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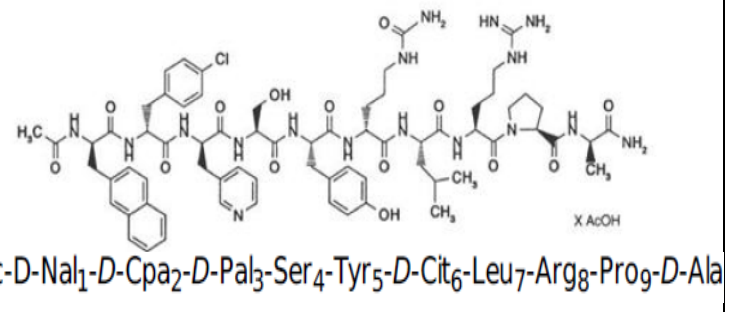
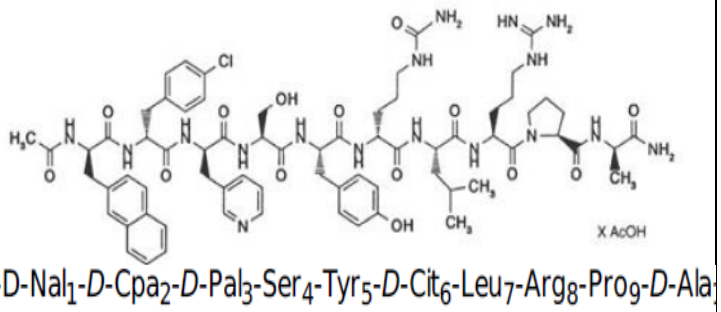
Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
CETROTIDE - cetrorelix acetate **EMD Serono, Inc.** --- Cetrotide ® 0.25 mg (cetrorelix acetate for injection) **FOR SUBCUTANEOUS USE ONLY** **DESCRIPTION** Cetrotide® (cetrorelix acetate for injection) is a synthetic decapeptide with gonadotropinreleasing hormone (GnRH) antagonistic activity. Cetrorelix acetate is an analog of native GnRH with substitutions of amino acids at positions 1, 2, 3, 6, and 10. The molecular formula is Acetyl-D-3-(2′-naphtyl)-alanine-D-4-chlorophenylalanine-D-3-(3′-pyridyl)- alanine-L-serine-L-tyrosine-D-citruline-L-leucine-L-arginine-L-proline-D-alanine-amide, and the molecular weight is 1431.06, calculated as the anhydrous free base. The structural formula is as follows: Cetrorelix acetate  (Ac-D-Nal$_1$-*D*-Cpa$_2$-*D*-Pal$_3$-Ser$_4$-Tyr$_5$-*D*-Cit$_6$-Leu$_7$-Arg$_8$-Pro$_9$-*D*-Ala	**Cetrorelix Acetate Injection, Ready to Use Prefilled syringe, 0.25 mg/mL** **FOR SUBCUTANEOUS USE ONLY** **DESCRIPTION** Cetrorelix Acetate Injection is a synthetic decapeptide with gonadotropinreleasing hormone (GnRH) antagonistic activity. Cetrorelix acetate is an analog of native GnRH with substitutions of amino acids at positions 1, 2, 3, 6, and 10. The molecular formula is Acetyl-D-3-(2′-naphtyl)-alanine-D-4-chlorophenylalanine-D-3-(3′-pyridyl)- alanine-L-serine-L-tyrosine-D-citruline-L-leucine-L-arginine-L-proline-D-alanine-amide, and the molecular weight is 1431.06, calculated as the anhydrous free base. The structural formula is as follows: Cetrorelix acetate  (Ac-D-Nal$_1$-*D*-Cpa$_2$-*D*-Pal$_3$-Ser$_4$-Tyr$_5$-*D*-Cit$_6$-Leu$_7$-Arg$_8$-Pro$_9$-*D*-Ala	RLD proprietary name replaced with the generic product specific information based on the prefilled syringe.
Cetrotide® (cetrorelix acetate for injection) 0.25 mg is a sterile lyophilized powder intended for subcutaneous injection after reconstitution with Sterile Water for Injection, USP (pH 5-8), that comes supplied in a 1.0 mL pre-filled syringe. Each vial of Cetrotide® 0.25 mg contains 0.26-0.27 mg cetrorelix acetate, equivalent to 0.25 mg cetrorelix, and 54.80 mg mannitol. **CLINICAL PHARMACOLOGY**	Cetrorelix acetate injection, 0.25 mg/mL is a sterile Ready to Use Prefilled solution intended for subcutaneous injection (pH 2.5-4.0), that comes supplied in a 1.0 mL pre-filled syringe. Each Ready to Use Prefilled Syringe of cetrorelix acetate injection, 0.25 mg/mL contains 0.26-0.27 mg cetrorelix acetate, equivalent to 0.25 mg cetrorelix, and 54.80 mg mannitol. **CLINICAL PHARMACOLOGY**	RLD proprietary name and description is replaced with the generic product specific information based on the prefilled syringe.

