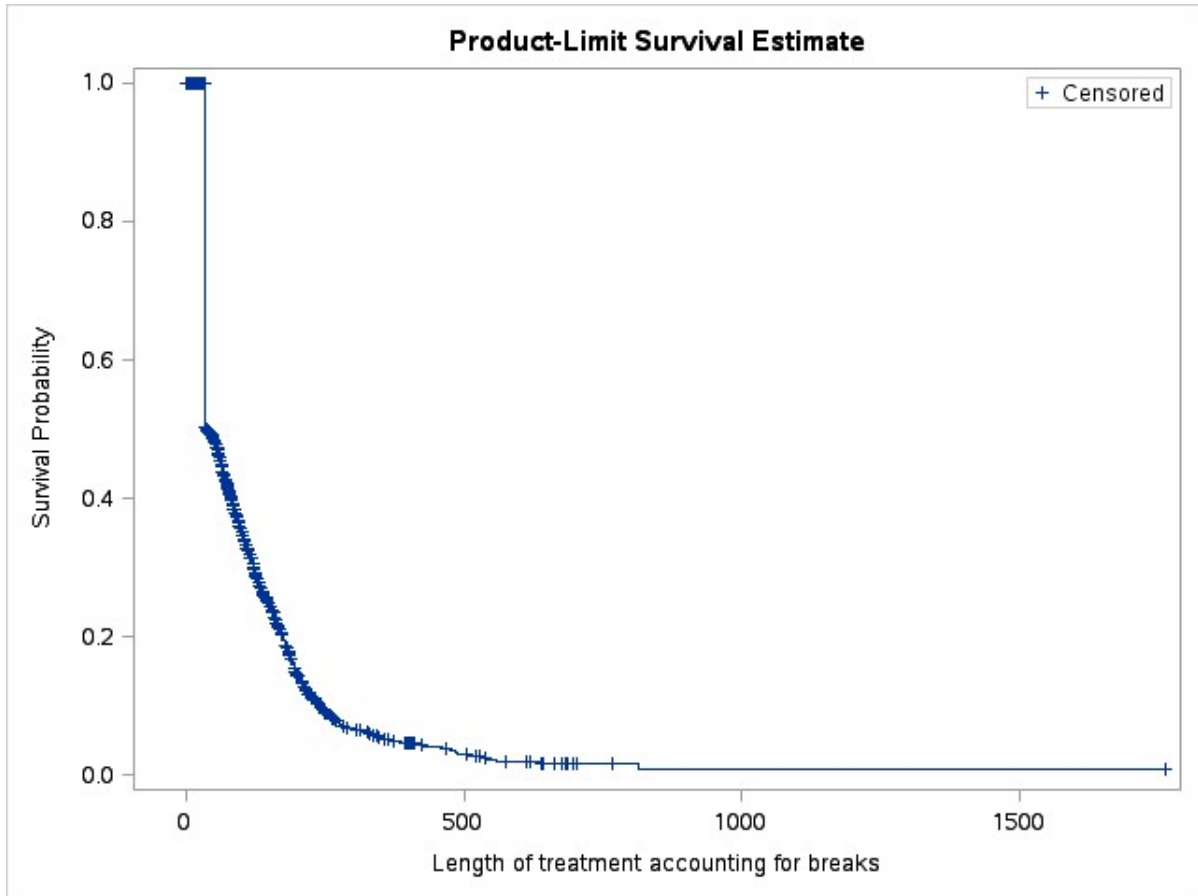
The PBS restriction for goserelin for endometriosis states that the treatment must be for the short-term (up to 6 months) and that only one course of not more than 6 months' therapy will be authorised.

For the 4,920 patients in the endometriosis cohort who were treated exclusively with goserelin, accounting for breaks shortens the 95<sup>th</sup> percentile duration from 406 days to 224 days. This suggests some patients have had breaks and reinitiated treatment. However, without accounting for breaks 82% of patients had stopped treatment after 6 months.

Length of treatment with nafarelin for female endometriosis patients in days not accounting for breaks



**Figure 12: Length of treatment with nafarelin for female endometriosis patients in days not accounting for breaks**



**Figure 13: Length of treatment with nafarelin for female endometriosis patients in days accounting for breaks**

**Table 14: Length of treatment with nafarelin for female endometriosis patients not accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
2,850	104	34	223.5	355	409	472	572.5	767	1,763

