

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cetrotide 0.25 mg powder and solvent for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 0.25 mg cetrorelix (as acetate).

After reconstitution with the solvent provided, each ml of the solution contains 0.25 mg cetrorelix.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

Appearance of the powder: white lyophilisate

Appearance of the solvent: clear and colourless solution

The pH of the reconstituted solution is 4.0 – 6.0

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention of premature ovulation in patients undergoing a controlled ovarian stimulation, followed by oocyte pick-up and assisted reproductive techniques.

In clinical trials Cetrotide was used with human menopausal gonadotropin (HMG), however, limited experience with recombinant follicle-stimulating hormone (FSH) suggested similar efficacy.

4.2 Posology and method of administration

Cetrotide should only be prescribed by a specialist experienced in this field.

The first administration of Cetrotide should be performed under the supervision of a physician and under conditions where treatment of possible allergic/pseudo-allergic reactions (including life-threatening anaphylaxis) is immediately available. The following injections may be self-administered as long as the patient is made aware of the signs and symptoms that may indicate hypersensitivity, the consequences of such a reaction and the need for immediate medical intervention.

The contents of 1 vial (0.25 mg cetrorelix) are to be administered once daily, at 24 h intervals, either in the morning or in the evening. Following the first administration, it is advised that the patient be kept under medical supervision for 30 minutes to ensure there is no allergic/pseudo-allergic reaction to the injection.

Cetrotide is for subcutaneous injection into the lower abdominal wall.

The injection site reactions may be minimised by rotating the injection sites, delaying injection at the same site and injecting the product in a slow rate to facilitate the progressive absorption of the product.

Administration in the morning: Treatment with Cetrotide should commence on day 5 or 6 of ovarian stimulation (approximately 96 to 120 hours after start of ovarian stimulation) with urinary or recombinant gonadotropins and is to be continued throughout the gonadotropin treatment period including the day of ovulation induction.

Administration in the evening: Treatment with Cetrotide should commence on day 5 of ovarian stimulation (approximately 96 to 108 hours after start of ovarian stimulation) with urinary or recombinant gonadotropins and is to be continued throughout the gonadotropin treatment period until the evening prior to the day of ovulation induction.

Additional information on special populations:

There is no relevant indication for the use of Cetrotide in children or geriatric populations.

For instructions for preparation, see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substance or any structural analogues of gonadotropin-releasing hormone (GnRH), extrinsic peptide hormones or to any of the excipients.
- Pregnancy and lactation.
- Postmenopausal women.
- Patients with moderate and severe renal and hepatic impairment.

4.4 Special warnings and precautions for use

Special care should be taken in women with signs and symptoms of active allergic conditions or known history of allergic predisposition. Treatment with Cetrotide is not advised in women with severe allergic conditions.

During or following ovarian stimulation an ovarian hyperstimulation syndrome can occur. This event must be considered as an intrinsic risk of the stimulation procedure with gonadotropins.

An ovarian hyperstimulation syndrome should be treated symptomatically, e.g. with rest, intravenous electrolytes/colloids and heparin therapy.

Luteal phase support should be given according to the reproductive medical centre's practice.

There is limited experience up to now with the administration of Cetrotide during a repeated ovarian stimulation procedure. Therefore Cetrotide should be used in repeated cycles only after a careful risk/benefit evaluation.

4.5 Interaction with other medicinal products and other forms of interaction

In vitro investigations have shown that interactions are unlikely with medicinal products that are metabolised by cytochrome P450 or glucuronised or conjugated in some other way. However, although there has been no evidence of drug-interactions, especially with commonly used medicinal products, gonadotropins or products that may induce histamine release in susceptible individuals, the possibility of an interaction cannot be totally excluded.

4.6 Pregnancy and lactation

Cetrotide is not intended to be used during pregnancy and lactation (see section 4.3).

Studies in animals have indicated that cetrorelix exerts a dose related influence on fertility, reproductive performance and pregnancy. No teratogenic effects occurred when the medicinal product was administered during the sensitive phase of gestation.