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GnRH induces the production and release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the gonadotrophic cells of the anterior pituitary. Due to a positive estradiol (E2) feedback at midcycle, GnRH liberation is enhanced resulting in an LH-surge. This LH-surge induces the ovulation of the dominant follicle, resumption of oocyte meiosis and subsequently luteinization as indicated by rising progesterone levels.	GnRH induces the production and release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the gonadotrophic cells of the anterior pituitary. Due to a positive estradiol (E2) feedback at midcycle, GnRH liberation is enhanced resulting in an LH-surge. This LH-surge induces the ovulation of the dominant follicle, resumption of oocyte meiosis and subsequently luteinization as indicated by rising progesterone levels.	
Cetrotide® competes with natural GnRH for binding to membrane receptors on pituitary cells and thus controls the release of LH and FSH in a dose-dependent manner. The onset of LH suppression is approximately one hour with the 3 mg dose and two hours with the 0.25 mg dose. This suppression is maintained by continuous treatment and there is a more pronounced effect on LH than on FSH. An initial release of endogenous gonadotropins has not been detected with Cetrotide®, which is consistent with an antagonist effect.	Cetrorelix acetate injection competes with natural GnRH for binding to membrane receptors on pituitary cells and thus controls the release of LH and FSH in a dose-dependent manner. The onset of LH suppression is approximately one hour with the 3 mg dose and two hours with the 0.25 mg dose. This suppression is maintained by continuous treatment and there is a more pronounced effect on LH than on FSH. An initial release of endogenous gonadotropins has not been detected with cetrorelix acetate injection, which is consistent with an antagonist effect.	RLD proprietary name replaced with prefilled syringe generic product name.
The effects of Cetrotide® on LH and FSH are reversible after discontinuation of treatment. In women, Cetrotide® delays the LH-surge, and consequently ovulation, in a dose-dependent fashion. FSH levels are not affected at the doses used during controlled ovarian stimulation. Following a single 3 mg dose of Cetrotide®, duration of action of at least 4 days has been established. A dose of Cetrotide® 0.25 mg every 24 hours has been shown to maintain the effect.	The effects of Cetrorelix acetate injection on LH and FSH are reversible after discontinuation of treatment. In women, Cetrorelix acetate injection delays the LH-surge, and consequently ovulation, in a dose-dependent fashion. FSH levels are not affected at the doses used during controlled ovarian stimulation. Following a single 3 mg dose of Cetrorelix acetate injection, duration of action of at least 4 days has been established. A dose of Cetrorelix acetate injection, 0.25 mg/mL every 24 hours has been shown to maintain the effect.	RLD proprietary name replaced with prefilled syringe generic product name
Pharmacokinetics The pharmacokinetic parameters of single and multiple doses of Cetrotide® (cetrorelix acetate for injection) in adult healthy female subjects are summarized in Table 1.	**Pharmacokinetics** The pharmacokinetic parameters of single and multiple doses of Cetrorelix acetate injection in adult healthy female subjects are summarized in Table 1.	RLD proprietary name replaced with prefilled syringe generic product name.
Table 1: Pharmacokinetic parameters of Cetrotide® following 3 mg single or 0.25 mg single and multiple (daily for 14 days) subcutaneous (sc) administration.	**Table 1: Pharmacokinetic parameters of Cetrorelix Acetate Injection following 3 mg single or 0.25 mg single and multiple (daily for 14 days) subcutaneous (sc) administration.**	