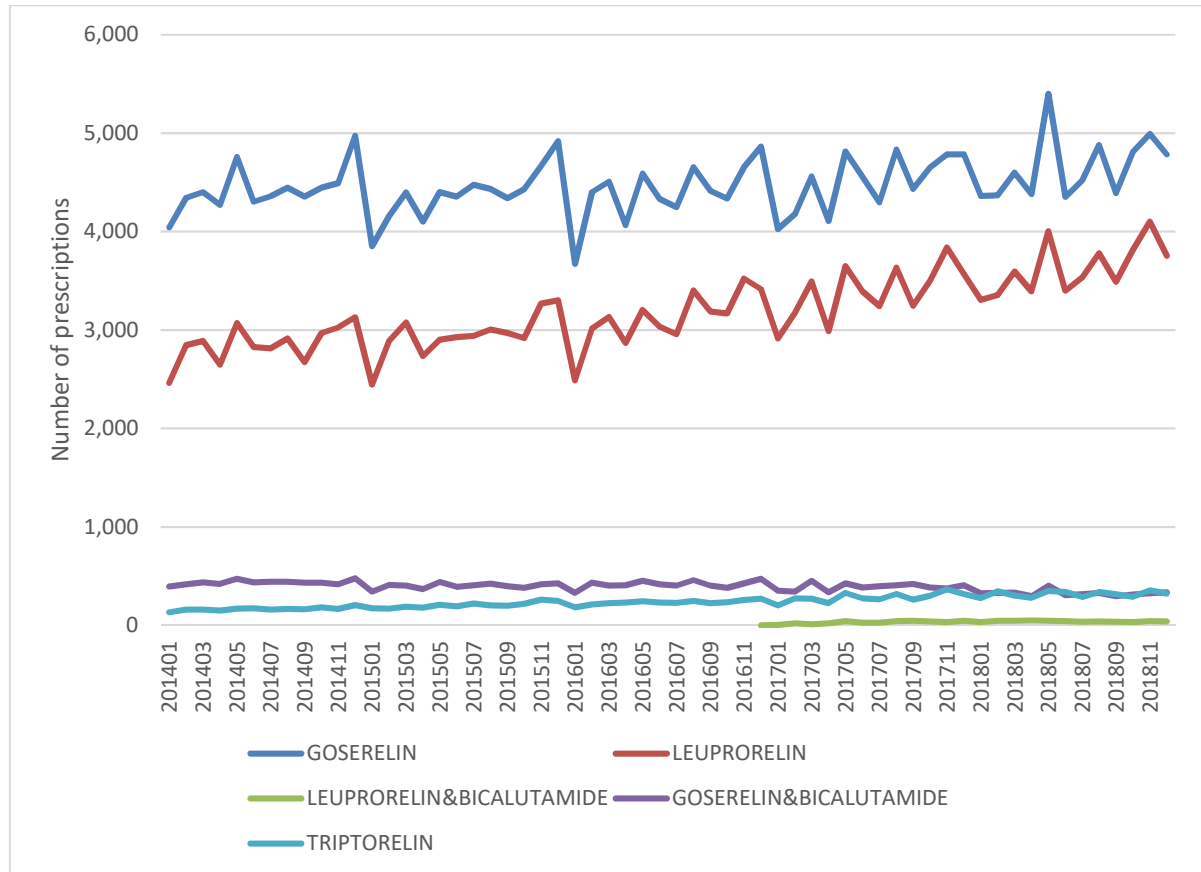
**Table 15: Length of treatment with nafarelin for female endometriosis patients accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
2,850	84	34	187	234	248	277	356.5	477	1,763

The PBS restriction for nafarelin allows initial treatment, for up to six months, and subsequent treatment, for up to six months where the subsequent treatment must be more two years after the end of the previous course of treatment. For patients who were only supplied nafarelin, without accounting for breaks, 85% of patients have stopped treatment after 6 months of treatment and 95.2% have stopped after one year. When