4.7 Effects on ability to drive and use machines

Cetrotide has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

The most commonly reported side effects are local injection site reactions such as erythema, swelling and pruritus that are usually transient in nature and mild in intensity. In clinical trials, these effects were observed with a frequency of 9.4% following multiple injections of Cetrotide 0.25 mg.

Mild to moderate ovarian hyperstimulation syndrome (OHSS) (WHO grade I or II) have been commonly reported and should be considered as an intrinsic risk of the stimulation procedure. Inversely, severe OHSS remains uncommon.

Uncommonly, cases of hypersensitivity reactions including pseudo-allergic/anaphylactoid reactions have been reported.

The adverse reactions reported below are classified according to frequency of occurrence as follows:

Very Common	$\geq 1/10$
Common	$\geq 1/100$ to $< 1/10$
Uncommon	$\geq 1/1,000$ to $< 1/100$
Rare	$\geq 1/10,000$ to $< 1/1,000$
Very rare	$< 1/10,000$

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Immune system disorders	Uncommon	Systemic allergic/pseudo-allergic reactions including life-threatening anaphylaxis.
Nervous system disorders	Uncommon	Headache
Gastrointestinal disorders	Uncommon	Nausea
Reproductive system and breast disorders	Common	Mild to moderate ovarian hyperstimulation syndrome (WHO grade I or II) can occur which is an intrinsic risk of the stimulation procedure (see section 4.4).
	Uncommon	Severe ovarian hyperstimulation syndrome (WHO grade III)
General disorders and administration site conditions	Common	Local reactions at the injection site (e.g. erythema, swelling and pruritus) have been reported. Usually they were transient in nature and of mild intensity. The frequency as reported in clinical trials was 9.4% following multiple injections of 0.25 mg cetrotide.

4.9 Overdose

Overdosage in humans may result in a prolonged duration of action but is unlikely to be associated with acute toxic effects.

In acute toxicity studies in rodents non-specific toxic symptoms were observed after intraperitoneal administration of cetrorelix doses more than 200 times higher than the pharmacologically effective dose after subcutaneous administration.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-gonadotropin-releasing hormones, ATC code: H01CC02.

Cetrorelix is a luteinising hormone releasing hormone (LHRH) antagonist. LHRH binds to membrane receptors on pituitary cells. Cetrorelix competes with the binding of endogenous LHRH to these receptors. Due to this mode of action, cetrorelix controls the secretion of gonadotropins (LH and FSH).

Cetrorelix dose-dependently inhibits the secretion of LH and FSH from the pituitary gland. The onset of suppression is virtually immediate and is maintained by continuous treatment, without initial stimulatory effect.

In females, cetrorelix delays the LH surge and consequently ovulation. In women undergoing ovarian stimulation the duration of action of cetrorelix is dose dependent. Following a single dose of 3 mg of cetrorelix a duration of action of at least 4 days has been evaluated. On day 4 the suppression was approximately 70%. At a dose of 0.25 mg per injection repeated injections every 24 hours will maintain the effect of cetrorelix.

In animals as well as in humans, the antagonistic hormonal effects of cetrorelix were fully reversible after termination of treatment.

5.2 Pharmacokinetic properties

The absolute bioavailability of cetrorelix after subcutaneous administration is about 85%.

The total plasma clearance and the renal clearance are $1.2 \text{ ml} \times \text{min}^{-1} \times \text{kg}^{-1}$ and $0.1 \text{ ml} \times \text{min}^{-1} \times \text{kg}^{-1}$, respectively. The volume of distribution (V_d) is $1.1 \text{ l} \times \text{kg}^{-1}$. The mean terminal half-lives following intravenous and subcutaneous administration are about 12 h and 30 h, respectively, demonstrating the effect of absorption processes at the injection site. The subcutaneous administration of single doses (0.25 mg to 3 mg cetrorelix) and also daily dosing over 14 days show linear kinetics.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

No target organ toxicity could be observed from acute, subacute and chronic toxicity studies in rats and dogs following subcutaneous administration of cetrorelix. No signs of medicinal product-related local irritation or incompatibility were noted in dogs after intravenous, intra-arterial and paravenous injection when cetrorelix was administered in doses clearly above the intended clinical use in man.