	Single dose 3 mg	Single dose 0.25 mg	Multiple do 0.25 mg

	Single dose 3 mg	Single dose 0.25 mg	Multiple dose 0.25

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No. of subjects	12	12	12				**mg**	
tmax* [h]	1.5 (0.5-2)	1.0 (0.5-1.5)	1.0 (0.5-2)	No. of subjects	12	12	12	
t1/2 * [h]	62.8 (38.2-108)	5.0 (2.4-48.8)	20.6 (4.1-179.3)	tmax* [h]	1.5 (0.5-2)	1.0 (0.5-1.5)	1.0 (0.5-2)	
Cmax [ng/ml]	28.5 (22.5-36.2)	4.97 (4.17-5.92)	6.42 (5.18-7.96)	t1/2 * [h]	62.8 (38.2-108)	5.0 (2.4-48.8)	20.6 (4.1-179.3)	
AUC [ng·h/ml]	536 (451-636)	31.4 (23.4-42.0)	44.5 (36.7-54.2)	Cmax [ng/ml]	28.5 (22.5-36.2)	4.97 (4.17-5.92)	6.42 (5.18-7.96)	
CL† [ml/min·kg]	1.28‡			AUC [ng·h/ml]	536 (451-636)	31.4 (23.4-42.0)	44.5 (36.7-54.2)	
Vz† [l/kg]	1.16‡			CL† [ml/min·kg]	1.28‡			
				Vz† [l/kg]	1.16‡			

tmax Time to reach observed maximum plasma concentration
t1/2 Elimination half-life
Cmax Maximum plasma concentration; multiple dose Css, max
AUC Area under the curve; single dose AUC0-inf, multiple dose AUCt
CL Total plasma clearance
Vz Volume of distribution
Geometric mean (95% Clln),
* median (min-max)
† arithmetic mean,
‡ Based on iv administration (n=6, separate study 0013)

Absorption

Cetrotide® is rapidly absorbed following subcutaneous injection, maximal plasma concentrations being achieved approximately one to two hours after administration. The mean absolute bioavailability of Cetrotide® following subcutaneous administration to healthy female subjects is 85%.

Distribution

The volume of distribution of Cetrotide® following a single intravenous dose of 3 mg is about 1 l/kg. In vitro protein binding to human plasma is 86%.

Cetrotide® concentrations in follicular fluid and plasma were similar on the day of oocyte pick-up in patients undergoing controlled ovarian stimulation. Following subcutaneous administration of Cetrotide® 0.25 mg and 3 mg, plasma

tmax Time to reach observed maximum plasma concentration
t1/2 Elimination half-life
Cmax Maximum plasma concentration; multiple dose Css, max
AUC Area under the curve; single dose AUC0-inf, multiple dose AUCt
CL Total plasma clearance
Vz Volume of distribution
Geometric mean (95% Clln),
* median (min-max)
† arithmetic mean,
‡ Based on iv administration (n=6, separate study 0013)

Absorption

Cetrorelix acetate injection is rapidly absorbed following subcutaneous injection, maximal plasma concentrations being achieved approximately one to two hours after administration. The mean absolute bioavailability of Cetrorelix acetate injection following subcutaneous administration to healthy female subjects is 85%.

Distribution

The volume of distribution of Cetrorelix acetate injection following a single intravenous dose of 3 mg is about 1 l/kg. In vitro protein binding to human plasma is 86%.

Cetrorelix acetate injection concentrations in follicular fluid and plasma were similar on the day of oocyte pick-up in patients undergoing controlled ovarian stimulation. Following