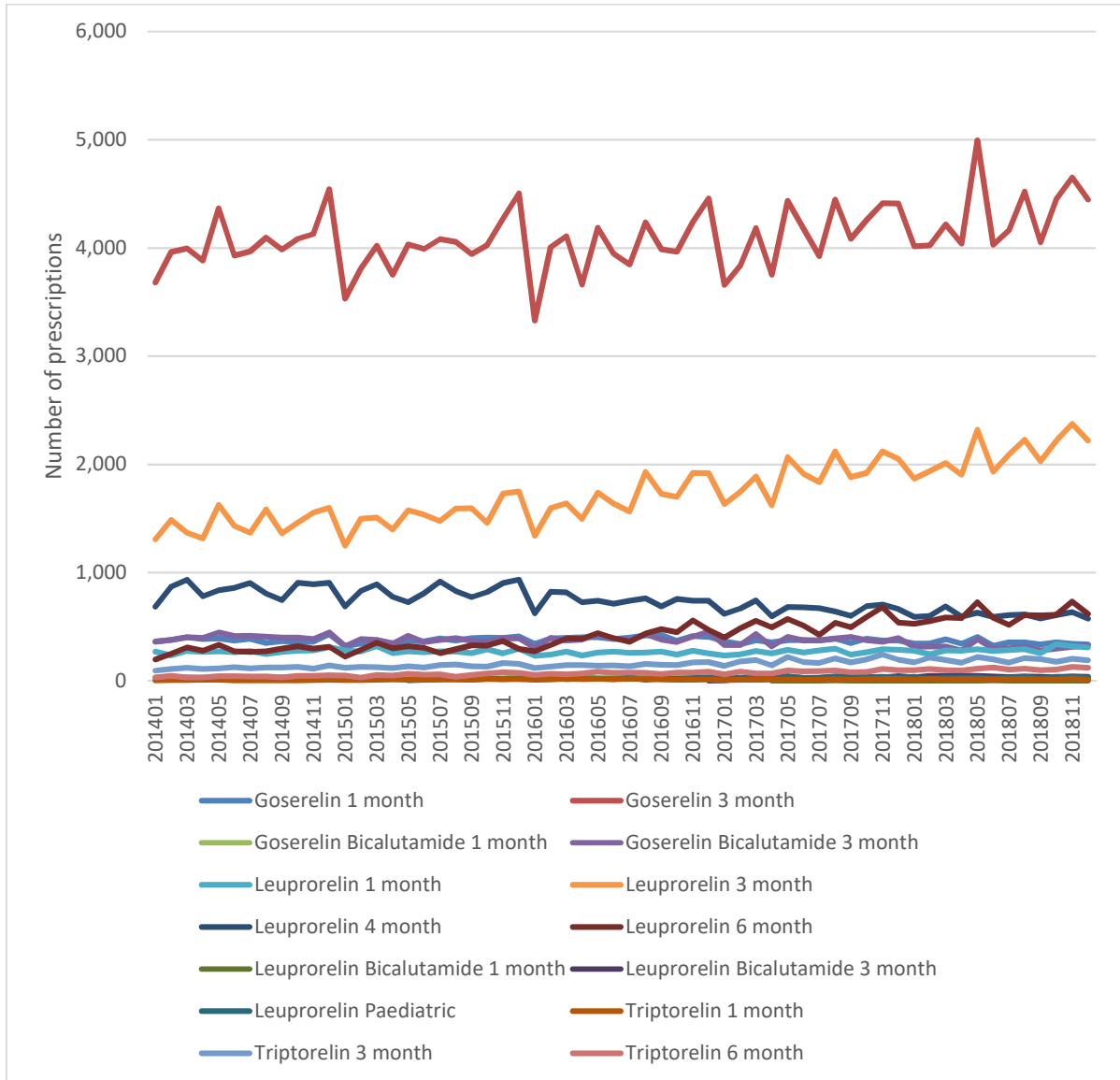
breaks are accounted for, 87.2% have stopped after six months of treatment, and 97.7% of patients had stopped after one year of treatment.

