NEW ZEALAND DATA SHEET

1. PRODUCT NAME

ZOLADEX® 3.6 mg Depot Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Goserelin (present as goserelin acetate) 3.6 mg injection.

3. PHARMACEUTICAL FORM

Injection (depot)

A sterile, white to cream coloured cylindrical implant in which goserelin acetate (equivalent to 3.6 mg of peptide base) is dispersed in a biodegradable matrix. It is supplied in a single dose syringe applicator. The SafeSystem™ incorporates a protective needle sleeve that automatically locks in place following administration of the implant to aid in the prevention of needle stick injury.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

ZOLADEX 3.6 mg is indicated for the management of:

1. Prostate cancer suitable for hormonal manipulation.
2. Adjuvant and neoadjuvant therapy in combination with radiotherapy for the management of locally advanced prostate cancer in men suitable for hormonal manipulation.
3. Pre- and peri-menopausal women with hormone receptor positive breast cancer suitable for hormonal manipulation.
4. Endometriosis:- ZOLADEX alleviates symptoms including pain, and reduces the size and number of endometrial lesions.
5. Uterine fibroids:- ZOLADEX shrinks the lesions, reduces symptoms including pain, and causes cessation of menses in the majority of patients thereby improving haematological status when previous heavy menstrual loss has caused anaemia.
6. Endometrial thinning:- Use as an endometrial thinning agent prior to endometrial ablation. As a prethinning agent ZOLADEX 3.6 mg should be administered as two implants, four weeks apart, with surgery planned for between zero and two weeks after the second implant injection.
7. Assisted reproduction:- Pituitary down regulation in preparation for superovulation.

4.2 DOSE AND METHOD OF ADMINISTRATION

Caution should be taken while inserting ZOLADEX into the anterior abdominal wall due to the proximity of underlying inferior epigastric artery and its branches.

Use extra care when administering ZOLADEX to patients with a low BMI and/or who are receiving full anticoagulation medication (see section 4.4).

For correct administration of ZOLADEX, see instructions on the administration card (also see Method of administration below).

Adults

One 3.6 mg implant of ZOLADEX injected subcutaneously into the anterior abdominal wall, every 28 days.

Use of ZOLADEX in treatment of benign gynaecological conditions should be limited to six months because of possible osteoporotic effects.

Adjuvant and/or neoadjuvant Zoladex therapy in combination with radiotherapy may include short-term use of an anti-androgen to prevent flare (see ACTIONS).

Assisted reproduction

Once pituitary down regulation has been achieved with ZOLADEX, superovulation and oocyte retrieval should be carried out in accordance with normal practice.

Elderly

No dosage adjustment is necessary for in the elderly.

Renal and hepatic Impairment

No dosage adjustment is necessary for patients with renal or hepatic impairment.

Children

Not indicated for use in children.

Method of administration

For correct administration of ZOLADEX, see instructions on the pouch/carton.

Use as directed by the prescriber. Use extra care when administering ZOLADEX to patients with a low BMI and/or who are receiving full anticoagulation medication (see section 4.4).

Use only if pouch is undamaged. Use immediately after opening pouch.

The following information is intended for medical or healthcare professionals only:

ZOLADEX is administered by subcutaneous injection - read and understand all the instructions fully prior to administration

1. Put the patient in a comfortable position with the upper part of the body slightly raised.
   Prepare the injection site according to the local policy and procedure.

NOTE: Caution should be taken while injecting ZOLADEX into the anterior abdominal wall due to the proximity of underlying inferior epigastric artery and its branches; very thin patients may be at higher risk of vascular injury.

2. Examine the foil pouch and syringe for damage. Remove the syringe from the opened foil pouch and hold the syringe at a slight angle to the light.
   Check that at least part of the ZOLADEX implant is visible. **(Figure 1).**

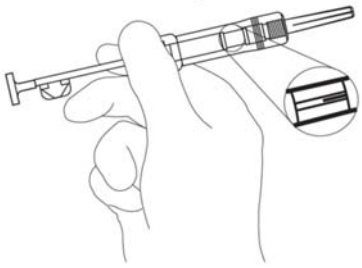

Figure 1.

