AstraZeneca UK Limited
Horizon Place, 600 Capability Green
Luton, LU1 3LU, Bedfordshire
T: +01582 836000
www.astrazeneca.co.uk

27th January 2016

Important information for Healthcare Professionals

Zoladex (goserelin) 3.6 mg Implant, MA044/00901
Zoladex LA (goserelin) 10.8 mg Implant, MA044/00902

Dear Healthcare Professional,

AstraZeneca Pharmaceuticals Ltd in agreement with the Medicines Authority would like to inform you of updated information regarding the **special warnings and precaution for use during the administration of Zoladex and Zoladex LA**.

Zoladex and Zoladex LA are both administered by subcutaneous injection - it is important to read and understand all the instructions fully prior to administration. The instructions for product administration are now included in the Summary of Product Characteristics, in addition to the Instruction Card contained inside the product carton.

The method of administration is included in the Annex to this letter.

Therapeutic indications[1,2]

Zoladex 3.6mg Implant is indicated for:

(i) Prostate cancer: Zoladex 3.6 mg is indicated in the management of prostate cancer suitable for hormonal manipulation.

(ii) Breast cancer: Zoladex 3.6 mg is indicated in the management of breast cancer in pre and perimenopausal women suitable for hormonal manipulation.

(iii) Endometriosis: In the management of endometriosis, Zoladex 3.6 mg alleviates symptoms, including pain, and reduces the size and number of endometrial lesions.

(iv) Uterine fibroids: In the management of fibroids, Zoladex 3.6 mg shrinks the lesions, improves the patient's haematological status and reduces symptoms, including pain. It is used as an adjunct to surgery to facilitate the operative technique and reduce operative blood loss.

(v) 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 depots, four weeks apart, with surgery planned for between zero and two weeks after the second depot injection.

(vi) Assisted reproduction: Pituitary down regulation in preparation for superovulation.

Zoladex LA 10.8 mg Implant is indicated for:

(i) Prostate cancer: Zoladex LA is indicated in the management of prostate cancer suitable for hormonal manipulation.

(ii) Endometriosis: Zoladex LA is indicated in the management of endometriosis including alleviation of symptoms, such as pain, and reduction in the size and number of endometrial lesions.

(iii) Uterine fibroids: Zoladex LA is indicated in the management of fibroids including shrinkage of lesions, improvement in the patient's haematological status and reduction of symptoms, such as pain. It can be used as an adjunct to surgery to facilitate the operative technique and reduce operative blood loss.

Update to the Summary of Product Characteristics[1]

4.2 Posology 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.

The Zoladex and Zoladex LA Instruction Cards also include the above safety warnings.

4.4 Special warnings and precautions for use

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.

Please ensure that all relevant staff are made aware of the content of this letter and that the information is communicated to staff responsible for the administration of Zoladex and Zoladex LA.

Reporting of suspected adverse reactions

Adverse Drug Reaction and medication errors should be reported. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and sent to ADR reporting/Post-Licensing Directorate/Medicines Authority, 203, Level 3, Rue D'Argens, Gzira GZR 1368, Malta or sent by email to: Postlicensing.medicinesauthority@gov.mt

Adverse events should also be reported to Associated Drug Co. Ltd Tel: 22778115

Contact Details

Should you have any queries or require additional information regarding the use of Zoladex or Zoladex LA, please contact Associated Drug Co. Ltd on 0035622778115.

Yours sincerely,

Dr Jonathan Day MBBS PhD FFPM FESC MRCS
Director Medical and Healthcare Affairs
AstraZeneca
Global Commercial | UK Marketing Company

Prescribing Information

Please refer to the Summary of Product Characteristics (SmPC) for full prescribing information and instructions on the administration of Zoladex and Zoladex LA. http://www.medicinesauthority.gov.mt/search-medicine-results?modSearch=sim&field=BDC9AB8B9B66D2

1. Zoladex: http://www.medicinesauthority.gov.mt/search-medicine-results?modSearch=sim&field=BDC9AB8B9B66D2
2. Zoladex LA: http://www.medicinesauthority.gov.mt/search-medicine-results?modSearch=sim&field=BDC9AB8B9B66D2

The instructions for administration of Zoaldex and Zoladex LA are also available on the Instruction Card contained inside the product carton.

Annex to letter: Method of administration as per the SmPC.

Zoladex and Zoladex LA – Method of Administration[1]

The method of administration for Zoladex and Zoladex LA is the same. Both products are administered by subcutaneous injection - please 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 and Zoladex LA 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).**

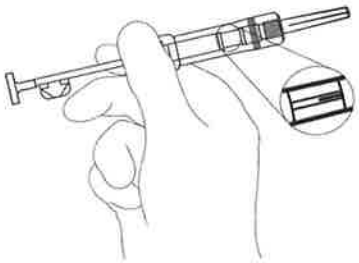

Figure 1.

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.**

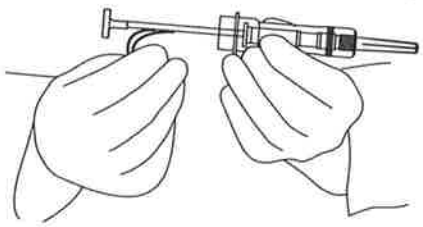

Figure 2.

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).**

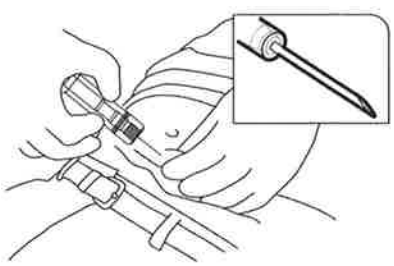

Figure 3.

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.

   Dispose of the syringe in an approved sharps collector.

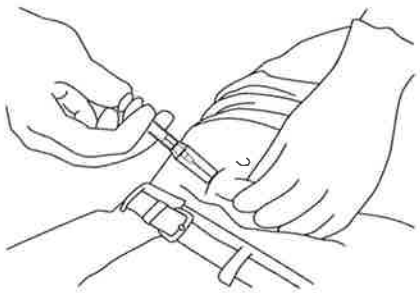

Figure 5.

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