**Utilisation of GnRH agonists in male patients**



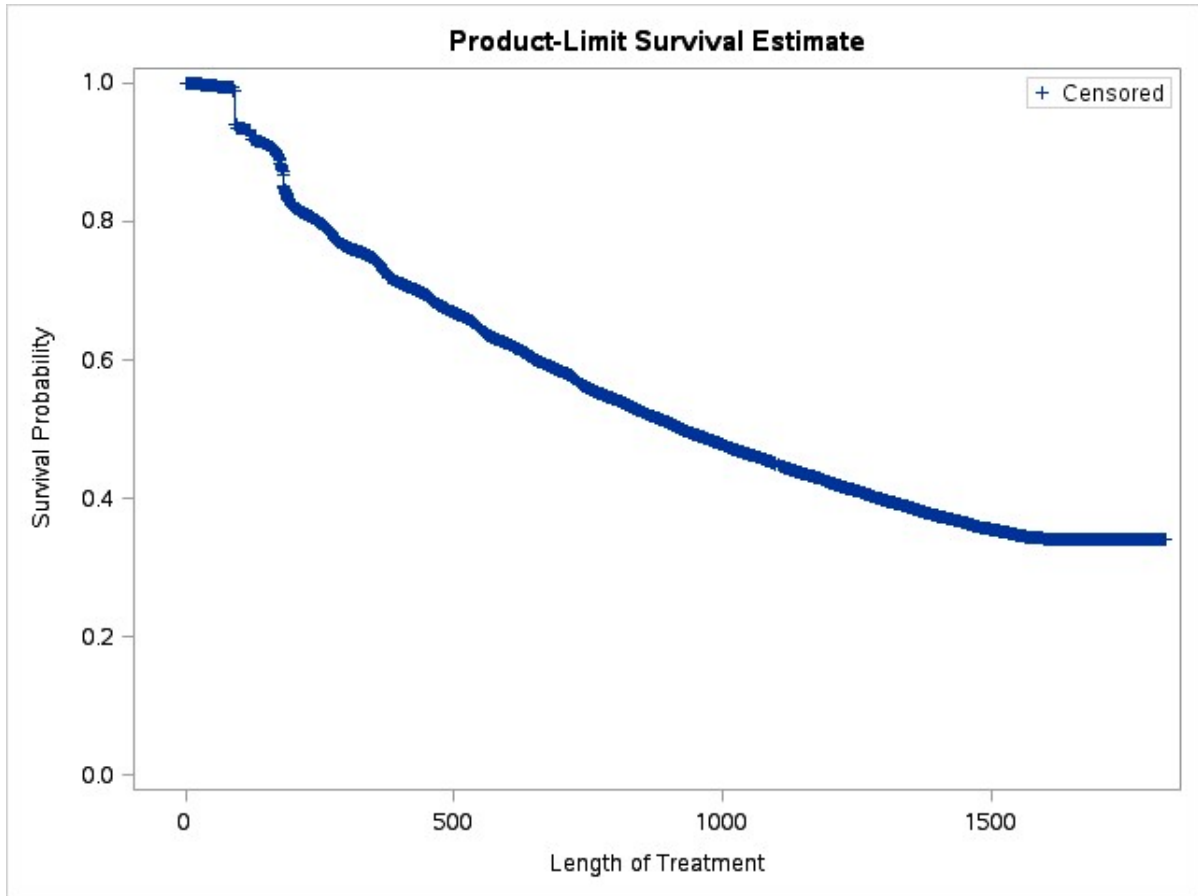
**Figure 14: Prescriptions for male patients by medicine and month of supply**

Goserelin is the most used medicine in male patients but its use appears to be stable. The second most used medicine is leuprorelin and its use is growing. In 2018 there were 55,846 prescriptions of goserelin and 43,535 prescriptions of leuprorelin supplied to males. In 2018 less than five prescriptions of nafarelin were supplied to males, which may be due to miscoding.



**Figure 15: Prescriptions for male patients by product and month of supply**

In male patients, the most commonly used product is 3 monthly implants of goserelin, and the second most commonly used product is 3 monthly implants of leuprorelin.



**Figure 16: Length of treatment in days for male patients not accounting for breaks**

**Table 16: Length of treatment in days for male patients not accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
71,882	716	546	1,729	1,777	1,787	1,795	1,804	1,813	1,825

**Table 17: Length of treatment in days for male patients accounting for breaks**

n	mean	median	P90	P95	P96	P97	P98	P99	P100
71,882	622	448	1,579	1,764	1,775	1,785	1,797	1,811	1,825

For male patients, the mean duration of treatment is close to two years, and the median is approximately 1.5 years. Some patients have been treated for the entire five year period.