3. Grasp the plastic safety tab and pull away from the syringe, and discard. **(Figure 2).**
   Remove needle cover. **Unlike liquid injections, there is no need to remove air bubbles as attempts to do so may displace the ZOLADEX implant.**

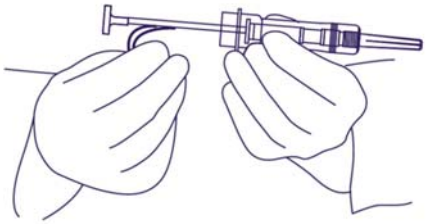

Figure 2.

4. Holding the syringe around the protective sleeve, using an aseptic technique, pinch the patient's skin and insert the needle at a slight angle (30 to 45 degrees) to the skin.
   With the opening of the needle facing up, **insert needle into the subcutaneous tissue** of the anterior abdominal wall below the navel line, until the protective sleeve touches the patient's skin. **(Figure 3).**

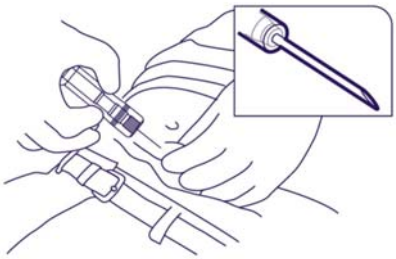

Figure 3.

NOTE: The ZOLADEX syringe cannot be used for aspiration. If the hypodermic needle penetrates a large vessel, blood will be seen instantly in the syringe chamber. If a vessel is penetrated, withdraw the needle and immediately control any resultant bleeding, monitoring the patient for signs or symptoms of abdominal haemorrhage. After ensuring the patient is haemodynamically stable another ZOLADEX implant may be injected with a new syringe elsewhere. Use extra care when administering ZOLADEX to patients with a low BMI and/or to patients receiving full dose anticoagulation.

5. **Do not penetrate into muscle or peritoneum.** Incorrect grip and angle of presentation is shown **(Figure 4.)**

Figure 4.

6. Depress the plunger **fully**, until you can depress no more, to discharge the ZOLADEX implant and to activate the protective sleeve. You may hear a 'click' and will feel the protective sleeve automatically begin to slide to cover the needle. If the plunger is not depressed fully, the protective sleeve will **NOT** activate.

   NOTE: The needle does not retract.

7. Holding the syringe as shown in **Figure 5,** withdraw the needle and allow protective sleeve to continue to slide and cover needle.
   1. Dispose of the syringe in an approved sharps collector.

Figure 5.

NOTE: In the unlikely event of the need to surgically remove a ZOLADEX implant, it may be localized by ultrasound.

4.3 CONTRAINDICATIONS

Known severe hypersensitivity to the active substance or to any of the excipients of this product.

Pregnancy and lactation (see section 4.6).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

ZOLADEX 3.6 mg is not indicated for use in children, as safety and efficacy have not been established in this group of patients.

Injection site injury has been reported with ZOLADEX, including events of pain, haematoma, haemorrhage and vascular injury. Monitor affected patients for signs or symptoms of abdominal haemorrhage. In very rare cases, administration error resulted in vascular injury and haemorrhagic shock requiring blood transfusions and surgical intervention. Extra care should be taken when administering ZOLADEX to patients with a low BMI and/or receiving full anticoagulation medications.

The use of ZOLADEX 3.6 mg in men at particular risk of developing ureteric obstruction or spinal cord compression should be considered carefully and the patients monitored closely during the first month of therapy. If spinal cord compression or renal impairment due to ureteric obstruction are present or develop, specific standard treatment of these complications should be instituted. Isolated cases have been reported.

Initially ZOLADEX, like other LHRH agonists, transiently increases serum testosterone. Some patients may experience a temporary increase in bone pain, which can be managed symptomatically.

A reduction in glucose tolerance has been observed in males receiving LHRH agonists. This may manifest as diabetes or loss of glycaemic control in those with pre-existing diabetes mellitus. Consideration should therefore be given to monitoring blood glucose.

An increased risk of developing myocardial infarction and sudden cardiac death has been reported in association with use of GnRH agonists in men. The risk appears low based on the reported odds ratios, and should be evaluated carefully along with cardiovascular risk factors when determining a treatment for patients with prostate cancer. Patients receiving a GnRH agonist should be monitored for symptoms and signs suggestive of development of cardiovascular disease.