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concentrations of cetrorelix were below or in the range of the lower limit of quantitation on the day of oocyte pick-up and embryo transfer. **Metabolism** After subcutaneous administration of 10 mg Cetrotide® to females and males, Cetrotide® and small amounts of (1-9), (1-7), (1-6), and (1-4) peptides were found in bile samples over 24 hours. In in vitro studies, Cetrotide® was stable against phase I- and phase II-metabolism. Cetrotide® was transformed by peptidases, and the (1-4) peptide was the predominant metabolite. **Excretion** Following subcutaneous administration of 10 mg cetrorelix to males and females, only unchanged cetrorelix was detected in urine. In 24 hours, cetrorelix and small amounts of the (1-9), (1-7), (1-6), and (1-4) peptides were found in bile samples. 2-4% of the dose was eliminated in the urine as unchanged cetrorelix, while 5-10% was eliminated as cetrorelix and the four metabolites in bile. Therefore, only 7-14% of the total dose was recovered as unchanged cetrorelix and metabolites in urine and bile up to 24 hours. The remaining portion of the dose may not have been recovered since bile and urine were not collected for a longer period of time. **Special Populations** Pharmacokinetic investigations have not been performed either in subjects with impaired renal or liver function, or in the elderly, or in children (see PRECAUTIONS). Pharmacokinetic differences in different races have not been determined. There is no evidence of differences in pharmacokinetic parameters for Cetrotide® between healthy subjects and patients undergoing controlled ovarian stimulation.	subcutaneous administration of Cetrorelix acetate injection, 0.25 mg and 3 mg, plasma concentrations of cetrorelix were below or in the range of the lower limit of quantitation on the day of oocyte pick-up and embryo transfer. **Metabolism** After subcutaneous administration of 10 mg Cetrorelix acetate injection to females and males, Cetrorelix acetate injection and small amounts of (1-9), (1-7), (1-6), and (1-4) peptides were found in bile samples over 24 hours. In in vitro studies, Cetrorelix acetate injection was stable against phase I- and phase II-metabolism. Cetrorelix acetate injection was transformed by peptidases, and the (1-4) peptide was the predominant metabolite. **Excretion** Following subcutaneous administration of 10 mg cetrorelix to males and females, only unchanged cetrorelix was detected in urine. In 24 hours, cetrorelix and small amounts of the (1-9), (1-7), (1-6), and (1-4) peptides were found in bile samples. 2-4% of the dose was eliminated in the urine as unchanged cetrorelix, while 5-10% was eliminated as cetrorelix and the four metabolites in bile. Therefore, only 7-14% of the total dose was recovered as unchanged cetrorelix and metabolites in urine and bile up to 24 hours. The remaining portion of the dose may not have been recovered since bile and urine were not collected for a longer period of time. **Special Populations** Pharmacokinetic investigations have not been performed either in subjects with impaired renal or liver function, or in the elderly, or in children (see PRECAUTIONS). Pharmacokinetic differences in different races have not been determined. There is no evidence of differences in pharmacokinetic parameters for Cetrorelix acetate injection between healthy subjects and patients undergoing controlled ovarian stimulation.	RLD proprietary name replaced with prefilled syringe generic product name. RLD proprietary name replaced with prefilled syringe generic product name.

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Drug-Drug Interactions No formal drug-drug interaction studies have been performed with Cetrotide® (see PRECAUTIONS).	**Drug-Drug Interactions** No formal drug-drug interaction studies have been performed with Cetrorelix acetate injection (see PRECAUTIONS).	
Clinical Studies Seven hundred thirty two (732) patients were treated with Cetrotide® in five (two Phase 2 dose-finding and three Phase 3) clinical trials. The clinical trial population consisted of Caucasians (95.5%) and Black, Asian, Arabian and others (4.5%). Women were between 19 and 40 years of age (mean: 32). The studies excluded subjects with polycystic ovary syndrome (PCOS), subjects with low or no ovarian reserve, and subjects with stage III-IV endometriosis.	**Clinical Studies** Seven hundred thirty two (732) patients were treated with Cetrorelix acetate injection in five (two Phase 2 dose-finding and three Phase 3) clinical trials. The clinical trial population consisted of Caucasians (95.5%) and Black, Asian, Arabian and others (4.5%). Women were between 19 and 40 years of age (mean: 32). The studies excluded subjects with polycystic ovary syndrome (PCOS), subjects with low or no ovarian reserve, and subjects with stage III-IV endometriosis.	RLD proprietary name replaced with prefilled syringe generic product name.
Two dose regimens were investigated in these clinical trials, either a single dose per treatment cycle or multiple dosing. In the Phase 2 studies, a single dose of 3 mg was established as the minimal effective dose for the inhibition of premature LH surges with a protection period of at least 4 days. When Cetrotide® is administered in a multidose regimen, 0.25 mg was established as the minimal effective dose. The extent and duration of LH-suppression is dose dependent.	Two dose regimens were investigated in these clinical trials, either a single dose per treatment cycle or multiple dosing. In the Phase 2 studies, a single dose of 3 mg was established as the minimal effective dose for the inhibition of premature LH surges with a protection period of at least 4 days. When Cetrorelix acetate injection is administered in a multidose regimen, 0.25 mg was established as the minimal effective dose. The extent and duration of LH-suppression is dose dependent.	RLD proprietary name replaced with prefilled syringe generic product name.
In the Phase 3 program, efficacy of the single 3 mg dose regimen of Cetrotide® and the multiple 0.25 mg dose regimen of Cetrotide® was established separately in two adequate and well controlled clinical studies utilizing active comparators. A third non- comparative clinical study evaluated only the multiple 0.25 mg dose regimen of Cetrotide®. The ovarian stimulation treatment with recombinant FSH or human menopausal gonadotropin (hMG) was initiated on day 2 or 3 of a normal menstrual cycle. The dose of gonadotropins was administered according to the individual patient's disposition and response.	In the Phase 3 program, efficacy of the single 3 mg dose regimen of Cetrorelix acetate injection and the multiple 0.25 mg dose regimen of Cetrorelix acetate injection was established separately in two adequate and well controlled clinical studies utilizing active comparators. A third non- comparative clinical study evaluated only the multiple 0.25 mg dose regimen of Cetrorelix acetate injection. The ovarian stimulation treatment with recombinant FSH or human menopausal gonadotropin (hMG) was initiated on day 2 or 3 of a normal menstrual cycle. The dose of gonadotropins was administered according to the individual patient's disposition and response.	RLD proprietary name replaced with prefilled syringe generic product name.
In the single dose regimen study, Cetrotide® 3 mg was administered on the day of controlled ovarian stimulation when adequate estradiol levels (400 pg/mL) were obtained, usually on day 7 (range day 5-12). If hCG was not given within 4 days of the 3 mg dose of Cetrotide®, then 0.25 mg of Cetrotide® was	In the single dose regimen study, Cetrorelix acetate injection 3 mg was administered on the day of controlled ovarian stimulation when adequate estradiol levels (400 pg/mL) were obtained, usually on day 7 (range day 5-12). If hCG was not	