## Analysis of expenditure

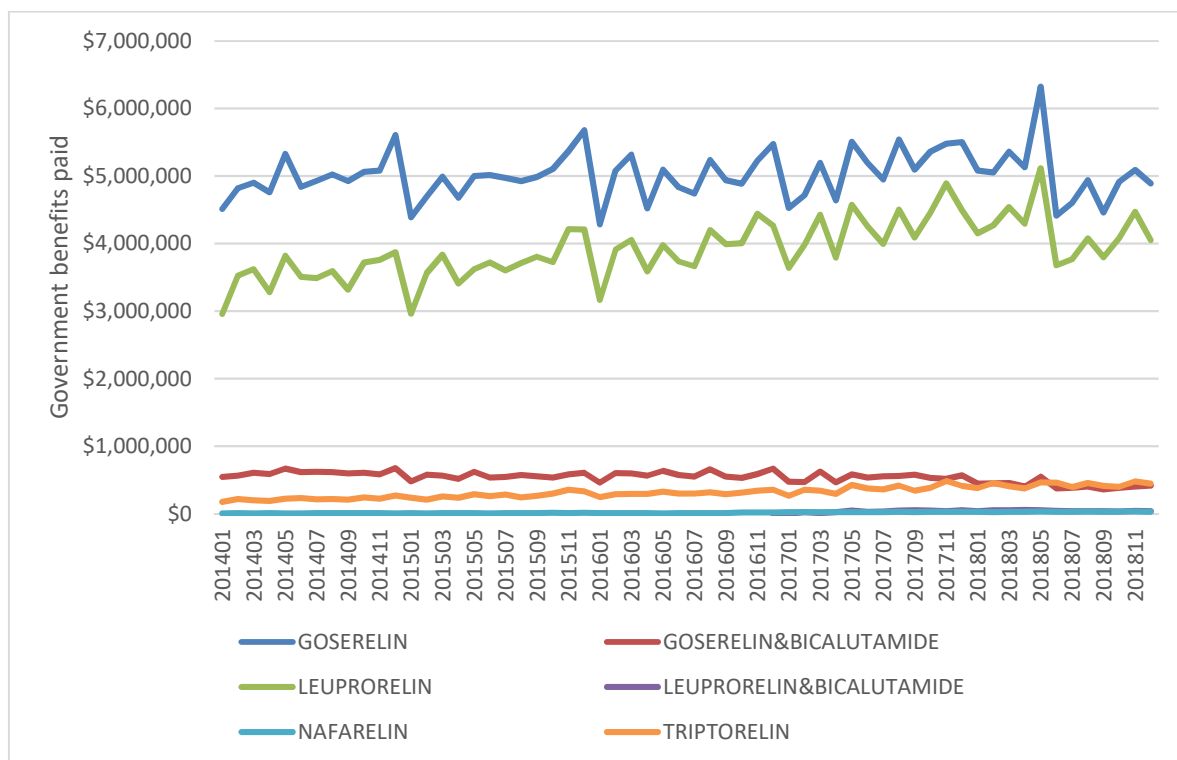


Figure 17: Cost of GnRH agonists by drug and month of supply

Table 18: Cost of GnRH agonists by medicine and year of supply

Year	Goserelin	Goserelin & bicalutamide	Leuprorelin	Leuprorelin & bicalutamide	Nafarelin	Triptorelin
2014	\$59,805,163	\$7,315,648	\$42,483,537		\$118,735	\$2,646,259
2015	\$59,828,102	\$6,722,258	\$44,395,539		\$140,533	\$3,293,103
2016	\$59,656,302	\$7,003,967	\$47,025,507	\$1,230	\$163,357	\$3,688,158
2017	\$61,724,252	\$6,484,245	\$51,113,098	\$438,509	\$329,318	\$4,482,370
2018	\$60,278,181	\$5,062,922	\$50,321,537	\$561,273	\$385,775	\$5,154,736

**Table 19: Cost and rate of growth of GnRH agonists by year of supply**

Year	Total	Rate of growth
2014	\$112,369,341	
2015	\$114,379,534	2%
2016	\$117,538,521	3%
2017	\$124,571,792	6%
2018	\$121,764,424	-2%

Similar to the number of prescriptions dispensed for GnRH agonists, the cost to government of goserelin is higher than the cost to government of leuprorelin. The cost to government of GnRH agonists has been slowly growing over time. The reduction of costs mid 2018 was due to a fifteen year anniversary price reduction of 14.5% which applied to products containing goserelin and leuprorelin on 1 June 2018.

## Discussion

GnRH agonists (goserelin, leuprorelin, triptorelin, nafarelin) are used in the treatment of carcinoma of the prostate, CPP, breast cancer, endometriosis, and anticipated premature ovarian failure. Nafarelin and triptorelin are also PBS listed for use in assisted reproduction, which was not included in this review. The GnRH agonist that is supplied the most often is goserelin. Goserelin is PBS listed for use in both male and female patients, for a range of conditions including locally advanced and metastatic prostate cancer, breast cancer, endometriosis and anticipated premature ovarian failure. It has the highest use in male patients, and the highest use in female patients.

The overall market of GnRH agonists is growing over time. The medicine that has recorded the highest increase in prescriptions is goserelin. This could be due to a combination of factors, including the change in restriction level to Restricted Benefits from 1 May 2015, increasing incidence of breast cancer<sup>10</sup>, the listing for hormone receptor positive breast cancer on 1 October 2015, and the listing for anticipated premature ovarian failure on 1 December 2017. There may also be potential use outside of the restriction, for example to treat patients with uterine fibroids. The number of prescriptions of goserelin appears stable in male patients, which may be because the incidence of prostate cancer is stable or decreasing.<sup>10</sup> This suggests the increased overall use of goserelin is due to increasing use in female patients.

Although the cost of GnRH agonists had been increasing with the increase of prescriptions, the cost decreased in 2018 because products containing goserelin and leuprorelin were subject to a 14.5% fifteen year anniversary price reduction.