The use of LHRH agonists may cause a reduction in bone mineral density. In women, current available data suggest that recovery of bone loss occurs on cessation of therapy in the majority. Preliminary data suggest the use of ZOLADEX in combination with tamoxifen in patients with breast cancer may reduce bone mineral loss. In patients receiving ZOLADEX for the treatment of endometriosis, the addition of hormone replacement therapy (a daily oestrogenic agent and a progestogenic agent) has been shown to reduce bone mineral density loss and vasomotor symptoms. In men, preliminary data suggest the use of a bisphosphonate in combination with a LHRH agonist may reduce bone mineral loss.

Following two years treatment for early breast cancer in women, the average loss of BMD was 6.2% and 11.5% at the femoral neck and lumbar spine respectively. This loss has been shown to be partially reversible at the one year off treatment follow-up with recovery to 3.4% and 6.4% relative to baseline at the femoral neck and lumbar spine respectively.

Currently, there are no clinical data on the effects of treating benign gynaecological conditions with ZOLADEX 3.6 mg for periods in excess of six months.

Androgen deprivation therapy may prolong the QT interval, although a causal association has not been established with ZOLADEX. In patients with a history of or who have risk factors for QT prolongation and in patients receiving concomitant medicinal products that may prolong the QT interval (see section 4.5) physicians should assess the benefit risk ratio including the potential for Torsade de Pointes prior to initiating ZOLADEX.

The use of ZOLADEX may cause an increase in cervical resistance and care should be taken when dilating the cervix.

Assisted reproduction

ZOLADEX 3.6 mg should only be administered as part of a regimen for assisted reproduction under the supervision of a specialist experienced in the area.

As with other LHRH agonists, there have been reports of ovarian hyperstimulation syndrome (OHSS) associated with use of ZOLADEX 3.6 mg in combination with gonadotrophins. The

stimulation cycle should be monitored carefully to identify patients at risk of developing OHSS. Human chorionic gonadotrophin (hCG) should be withheld if appropriate.

It is recommended that ZOLADEX 3.6 mg be used with caution in assisted reproduction regimens in patients with polycystic ovarian syndrome, as follicle recruitment may be increased.

ZOLADEX is not indicated for use in children as safety and efficacy has not been established in this group of patients.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

No pharmacological incompatibilities have been encountered.

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of ZOLADEX with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de Pointes should be carefully evaluated (see section 4.4).

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy

ZOLADEX 3.6 mg should not be used in pregnancy as there is a theoretical risk of abortion or foetal abnormality if LHRH agonists are used during pregnancy. Potentially fertile women should be examined carefully before treatment to exclude pregnancy. Non hormonal methods of contraception should be employed during therapy until menses is resumed.

Pregnancy should be excluded before ZOLADEX 3.6 mg is used for assisted reproduction. When ZOLADEX 3.6 mg is used in this setting, there is no clinical evidence to suggest a causal association between ZOLADEX and any subsequent abnormalities of oocyte development or pregnancy and outcome.

Breast-feeding

The use of ZOLADEX during breast feeding is not recommended.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

There is no evidence that ZOLADEX 3.6 mg results in impairment of ability to drive or operate machinery.

4.8 UNDESIRABLE EFFECTS

The following frequency categories for adverse drug reactions (ADRs) were calculated based on reports from ZOLADEX clinical trials and post-marketing sources.

Table 1 ZOLADEX 3.6 mg adverse drug reaction by frequency and System Organ Class (SOC)

