New

ZOLADEX LA 10.8 MG

(*goserelin*)

Name of the medicinal product

ZOLADEX LA 10.8 mg depot

Qualitative and quantitative composition

Goserelin acetate (equivalent to 10.8 mg goserelin)

Pharmaceutical form

Depot, pre-filled syringe

Indications

ZOLADEX LA 10.8 mg is indicated in the management of prostate cancer suitable for hormonal manipulation.

Dosage and 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 Warnings and Precautions].

For correct administration of ZOLADEX, see instructions on the instruction card (see Instructions for use, handling and disposal).

Adult Males (including the elderly)

One 10.8 mg depot of ZOLADEX LA injected subcutaneously into the anterior abdominal wall, every 12 weeks.

No dosage adjustment is necessary for patients with renal impairment.

No dosage adjustment is necessary for patients with hepatic impairment.

Females

ZOLADEX LA 10.8 mg is not indicated for use in females.

Children

ZOLADEX LA 10.8 mg is not indicated for use in children.

Contra-indications

ZOLADEX LA 10.8 mg should not be given to patients with a known hypersensitivity to the active substance, to other LHRH analogues, or to any of the excipients of this product.

Warnings and Precautions

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 [see Dosage and Administration].

ZOLADEX LA 10.8 mg is not indicated for use in females, since there is insufficient evidence of reliable suppression of serum oestradiol. For female patients requiring treatment with goserelin, refer to the prescribing information for ZOLADEX 3.6mg.
ZOLADEX LA 10.8 mg is not indicated for use in children, as safety and efficacy have not been established in this group of patients.

The use of ZOLADEX LA 10.8 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.
In men, preliminary data suggest the use of a bisphosphonate in combination with a LHRH agonist may reduce mineral loss.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.

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 Interactions) physicians should assess the benefit risk ratio including the potential for Torsade de Pointes prior to initiating ZOLADEX.

Interactions

None known.

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 Warnings and Precautions).

Pregnancy and Lactation

ZOLADEX LA 10.8 mg is not indicated for use in females.

Effect on ability to drive or operate machinery

There is no evidence that ZOLADEX LA 10.8 mg results in impairment of ability to drive or operate machinery.

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 LA 10.8 mg adverse drug reactions by frequency and System Organ Class (SOC)

Frequency Descriptor	**SOC**	**Males**
Very Common (≥10%)	Psychiatric disorders	Libido decreased[a]
	Vascular disorders	Hot flush[a]
	Skin and subcutaneous tissue disorders	Hyperhidrosis[a]
	Reproductive system and breast disorders	Erectile dysfunction
Common (≥1% and <10%)	Metabolism and nutrition disorders	Glucose tolerance impaired[b]
	Nervous system disorders	Paraesthesia
Common (continued)		Spinal cord compression
	Cardiac disorders	Cardiac failure[f], myocardial infarction[f]
	Vascular disorders	Blood pressure abnormal[c]
	Skin and subcutaneous tissue disorders	Rash[d]
	Musculoskeletal, connective tissue and bone disorders	Bone pain[e]

Frequency Descriptor	SOC	Males
	Reproductive system and breast disorders	Gynaecomastia
	General disorders and administration site conditions	Injection site reaction
	Investigations	Bone density decreased
		Weight increased
	Psychiatric disorders	Mood swings
Uncommon (≥0.1% and <1%)	Immune system disorders	Drug hypersensitivity
	Musculoskeletal, connective tissue and bone disorders	Arthralgia
	Renal and urinary disorders	Ureteric obstruction
	Reproductive system and breast disorders	Breast tenderness
Rare (≥0.01% and <0.1%)	Immune system disorders	Anaphylactic reaction
Very rare (<0.01%)	Neoplasms benign, malignant and unspecified (including cysts and polyps)	Pituitary tumour
	Endocrine disorders	Pituitary haemorrhage
	Psychiatric disorders	Psychotic disorder
Unknown	Skin and subcutaneous tissue disorders	Alopecia[9]
	Cardiac disorders	QT prolongation

[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] Particularly loss of body hair, an expected effect of lowered androgen levels.

Overdosage

There is limited experience of overdosage in humans. In cases where ZOLADEX has unintentionally been readministered 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 LA 10.8 mg. If overdosage occurs, this should be managed symptomatically.

Pharmacodynamic Properties

Mode of action: ZOLADEX (D-Ser(Bu^t)^6 Azgly^{10} LHRH) is a synthetic analogue of naturally occurring luteinising hormone releasing hormone (LHRH). On chronic administration ZOLADEX LA 10.8 mg results in inhibition of pituitary LH secretion leading to a fall in serum testosterone concentrations in males. Initially, ZOLADEX LA 10.8 mg, like other LHRH agonists, transiently increases serum testosterone concentration.

In men by around 21 days after the first depot injection testosterone concentrations have fallen to within the castrate range and remain suppressed with treatment every 12 weeks.

Pharmacokinetic Properties

Administration of ZOLADEX LA 10.8 mg every 12 weeks ensures that exposure to goserelin is maintained with no clinically significant 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 in a 10.8 mg depot formulation every 12 weeks, this change will not lead to any accumulation. Hence, no change in dosing is necessary in these patients. There is no significant change in pharmacokinetics in patients with hepatic failure.

Preclinical Safety Data

Following long-term repeated dosing with ZOLADEX, an increased incidence of benign pituitary tumours has been observed in male rats. Whilst 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. This is 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.

Precautions for Storage

Do not store above 25°C.

Instructions for use, handling and disposal

For correct administration of ZOLADEX, see instructions on the instruction card.

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 Warnings and Precautions].

Use only if pouch is undamaged. Use immediately after opening pouch.
Dispose of the syringe in an approved sharps collector.

Pack size

Please refer to the outer carton for pack size.

Shelf life

Please refer to expiry date on the outer carton.

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