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<sup>10</sup> Australian Institute of Health and Welfare 2019. Cancer in Australia 2019. Cancer series no.119. Cat. no. CAN 123. Canberra: AIHW., p51, <https://www.aihw.gov.au/getmedia/8c9fcf52-0055-41a0-96d9-f81b0feb98cf/aihw-can-123.pdf.aspx?inline=true>

More prescriptions of GnRH agonists are supplied to males than females. The mean and median age of male and female patients treated with GnRH agonists is different, the median age of females was 41 and the median age of males was 78. This difference is likely due to the conditions treated by GnRH agonists in males and females. In males GnRH agonists are mainly used to treat prostate cancer, the incidence of which is reported to peak between the ages of 65 and 69.<sup>11</sup> In females GnRH agonists suppress hormones to levels comparable with those observed in postmenopausal women.<sup>7</sup> They are used to treat conditions, such as endometriosis and premature ovarian failure, that generally affect pre- and perimenopausal women. GnRH agonists are also PBS listed for use in hormone receptive breast cancer, although the registered indication for goserelin does not include use in post-menopausal women.<sup>7</sup>

The comparison of use of GnRH agonists between different indications was complicated by the change in restriction level to Restricted Benefits from 1 May 2015 for goserelin and from 1 October 2016 for leuprorelin, triptorelin and nafarelin, particularly for female patients. Identifying the patient cohorts for breast cancer or endometriosis relied on patients being supplied other medicines for these indications, such as chemotherapy medicines used to treat breast cancer, and prescriber type on GnRH prescriptions. There may be patients treated for premature ovarian failure included in the endometriosis cohort, as there is overlap in the types of doctors who treat both diseases, and overlap in medicines other than GnRH agonists used to treat both diseases.

Of the 5,898 female patients identified as being supplied goserelin for breast cancer, the duration of treatment was approximately 1.2 years, without accounting for breaks.

For endometriosis, the length of treatment permitted under the PBS restrictions for goserelin and nafarelin are different. For goserelin, only one course of not more than six months is permitted. For nafarelin, patients may have an initial course of up to six months, and subsequent treatment, for up to 6 months, where the subsequent treatment must be more than two years after the end of the previous course of treatment. The majority of patients (approximately 80%) who were determined to be treated for endometriosis are not treated for longer than six months. However, there may be patients in this cohort who are being treated for conditions other than endometriosis, i.e. premature ovarian failure patients as noted above.

The duration of treatment with goserelin for premature ovarian failure was not investigated, primarily because the data was too premature as it was PBS listed on 1 December 2017.

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<sup>11</sup> Australian Institute of Health and Welfare (AIHW) 2018 Cancer Data in Australia; Australian Cancer Incidence and Mortality (ACIM) books: prostate cancer Canberra: AIHW. <<https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/>>.

## DUSC consideration

DUSC noted that goserelin and leuprorelin dominate the GnRH agonist market, and that goserelin use is two times higher than leuprorelin and appears to be growing. DUSC noted that since the restriction changes, the utilisation of nafarelin and triptorelin has also increased. In 2016 there were 1,743 prescriptions of nafarelin dispensed, and in 2018 there were 4,349 dispensed. In 2016 there were 2,821 prescriptions of triptorelin dispensed, and in 2018 there were 3,886 dispensed. DUSC commented that in addition to the change in restrictions there were likely to be other contributing factors influencing the uptake of these medicines. DUSC commented that ovarian function suppression can be achieved with GnRH agonists which can be beneficial in reducing the recurrence of early breast cancer. DUSC considered that the clinical evidence demonstrating this benefit, such as the findings from the Suppression of Ovarian Function Trial (SOFT) and the Tamoxifen and Exemestane Trial (TEXT) first published in 2014 may have encouraged a greater uptake of GnRH agonists. DUSC further noted that the overall survival data from the SOFT and TEXT trials was published in 2018 which may further influence utilisation.

DUSC noted the response from the sponsor of some leuprorelin products, where it was commented that the change to a Restricted Benefit listing may not have had an impact on the annual increase in leuprorelin's prescription volume. The sponsor response noted leuprorelin is mainly used to treat prostate cancer in older men, and the growth may be due to an ageing population.

DUSC noted there were approximately 16,000 new patients treated in 2018, but that the number of new patients appears stable, however the number of prevalent treated patients is growing. DUSC noted there are more males initiating than females, and more males treated than females.

DUSC noted that GnRH agonists are mainly used in women aged 15 to 59 years, and in men aged 45 to 99 years. DUSC noted the age at first prescription for female and male patients corresponded with the onset of conditions that are PBS listed for treatment.