Frequency Descriptor	SOC	Males	Females
Very Common (~~≥10%~~)	Psychiatric disorders	Libido decreased[a]	Libido decreased[a]
	Vascular disorders	Hot flush[a]	Hot flush[a]
	Skin and subcutaneous tissue disorders	Hyperhidrosis[a]	Hyperhidrosis[a],acne[i]
	Reproductive system and breast disorders	Erectile dysfunction	N/A
		N/A	Vulvovaginal dryness
		N/A	Breast enlargement
	General disorders and administration site conditions	(see Common)	Injection site reactions
Common (≥ 1%~~-~~and <10%)	Metabolism and nutrition disorders	Glucose tolerance impaired[b]	NA
	Psychiatric disorders	Mood swings	Mood altered, depression
	Nervous system disorders	Paraesthesia	Paraesthesia
		Spinal cord compression	N/A
		N/A	Headache
	Cardiac disorders	Cardiac failure[f] Myocardial infarction[f]	N/A
	Vascular disorders	Blood pressure abnormal[c]	Blood pressure abnormal[c]
	Skin and subcutaneous tissue disorders	Rash[d]	Rash[d], alopecia[g]
	Musculoskeletal, connective tissue and bone disorders	Bone pain[e]	N/A
		(see Uncommon)	Arthralgia
	Reproductive system and breast disorders	Gynaecomastia	N/A
	General disorders and administration site conditions	N/A	Tumour flare, tumour pain
		Injection site reaction	(see Very Common)
	Investigations	Density decreased, weight increased	Bone density decreased, weight increased
Uncommon (≥0.1% and <1%)	Immune system disorders	Drug hypersensitivity	Drug hypersensitivity
	Musculoskeletal, connective tissue and bone disorders	Arthralgia	(see Common)
	Renal and urinary disorders	Ureteric obstruction	N/A
	Reproductive system and breast disorders	Breast tenderness	N/A

Frequency Descriptor	SOC	Males	Females
	Metabolism and nutrition disorders	N/A	Hypercalcaemia
Rare (≥0.01% and <0.1%)	Immune system disorders	Anaphylactic reaction	Anaphylactic reaction
	Reproductive system and breast disorders	N/A	Ovarian cyst
		N/A	Ovarian hyper-stimulation syndrome
Very Rare (<0.01%)	Neoplasms benign, malignant and unspecified (including cysts and polyps)	Pituitary tumour	Pituitary tumour
	Endocrine disorders	Pituitary haemorrhage	Pituitary haemorrhage
	Psychiatric disorders	Psychotic disorder	Psychotic disorder
Unknown	Neoplasms benign, malignant and unspecified (including cysts and polyps)	N/A	Degeneration of uterine fibroid
	Skin and subcutaneous tissue disorders	Alopecia[h]	(see Common)

a These are pharmacological effects which seldom require withdrawal of therapy.
b A reduction in glucose tolerance has been observed in males receiving LHRH agonists. This may manifest as diabetes or loss of glycaemic control in those with pre-existing diabetes mellitus.
c These may manifest as hypotension or hypertension, have been occasionally observed in patients administered ZOLADEX. The changes are usually transient, resolving either during continued therapy or after cessation of therapy with ZOLADEX. Rarely, such changes have been sufficient to require medical intervention, including withdrawal of treatment from ZOLADEX
d These are generally mild, often regressing without discontinuation of therapy.
e Initially, prostate cancer patients may experience a temporary increase in bone pain, which can be managed symptomatically.
f Observed in a pharmaco-epidemiology study of LHRH agonists used in the treatment of prostate cancer. The risk appears to be increased when used in combination with anti-androgens.
g Loss of head hair has been reported in females, including younger patients treated for benign conditions. This is usually mild but occasionally can be severe.
h Particularly loss of body hair, an expected effect of lowered androgen levels.
i In most cases acne was reported within one month after the start of ZOLADEX.

Reduction in glucose tolerance, manifesting as diabetes or loss of glycaemic control in those with pre-existing diabetes, has been reported during treatment with GnRH agonists including ZOLADEX (see section 4.4).

A small increased risk of developing myocardial infarction and sudden cardiac death has been reported in association with use of GnRH agonists in men.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 OVERDOSE

There is limited experience of overdosage in humans. In cases where ZOLADEX has unintentionally been re-administered early or given at a higher dose, no clinically relevant adverse effects have been seen. Animal tests suggest that no effect other than the intended therapeutic effects on sex hormone concentrations and on the reproductive tract will be evident with higher doses of ZOLADEX. If overdosage occurs, this should be managed symptomatically.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PARTICULARS

5.1 PHARMACODYNAMIC PROPERTIES

ZOLADEX (d-Ser(But)^{6}Azgly^{10} LHRH) is a synthetic analogue of naturally occurring luteinising-hormone releasing hormone (LHRH). On chronic administration ZOLADEX results in inhibition of pituitary LH secretion leading to a fall in serum testosterone concentrations in males and serum oestradiol concentrations in females. Initially, ZOLADEX, like other LHRH agonists, may transiently increase serum testosterone concentration in men and serum oestradiol concentration in women.