Cetrorelix showed no mutagenic or clastogenic potential in gene and chromosome mutation assays.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:

Mannitol

Solvent:

Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

2 years.

The solution should be used immediately after preparation.

6.4 Special precautions for storage

Do not store above 25 °C. Keep the vial(s) in the outer carton in order to protect from light.

6.5 Nature and contents of container

Packs with 1 or 7 Type I glass vials sealed with a rubber stopper.

Additionally for each vial the packs contain:

1 pre-filled syringe (Type I glass cartridge closed with rubber stoppers) with 1 ml solvent for parenteral use

1 injection needle (20 gauge)

1 hypodermic injection needle (27 gauge)

2 alcohol swabs.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Cetrotide should only be reconstituted with the solvent provided, using a gentle, swirling motion. Vigorous shaking with bubble formation should be avoided.

The reconstituted solution is without particles and clear. Do not use if the solution contains particles or if the solution is not clear.

Withdraw the entire contents of the vial. This ensures a delivery to the patient of a dose of at least 0.23 mg cetrotirelix.

The solution should be used immediately after reconstitution.

7. MARKETING AUTHORISATION HOLDER

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56 Marsh Wall
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8. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/001
EU/1/99/100/002

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 April 1999
Date of first renewal: 15 April 2004
Date of latest renewal: 13 April 2009

10. DATE OF REVISION OF THE TEXT

07/2009

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**BOX OF 1 VIAL AND 1 PRE-FILLED SYRINGE****1. NAME OF THE MEDICINAL PRODUCT**

Cetrotide 0.25 mg powder and solvent for solution for injection
cetorelix

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 vial with powder contains:
0.25 mg cetorelix (as acetate).

3. LIST OF EXCIPIENTS

Excipient: Mannitol.
1 pre-filled syringe with solvent contains: 1 ml water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 vial with powder for solution for injection.
1 pre-filled syringe with solvent for parenteral use.
Additionally, the pack contains:
1 injection needle (20 gauge)
1 hypodermic injection needle (27 gauge)
2 alcohol swabs.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C. Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Merck Serono Europe Limited
56 Marsh Wall
London E14 9TP
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE**16. INFORMATION IN BRAILLE**

cetrotide 0.25 mg

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**BOX OF 7 VIALS AND 7 PRE-FILLED SYRINGES****1. NAME OF THE MEDICINAL PRODUCT**

Cetrotide 0.25 mg powder and solvent for solution for injection
cetorelix

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 vial with powder contains:
0.25 mg cetorelix (as acetate).

3. LIST OF EXCIPIENTS

Excipient: Mannitol.
1 pre-filled syringe with solvent contains: 1 ml water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

7 vials with powder for solution for injection.
7 pre-filled syringes with solvent for parenteral use.
Additionally, the pack contains :
7 injection needle (20 gauge)
7 hypodermic injection needle (27 gauge)
14 alcohol swabs.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C. Keep the vial(s) in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

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12. MARKETING AUTHORISATION NUMBER(S)

EU/1/99/100/002

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE**16. INFORMATION IN BRAILLE**

cetrotide 0.25 mg

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**CETROTIDE 0.25 MG VIAL LABEL****1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Cetrotide 0.25 mg powder for solution for injection
cetrotide
Subcutaneous use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.25 mg

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS SOLVENT PRE-FILLED SYRINGE LABEL
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1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION
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Solvent for Cetrotide 0.25 mg
Water for injections

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT
--

1 ml

6. OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Cetrotide 0.25 mg powder and solvent for solution for injection Cetorelix acetate

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Cetrotide is and what it is used for
2. Before you use Cetrotide
3. How to use Cetrotide
4. Possible side effects
5. How to store Cetrotide
6. Further information
How to mix and inject Cetrotide

1. WHAT CETROTIDE IS AND WHAT IT IS USED FOR

What Cetrotide is

Cetrotide contains a medicine called ‘cetorelix acetate’. This medicine stops your body from releasing an egg from your ovary (ovulation) during your menstrual cycle. Cetrotide belongs to a group of medicines called ‘anti-gonadotropin-releasing hormones’.