DUSC noted that in female patients, use is dominated by goserelin 3.6 mg, and used primarily in women aged 15 to 59 years. DUSC noted that the PBS restriction for goserelin for endometriosis allows no more than 6 month's treatment, and that the PBS restriction for nafarelin allows up to 6 months of initial treatment and up to 6 months of subsequent treatment. DUSC noted that approximately 80% of endometriosis patients stop treatment by six months after first initiation. DUSC commented that the findings from the report showed no major concerns with people using goserelin or nafarelin outside of the PBS restrictions. DUSC also commented that these medicines can cause unpleasant side effects in women, which likely affects the length of treatment.

DUSC noted that in male patients, use is dominated by goserelin, and there has been growth in the use of leuprorelin. DUSC noted the three monthly implants are the most commonly used products in male patients for both goserelin and leuprorelin. DUSC commented that the duration of use was higher in male patients than female patients, with

some patients continuing on therapy over the entire length of the data extraction period to 5 years, which contributed to the higher number of male prevalent patients.

DUSC commented that the market is growing, but the analyses of utilisation by age showed that the use of the GnRH agonists reflects their PBS listed indications. DUSC further commented that the durations of therapy were reasonable. Overall, DUSC considered that the review's findings did not indicate that the GnRH agonists are being used outside of the PBS restrictions.

## **DUSC actions**

DUSC requested that the report be provided to the PBAC.

## **Context for analysis**

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

## **Sponsors' comments**

AstraZeneca Pty Ltd: The sponsor has no comment.

Mundipharma Pty Limited: The sponsor has no comment.

AbbVie Pty Ltd: The sponsor has no comment.

Ipsen Pty Ltd: The sponsor has no comment.

Pfizer Australia Pty Ltd: The sponsor has no comment.

## **Disclaimer**

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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## Appendix A

**Table A.1: PBS listing as at March 2019**

Item	Name, form & strength, pack size	Max. quant	Rpts	DPMQ	Brand name and manufacturer
1454M	goserelin 3.6 mg implant, 1	1	5	\$264.45	Zoladex Implant, AstraZeneca Pty Ltd
8093Y	goserelin 10.8 mg implant, 1	1	5	\$899.89	Zoladex 10.8 Implant, AstraZeneca Pty Ltd
9064C	goserelin 3.6 mg implant [1 implant] (& bicalutamide 50 mg tablet [28 tablets], 1 pack	1	5	\$413.76	ZolaCos CP 3.6/50, AstraZeneca Pty Ltd
9065D	goserelin 10.8 mg implant [1 implant] (& bicalutamide 50 mg tablet [28 tablets], 1 pack	1	5	\$1,048.56	ZolaCos CP 10.8/50(28), AstraZeneca Pty Ltd
9066E	goserelin 10.8 mg implant [1 implant] (& bicalutamide 50 mg tablet [84 tablets], 1 pack	1	5	\$1,326.29	ZolaCos CP 10.8/50(84), AstraZeneca Pty Ltd
10255R	leuprorelin acetate 30 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	1	0	\$1,186.61	Lucrin Depot Paediatric 30 mg PDS, AbbVie Pty Ltd
10256T	leuprorelin acetate 30 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	1	0	\$1,186.61	Lucrin Depot Paediatric 30 mg PDS, AbbVie Pty Ltd
10656W	leuprorelin acetate 45 mg injection: modified release [1] (& inert substance diluent [1 syringe], 1 pack	1	0	\$1,739.96	Lucrin Depot 6-Month, AbbVie Pty Ltd
8707G	leuprorelin acetate 7.5 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	1	5	\$337.75	Eligard 1 month, Mundipharma Pty Limited
8708H	leuprorelin acetate 22.5 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	1	1	\$899.89	Eligard 3 month, Mundipharma Pty Limited
8709J	leuprorelin acetate 30 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	1	1	\$1,186.61	Eligard 4 month, Mundipharma Pty Limited
8859G	leuprorelin acetate 45 mg modified release injection [1 syringe] (& inert substance diluent [1 syringe], 1 pack	1	1	\$1,739.96	Eligard 6 month, Mundipharma Pty Limited
8875D	leuprorelin acetate 7.5 mg injection: modified release [1] (& inert substance diluent [2 mL syringe], 1 pack	1	5	\$337.75	Lucrin Depot 7.5mg PDS, AbbVie Pty Ltd
8876E	leuprorelin acetate 22.5 mg injection: modified release [1] (& inert substance diluent [2 mL syringe], 1 pack	1	1	\$899.89	Lucrin Depot 3 Month PDS, AbbVie Pty Ltd