In men, by around 21 days after the first implant injection, testosterone concentrations have decreased to within the castrate range and remain suppressed with continuous treatment every 28 days. This inhibition leads to prostate tumour regression and symptomatic improvement in the majority of patients.

In women serum oestradiol concentrations are suppressed by around 21 days after the first depot injection and, with continuous treatment every 28 days remain suppressed at levels comparable with those observed in post menopausal women. This suppression is associated with endometrial thinning, suppression of follicular development within the ovary and a response in hormone dependent breast cancer (tumours that are ER-positive and/or PgR-positive), endometriosis and uterine fibroids and will result in amenorrhoea in the majority of patients. ZOLADEX results in cessation of menses in the majority of patients and so leads to an improvement in haematological status when this has been affected by the patient's fibroids. Menses usually return on average at 10 to 15 weeks post treatment. Fibroid regrowth has also been seen at 12 weeks post treatment. During early treatment with ZOLADEX some women may experience vaginal bleeding of variable duration and intensity. Such bleeding probably represents oestrogen withdrawal bleeding and is expected to stop spontaneously. Rarely, some women may enter the menopause during treatment with LHRH analogues and not resume menses on cessation of therapy.

Clinical efficacy and safety

<u>Effect in prostate cancer – Adjuvant and neoadjuvant ZOLADEX therapy in combination with radiotherapy</u>

Four phase III, open-labelled, randomised, controlled, multi-centred clinical trials have been conducted to evaluate the added value of adjuvant and/or neoadjuvant ZOLADEX therapy in combination with radiotherapy in patients with histologically proven prostate cancer. The majority of patients had locally advanced disease (T2 N+, T3 or T4, N0/Nx, M0). All studies have been performed by two independent collaborative oncology groups (European Organisation for Research and Treatment of Cancer [EORTC] and the Radiation Therapy

Oncology Group [RTOG]), and have reported results from median follow-up of more than 5 years. Table 2 summarises the study design, patient populations and median follow-up periods for these studies.

Table 2: Study design, patient population and median follow-up period for adjuvant and/or neoadjuvant ZOLADEX combined with radiotherapy clinical trials.

	Adjuvant		*Neo-adjuvant*	*Neo and adjuvant*
Trial	*RTOG 85-31 (n=945)*	*EORTC 22863 (n=415)*	*RTOG 86-10 (n=456)*	*RTOG 92-02 (n=1514)*
Treatment	ZOLADEX * + RT	ZOLADEX *# + RT	ZOLADEX *§ + RT	ZOLADEX *§ (neo) + RT + ZOLADEX * alone (adjuvant)
Comparator	RT alone + ZOLADEX at relapse	RT alone	RT alone	ZOLADEX *§ (neo) only + RT
Duration	Last week of RT continued indefinitely	Day 1 of RT continued for 3 years post RT	2 months prior to & during RT	2 months prior to, during & 2 years post RT 2 months prior to & during RT
Patient population	T1-2N+ & T3 (any N); Lesions <25cm^3; prior prostatectomy allowed^	T1-2N0-X (G3) & T3-4N0 (any G)	T2b-4M0; N+ allowed†; Lesions ≥25cm^3	T2c-T4; PSA <150ng/mL; N+ allowed†; KS ≥70
Median follow-up	7.6 years[a]	5.5 years[b]	6.7 years[c]	5.8 years[d]

*T, N – Tumour, node in accordance with the UICC classification; G – WHO grade; *3.6 mg sc every 4 weeks; # plus 1 month of oral cyproterone acetate 150mg/day initiated 1 week prior to ZOLADEX to prevent flare; RT – radiotherapy; § combined with oral flutamide (250mg three times daily); ^ if penetration to the margins of resection and/or seminal vesicle involvement + Karnofsky performance status >60%; † if below the common iliac chain; KS – Karnofsky score.*