What Cetrotide is used for

Cetrotide is one of the medicines used during ‘assisted reproductive techniques’ to help you get pregnant. It stops eggs being released straight away. This is because if the eggs are released too early (premature ovulation) it may not be possible for your doctor to collect them.

How Cetrotide works

Cetrotide blocks a natural hormone in your body called LHRH (‘luteinising hormone releasing hormone’).

- LHRH controls another hormone, called LH (‘luteinising hormone’).
- LH stimulates ovulation during your menstrual cycle.

This means that Cetrotide stops the chain of events that leads to an egg being released from your ovary. When your eggs are ready to be collected, another medicine will be given to you that will release them (ovulation induction).

2. BEFORE YOU USE CETROTIDE

Do not use Cetrotide

- if you are allergic (hypersensitive) to cetorelix acetate or any of the other ingredients of Cetrotide listed in section 6.
- if you are allergic (hypersensitive) to medicines similar to Cetrotide (any other peptide hormones)
- if you are pregnant or breast-feeding
- if you have already reached your menopause
- if you have a moderate or severe kidney or liver disease.

Do not use Cetrotide if any of the above applies to you. If you are not sure, talk to your doctor before using this medicine.

Take special care with Cetrotide

Allergies

Tell your doctor before using Cetrotide if you have an active allergy or have had allergies in the past.

Ovarian Hyper-Stimulation Syndrome (OHSS)

Cetrotide is used together with other medicines that stimulate your ovaries to develop more eggs ready to be released. During or after you receive these medicines, you may develop Ovarian Hyper-Stimulation Syndrome (OHSS). This is when your follicles develop too much and become large cysts. For possible signs to look out for and what to do if this happens see section 4 '*Possible side effects*'.

Using Cetrotide during more than one cycle

Experience of using Cetrotide during more than one cycle is small. Your doctor will carefully look at the benefits and risks for you, if you need to have Cetrotide during more than one cycle.

Using other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

Do not use Cetrotide if you are pregnant, think you may be pregnant, or if you are breast-feeding. Ask your doctor or pharmacist for advice before taking any medicines

Driving and using machines

Cetrotide is not expected to affect you being able to drive and use machines.

3. HOW TO USE CETROTIDE

Always use Cetrotide exactly as your doctor has told you. Check with your doctor if you are not sure.

Using this medicine

This medicine is only for injection just under the skin of your belly (subcutaneous). To reduce skin irritation, select a different part of your belly each day.

- Your doctor must supervise your first injection. Your doctor or nurse will show you how to prepare and inject the medicine.
- You can carry out the following injections yourself as long as your doctor has made you aware of the symptoms that may indicate allergy and of the possibly serious or life threatening consequences that would need immediate treatment (Please see Section 4 '*Possible side effects*').
- Please carefully read and follow the instructions at the end of this leaflet called '*How to mix and inject Cetrotide*'.
- You start by using another medicine on day 1 of your treatment cycle. You then start using Cetrotide a few days later. (See next section '*How much to use*').

How much to use

Inject the contents of one vial (0.25 mg Cetrotide) once each day. It is best to use the medicine at the same time each day, leaving 24 hours between each dose.

You can choose to inject every morning **or** every evening.

- If you are injecting every morning: Start your injections on day 5 or 6 of the treatment cycle. Your doctor will tell you the exact date and time. You will keep using this medicine up until and including the morning that your eggs are collected (ovulation induction).