Item	Name, form & strength, pack size	Max. quant	Rpts	DPMQ	Brand name and manufacturer
8877F	leuprorelin acetate 30 mg injection: modified release [1] (&) inert substance diluent [2 mL syringe], 1 pack	1	1	\$1,186.61	Lucrin Depot 4 Month PDS, AbbVie Pty Ltd
10962Y	leuprorelin acetate 7.5 mg modified release injection [1 syringe] (&) inert substance diluent [1 syringe] (&) bicalutamide 50 mg tablet [28], 1 pack	1	5	\$416.01	Bi ELIGARD CP, Mundipharma Pty Limited
10963B	leuprorelin acetate 22.5 mg modified release injection [1 syringe] (&) inert substance diluent [1 syringe] (&) bicalutamide 50 mg tablet [28], 1 pack	1	0	\$978.15	Bi ELIGARD CP, Mundipharma Pty Limited
10969H	leuprorelin acetate 22.5 mg modified release injection [1 syringe] (&) inert substance diluent [1 syringe] (&) bicalutamide 50 mg tablet [84], 1 pack	1	1	\$1,128.04	Bi ELIGARD CP, Mundipharma Pty Limited
9378N	triptorelin 3.75 mg injection [1 vial] (&) inert substance diluent [2 mL ampoule], 1 pack	1	5	\$355.27	Diphereline, Ipsen Pty Ltd
9379P	triptorelin 11.25 mg injection [1 vial] (&) inert substance diluent [2 mL ampoule], 1 pack	1	1	\$946.98	Diphereline, Ipsen Pty Ltd
5297T	triptorelin 22.5 mg injection [1 vial] (&) inert substance diluent [2 mL ampoule], 1 pack	1	0	\$1827.47	Diphereline, Ipsen Pty Ltd
2962X	nafarelin 200 microgram/actuation nasal spray, 60 actuations	1	5	\$121.65	Synarel, Pfizer Australia Pty Ltd

Source: the [PBS website](#).

## Appendix B

**Table B.1: Medicines used as an indicator of breast cancer treatment**

Medicines
Anastrozole
Capecitabine
Cisplatin
Cyclophosphamide
Docetaxel
Doxorubicin
Doxorubicin hydrochloride
Epirubicin
Eribulin
Everolimus
Exemestane
Fluorouracil
Gemcitabine
Lapatinib
Lenograstim
Letrozole
Medroxyprogesterone
Megestrol
Mitozantrone
Nanoparticle albumin-bound paclitaxel
Paclitaxel
Pertuzumab
Ribociclib
Tamoxifen
Trastuzumab
Trastuzumab emtansine
Vinorelbine

**Table B.2: Specialities used as indicators of breast cancer and endometriosis**

<b>Prescriber type</b>	<b>Indicator</b>
Medical Oncology	Medical Oncology
Obstetrics and Gynaecology	Obstetrics and Gynaecology
Sexual Health Medicine	Obstetrics and Gynaecology
VRGP	GP
NONVRGP	GP
GP Unclassified	GP
GP Trainee	GP
Internal Medicine	Other
Haematology	Other
Rheumatology	Other
Surgery	Other
Paediatric Medicine	Other
Endocrinology	Other
Gastroenterology and Hepatology	Other
Pathology	Other
College Trainee - Physician	Other
Neurology	Other
Palliative Medicine	Other
Nephrology	Other
Dermatology	Other
Immunology and Allergy	Other
Psychiatry	Other
Nuclear Medicine	Other
Cardiology	Other
Geriatric Medicine	Other
Intensive Care	Other
Anaesthetics	Other
Nurse Practitioner	Other
Respiratory and Sleep Medicine	Other
Ophthalmology	Other
ENT	Other
Infectious Diseases	Other
Sport and Exercise Medicine	Other
Urogynaecology	Other
Public Health Medicine	Other
Rehabilitation Medicine	Other
Diagnostic Radiology	Other
Occupational & Environmental Medicine	Other
Addiction Medicine	Other
Clinical Genetics	Other
Optometrist	Other

## Appendix C

Table C.1 shows the number of initiating patients in each age group between 1 January 2014 and 31 December 2018.

**Table C.1: Age and gender of initiating patients**

	Female patients	Male patients
0-4 yrs	46	15
5-9 yrs	563	87
10-14 yrs	149	100
15-19 yrs	394	67
20-24 yrs	1,060	24
25-29 yrs	1,735	26
30-34 yrs	3,522	38
35-39 yrs	4,369	48
40-44 yrs	4,453	86
45-49 yrs	3,163	198
50-54 yrs	1,168	738
55-59 yrs	128	2,142
60-64 yrs	53	5,063
65-69 yrs	82	9,838
70-74 yrs	99	12,902
75-79 yrs	75	14,185
80-84 yrs	84	12,714
85-89 yrs	53	9,612
90-94 yrs	9	3,490
95-99 yrs	≤5	481
100+ yrs		30