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administered daily beginning 96 hours after the 3 mg injection until and including the day of hCG administration. In the two multiple dose regimen studies, Cetrotide® 0.25 mg was started on day 5 or 6 of COS. Both gonadotropins and Cetrotide® were continued daily (multiple dose regimen) until the injection of human chorionic gonadotropin (hCG). Oocyte pick-up (OPU) followed by in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) as well as embryo transfer (ET) were subsequently performed. The results for Cetrotide® are summarized below in Table 2.	given within 4 days of the 3 mg dose of Cetrorelix acetate injection, then 0.25 mg of Cetrorelix acetate injection was administered daily beginning 96 hours after the 3 mg injection until and including the day of hCG administration. In the two multiple dose regimen studies, Cetrorelix acetate injection, 0.25 mg was started on day 5 or 6 of COS. Both gonadotropins and Cetrorelix acetate injection were continued daily (multiple dose regimen) until the injection of human chorionic gonadotropin (hCG). Oocyte pick-up (OPU) followed by in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) as well as embryo transfer (ET) were subsequently performed. The results for Cetrorelix acetate injection are summarized below in Table 2.	RLD proprietary name replaced with prefilled syringe generic product name.

Table 2: Results of Phase 3 Clinical Studies with Cetrotide® 3 mg in a single dose (sd) regimen and 0.25 mg in a multiple dose (md) regimen

Parameter	Cetrotide® 3 mg (sd, active comparator study)	Cetrotide® 0.25 mg (md, active comparator study)	Cetrotide® 0.25 mg (md, non-comparative study)
No. of subjects	115	159	303
hCG administered [%]	98.3	96.2	96.0
Oocyte pick-up [%]	98.3	94.3	93.1
LH-surge [%] (LH ≥ 10 U/L and P* ≥ 1 ng/mL) †	0.0	1.9	1.0
Serum E2 [pg/ml] at day hCG‡, §	1125 (470-2952)	1064 (341-2531)	1185 (311-3676)

Table 2: Results of Phase 3 Clinical Studies with Cetrorelix Acetate Injection, 3 mg in a single dose (sd) regimen and 0.25 mg in a multiple dose (md) regimen