[a]Pilepich et al 2003a, Proc Am Soc Oncol 22: 1530 (including ASCO presentation slides), and Pilepich et al 2003b, Int J Radiation Oncol Biol Phys 57: S172-3; [b]Bolla et al 2002, Lancet 360: 103-8; [c]Pilepich et al 2001, Int J Radiation Oncol Biol Phys 50: 1243-1252 and Shipley et al 2002, In J Radiation Oncol Biol Phys 54: 1302-1310; [d]Hanks et al 2003, JCO 21: 3972-3978

Adjuvant ZOLADEX therapy long term (≥3 years) significantly improved disease-free survival and overall survival compared to radiotherapy alone (Tables 3 and 4). Neoadjuvant ZOLADEX therapy for two months prior and during radiotherapy significantly improved disease-free survival but not overall survival compared to radiotherapy alone (Table 5). A combination of neoadjuvant and adjuvant therapy (2 years) also significantly improved disease-free survival but not overall survival compared to radiotherapy alone (Table 6).

Table 3: Adjuvant ZOLADEX efficacy results for RTOG 85-31 (median follow-up: all patients 7.6 years ; alive patients 10 years)

Endpoint	*10 year estimates (%)*		*p value*
	ZOLADEX + RT	*RT alone*	
Overall survival	47*	38	0.0043
Disease-free survival	30	9	<0.0001

**ASCO presentation slides*

Table 4: Adjuvant ZOLADEX efficacy results for EORTC 22863 (median follow-up: all patients 5.5 years)

Endpoint	*5 year estimates (%)*		*Hazard ratio [95% CI]*
	ZOLADEX +RT	*RT alone*	
Overall survival	78	62	0.51 [0.36, 0.73]
Disease-free survival	74	40	0.34 [0.26, 0.46]

CI – confidence interval

Table 5: Neoadjuvant ZOLADEX efficacy results for RTOG 86-10 (median follow-up: all patients 6.7 years; alive patients 8.6 years)

Endpoint	*8 year estimates (%)*		*p value*
	ZOLADEX + RT	*RT alone*	
Overall survival	53 {53*}	44 {43*}	0.10 {0.08*}
Disease-free survival	49	34	0.004

**updated analyses (Shipley et al 2002 – all patients 6.7 years; alive patients 9.0 years)*

Table 6: Neoadjuvant and/or adjuvant ZOLADEX efficacy results for the total RTOG 92-02 population (median follow-up: all patients 5.8 years; alive patients 6.3 years)

Endpoint	*5 year estimates (%)*		*p value*
	Neo & adjuvant ZOLADEX	*Neo ZOLADEX only*	
Overall survival	80.0	78.5	ns
Disease-free survival	46	28	<0.0001

ns – not significant

5.2 PHARMACOKINETIC PROPERTIES

The bioavailability of ZOLADEX is almost complete. The implant formulation of ZOLADEX releases the medicine continuously with peak serum concentrations occurring approximately two weeks after administration. Administration of an implant every four weeks ensures that effective concentrations are maintained with no tissue accumulation.

ZOLADEX is poorly protein bound and has a serum elimination half-life of two to four hours in subjects with normal renal function.

The half-life is increased in patients with impaired renal function. For the compound given monthly in an implant formulation this change will have minimal effect. Hence, no change in dosing is necessary in these patients.

There is no significant change in pharmacokinetics in patients with hepatic failure.

5.3 PRECLINICAL SAFETY DATA

Following long-term repeated dosing with ZOLADEX, an increased incidence of benign pituitary tumours has been observed in male rats. While this finding is similar to that previously noted in this species following surgical castration, any relevance to humans has not been established.

In mice, long term repeated dosing with multiples of the human dose produced histological changes in some regions of the digestive system manifested by pancreatic islet cell hyperplasia and a benign proliferative condition in the pyloric region of the stomach, also reported as a spontaneous lesion in this species. The clinical relevance of these findings is unknown.

ZOLADEX is a synthetically derived peptide.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Polyglactin

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

3 years.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

There is one implant per pack.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Return unused and expired medicines to your local pharmacy for disposal.

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

AstraZeneca Limited
PO Box 87453
Meadowbank
Auckland 1742.
Telephone: (09) 306 5650

9. DATE OF FIRST APPROVAL

30 April 1987

10. DATE OF REVISION OF THE TEXT

8 May 2020

CDS 130515 + Aust PI

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
8	PO Box address updated.
10.	Trademark information updated.