OR

- If you are injecting every evening: Start your injections on day 5 of the treatment cycle. Your doctor will tell you the exact date and time. You will keep using this medicine up until and including the evening before your eggs are collected (ovulation induction).

If you use more Cetrotide than you should

Bad effects are not expected if you accidentally inject more of this medicine than you should. The effect of the medicine will last for longer. No specific measures are usually required.

If you forget to use Cetrotide

- If you forget a dose, inject it as soon as you remember and talk to your doctor.
- Do not inject a double dose to make up for a forgotten dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Cetrotide can cause side effects, although not everybody gets them.

Allergic reactions

- Warm, red skin, itching (often in your groin or armpits), red, itchy, raised areas (hives), runny nose, fast or uneven pulse, swelling of your tongue and throat, sneezing, wheezing, serious difficulty breathing or dizziness. You may be having a possible serious, life-threatening allergic reaction to the medicine. This is uncommon (affects less than 1% of the women).

If you notice any of the side effects above, stop using Cetrotide and contact your doctor immediately.

Ovarian Hyper-Stimulation Syndrome (OHSS)

This may occur due to the other medicines that you are using to stimulate your ovaries.

- Lower abdominal pain together with feeling sick (nausea) or being sick (vomiting) may be the symptoms of Ovarian Hyper-Stimulation Syndrome (OHSS). This may indicate that the ovaries over-reacted to the treatment and that large ovarian cysts developed. This event is common (affects between 1% and 10% of the women).
- The OHSS may become severe with clearly enlarged ovaries, decreased urine production, weight gain, difficulty breathing or fluid in your stomach or chest. This event is uncommon (affects less than 1% of the women).

If you notice any of the side effects above, contact your doctor immediately.

Other side effects

Common (affects between 1% and 10% of the women):

- Mild and short lasting skin irritation may occur at the injection site like redness, itching, or swelling.

Uncommon (affects less than 1% of the women):

- Feeling sick (nausea)
- Headache.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE CETROTIDE

Keep out of the reach and sight of children.

Do not use Cetrotide after the expiry date which is stated on the vial after EXP. The expiry date refers to the last day of that month.

The Cetrotide powder in the vial and the sterile water (solvent) in the pre-filled syringe have the same expiry date. It is printed on the labels and on the carton.

Do not store above 25°C.

Keep the vial in the outer carton in order to protect from light.

The solution should be used immediately after preparation.

Do not use Cetrotide if the white pellet in the vial has changed in appearance. Do not use it if the prepared solution in the vial is not clear and colourless or if it has particles in it.

If you have any further questions please ask your doctor or pharmacist.

6. FURTHER INFORMATION

What Cetrotide contains

- The active substance is cetrorelix acetate. Each vial contains 0.25 mg cetrorelix acetate.
- The other ingredient is mannitol.
- The solvent is sterile water for injection.

What Cetrotide looks like and contents of the pack

Cetrotide is a white powder for solution for injection in a glass vial with a rubber stopper. It is available in packs of one or seven vials (not all pack sizes may be marketed).

For each vial, the packs contain:

- one syringe pre-filled with sterile water for injection (solvent). This water is for mixing with the powder in the vial
- one needle with a **yellow** mark - for injecting the sterile water into the vial and drawing the made up medicine out from the vial
- one needle with a **grey** mark - for injecting the medicine into your belly
- two alcohol swabs for cleaning

Marketing Authorisation Holder

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Manufacturer

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HOW TO MIX AND INJECT CETROTIDE

- This section tells you how to mix the powder and the sterile water (solvent) together and then how to inject your medicine.
- Before starting to use this medicine, please read these instructions the whole way through first.
- This medicine is only for you – do not let anyone else use it.
- Use each needle, vial and syringe only once.

Before you start

1. Wash your hands

- It is important that your hands and the things you use are as clean as possible.

2. Lay out everything you need on a clean surface:

- one vial of powder
- one syringe pre-filled with sterile water (solvent)
- one needle with a **yellow** mark – for injecting the sterile water into the vial and drawing the made up medicine out from the vial
- one needle with a **grey** mark – for injecting the medicine into your belly
- two alcohol swabs.