Parameter	Cetrorelix Acetate Injection, 3 mg (sd, active comparator study)	Cetrorelix Acetate Injection, 0.25 mg (md, active comparator study)	Cetrorelix Acetate Injection, 0.25 mg (md, non-comparative study)
No. of subjects	115	159	303
hCG administered [%]	98.3	96.2	96.0
Oocyte pick-up [%]	98.3	94.3	93.1
LH-surge [%] (LH ≥ 10 U/L and P* ≥ 1 ng/mL) †	0.0	1.9	1.0
Serum E2 [pg/ml] at day hCG‡, §	1125 (470-2952)	1064 (341-2531)	1185 (311-3676)

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Serum LH [U/L] at day hCG‡, §	1.0 (0.5-2.5)	1.5 (0.5-7.6)	1.1 (0.5-3.5)	Serum LH [U/L] at day hCG‡, §	1.0 (0.5-2.5)	1.5 (0.5-7.6)	1.1 (0.5-3.5)	
No. of follicles ≥ 11 mm at day hCG¶	11.2±5.5	10.8±5.2	10.4±4.5	No. of follicles ≥ 11 mm at day hCG¶	11.2±5.5	10.8±5.2	10.4±4.5	
No. of oocytes: IVF¶ ICSI¶	9.2±5.2 10.0±4.2	7.6±4.3 10.1±5.6	8.5±5.1 9.3±5.9	No. of oocytes: IVF¶ ICSI¶	9.2±5.2 10.0±4.2	7.6±4.3 10.1±5.6	8.5±5.1 9.3±5.9	
Fertilization rate: IVF¶ ICSI¶	0.48±0.33 0.66±0.29	0.62±0.26 0.63±0.29	0.60±0.26 0.61±0.25	Fertilization rate: IVF¶ ICSI¶	0.48±0.33 0.66±0.29	0.62±0.26 0.63±0.29	0.60±0.26 0.61±0.25	
No. of embryos transferred¶	2.6±0.9	2.1±0.6	2.7±1.0	No. of embryos transferred¶	2.6±0.9	2.1±0.6	2.7±1.0	
Clinical pregnancy rate [%] per attempt per subject with ET	22.6 26.3	20.8 24.1	19.8 23.3	Clinical pregnancy rate [%] per attempt per subject with ET	22.6 26.3	20.8 24.1	19.8 23.3	
* Progesterone † Following initiation of Cetrotide® therapy ‡ Morning values § Median with 5th – 95th percentiles ¶ Mean ± standard deviation				* Progesterone † Following initiation of cetrorelix acetate injection therapy ‡ Morning values § Median with 5th – 95th percentiles ¶ Mean ± standard deviation				RLD proprietary name replaced with prefilled syringe generic product name.
In addition to IVF and ICSI, one pregnancy was obtained after intrauterine insemination. In the five Phase 2 and Phase 3 clinical trials, 184 pregnancies have been reported out of a total of 732 patients (including 21 pregnancies following the replacement of frozen- thawed embryos).				In addition to IVF and ICSI, one pregnancy was obtained after intrauterine insemination. In the five Phase 2 and Phase 3 clinical trials, 184 pregnancies have been reported out of a total of 732 patients (including 21 pregnancies following the replacement of frozen- thawed embryos).				
In the 3 mg regimen, 9 patients received an additional dose of 0.25 mg of Cetrotide® and two other patients received two additional doses of 0.25 mg Cetrotide®. The median number of days of Cetrotide® multiple dose treatment was 5 (range 1-15) in both studies.				In the 3 mg regimen, 9 patients received an additional dose of 0.25 mg of Cetrorelix acetate injection, and two other patients received two additional doses of 0.25 mg Cetrorelix acetate injection. The median number of days of Cetrorelix acetate injection multiple dose treatment was 5 (range 1-15) in both studies.				RLD proprietary name replaced with prefilled syringe generic product name.
No drug related allergic reactions were reported from these clinical studies.				No drug related allergic reactions were reported from these clinical studies.				