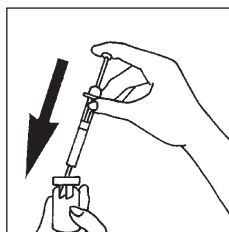
Mixing the powder and water to make up your medicine

1. Remove the plastic cap from the vial

- There will be a rubber stopper underneath – keep this in the vial.
- Wipe the rubber stopper and metal ring with your first alcohol swab.

2. Adding the water from the pre-filled syringe to the powder in the vial

- Unwrap the needle with the **yellow** mark on it.
- Remove the cap from the pre-filled syringe and screw the yellow needle onto it. Remove the cap from the needle.
- Push the yellow needle through the centre of the rubber stopper of the vial.
- Slowly push in the plunger of the syringe to inject the water into the vial. Do not use any other sort of water.
- Leave the syringe in the rubber stopper.

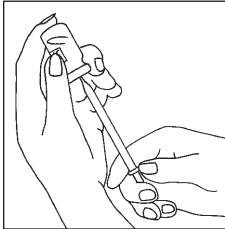


3. Mixing the powder and water in the vial

- While carefully holding the syringe and vial, swirl gently to mix the powder and water together. When it is mixed, it will look clear and have no particles in it.
- Do not shake or you will create bubbles in your medicine.

4. Re-filling the syringe with the medicine from the vial

- Turn the vial upside down.
- Pull the plunger out to draw the medicine from the vial back into the syringe.
- If any medicine is left in the vial, pull out the yellow needle until the end of the needle is just inside the rubber stopper. If you look from the side through the gap in the rubber stopper, you can control the movement of the needle and the liquid.
- Make sure that you collect all of your medicine from the vial.

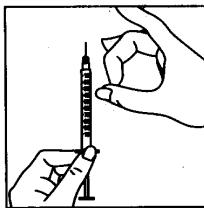


- Put the cap back on the yellow needle. Unscrew the yellow needle from the syringe and lay down the syringe.

Preparing the injection site and injecting your medicine

1. Removing air bubbles

- Unwrap the needle with the **grey** mark on it. Screw the grey needle onto the syringe and remove the cap from the grey needle.
- Hold the syringe with the grey needle pointing upwards and check for any air bubbles.
- To remove air bubbles, gently flick the syringe until all the air collects at the top - then slowly push the plunger in until the air bubbles are gone.
- Do not touch the grey needle and do not let the needle touch any surface.

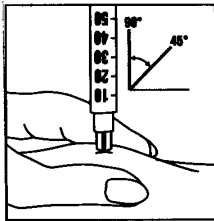


2. Clean the injection site

- Choose an injection site on your belly. It is best around the belly button (navel). To reduce skin irritation, select a different part of your belly each day.
- Clean the skin at your chosen injection site with your second alcohol swab - use a circular motion.

3. Piercing your skin

- Hold the syringe in one hand – like you would hold a pencil.
- Gently pinch up the skin around where you are going to inject and hold this firmly with your other hand.
- Slowly push the grey needle completely into your skin at an angle of about 45 to 90 degrees – then let go of your skin.



4. Injecting your medicine

- Gently pull back the plunger of the syringe. If blood appears, follow Step 5 below.
- If no blood appears, **slowly** push the plunger in to inject your medicine.
- When the syringe is empty, take out the grey needle slowly at the same angle.
- Use your second alcohol swab to gently apply pressure where you have just injected.

5. If blood appears:

- take out the grey needle slowly at the same angle
- use your second alcohol swab to gently apply pressure where you have just pierced your skin
- empty your medicine into a sink and follow Step 6 below
- wash your hands and start again with a new vial and pre-filled syringe.

6. Disposal

- Use each needle, vial and syringe only once.
- Put the cap back on the needles so that they are safe to be thrown away.
- Ask your pharmacist how to safely dispose of used needles, vial and syringe.