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INDICATIONS AND USAGE Cetrotide® is indicated for the inhibition of premature LH surges in women undergoing controlled ovarian stimulation.	**INDICATIONS AND USAGE** Cetrorelix acetate injection is indicated for the inhibition of premature LH surges in women undergoing controlled ovarian stimulation.	RLD proprietary name replaced with prefilled syringe generic product name.
CONTRAINDICATIONS Cetrotide® is contraindicated under the following conditions: 1. Hypersensitivity to cetrorelix acetate, extrinsic peptide hormones or mannitol. 2. Known hypersensitivity to GnRH or any other GnRH analogs. 3. Known or suspected pregnancy, and lactation (see PRECAUTIONS). 4. Severe renal impairment	**CONTRAINDICATIONS** Cetrorelix acetate injection is contraindicated under the following conditions: 1. Hypersensitivity to cetrorelix acetate, extrinsic peptide hormones or mannitol. 2. Known hypersensitivity to GnRH or any other GnRH analogs. 3. Known or suspected pregnancy, and lactation (see PRECAUTIONS). 4. Severe renal impairment	
WARNINGS **Cetrotide® should be prescribed by physicians who are experienced in fertility treatment. Before starting treatment with Cetrotide®, pregnancy must be excluded (see CONTRAINDICATIONS and PRECAUTIONS).**	**WARNINGS** **Cetrorelix acetate injection should be prescribed by physicians who are experienced in fertility treatment. Before starting treatment with Cetrorelix acetate injection, pregnancy must be excluded (see CONTRAINDICATIONS and PRECAUTIONS).**	RLD proprietary name replaced with prefilled syringe generic product name.
PRECAUTIONS **General** Cases of hypersensitivity reactions, including anaphylactoid reactions with the first dose, have been reported during post-marketing surveillance (see ADVERSE REACTIONS). A severe anaphylactic reaction associated with cough, rash, and hypotension, was observed in one patient after seven months of treatment with Cetrotide® (10 mg/day) in a study for an indication unrelated to infertility. 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.	**PRECAUTIONS** **General** Cases of hypersensitivity reactions, including anaphylactoid reactions with the first dose, have been reported during post-marketing surveillance (see ADVERSE REACTIONS). A severe anaphylactic reaction associated with cough, rash, and hypotension, was observed in one patient after seven months of treatment with Cetrorelix acetate injection (10 mg/day) in a study for an indication unrelated to infertility. Special care should be taken in women with signs and symptoms of active allergic conditions or known history of allergic predisposition. Treatment with Cetrorelix acetate injection is not advised in women with severe allergic conditions.	RLD proprietary name replaced with prefilled syringe generic product name.

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Information for Patients Prior to therapy with Cetrotide®, patients should be informed of the duration of treatment and monitoring procedures that will be required. The risk of possible adverse reactions should be discussed (see ADVERSE REACTIONS). Cetrotide® should not be prescribed if a patient is pregnant. If Cetrotide® is prescribed to patients for self-administration, information for proper use is given in the Patient Leaflet (see below).	**Information for Patients** Prior to therapy with Cetrorelix acetate injection, patients should be informed of the duration of treatment and monitoring procedures that will be required. The risk of possible adverse reactions should be discussed (see ADVERSE REACTIONS). Cetrorelix acetate injection should not be prescribed if a patient is pregnant. If Cetrorelix acetate injection is prescribed to patients for self-administration, information for proper use is given in the Patient Leaflet (see below).	RLD proprietary name replaced with prefilled syringe generic product name.
Laboratory Tests After the exclusion of preexisting conditions, enzyme elevations (ALT, AST, GGT, alkaline phosphatase) were found in 1-2% of patients receiving Cetrotide® during controlled ovarian stimulation. The elevations ranged up to three times the upper limit of normal. The clinical significance of these findings was not determined. During stimulation with human menopausal gonadotropin, Cetrotide® had no notable effects on hormone levels aside from inhibition of LH surges.	**Laboratory Tests** After the exclusion of preexisting conditions, enzyme elevations (ALT, AST, GGT, alkaline phosphatase) were found in 1-2% of patients receiving Cetrorelix acetate injection during controlled ovarian stimulation. The elevations ranged up to three times the upper limit of normal. The clinical significance of these findings was not determined. During stimulation with human menopausal gonadotropin, Cetrorelix acetate injection had no notable effects on hormone levels aside from inhibition of LH surges.	RLD proprietary name replaced with prefilled syringe generic product name.
Drug Interactions No formal drug interaction studies have been performed with Cetrotide®.	**Drug Interactions** No formal drug interaction studies have been performed with Cetrorelix acetate injection.	
Carcinogenesis, Mutagenesis, Impairment of Fertility Long-term carcinogenicity studies in animals have not been performed with cetrorelix acetate. Cetrorelix acetate was not genotoxic in vitro (Ames test, HPRT test, chromosome aberration test) or in vivo (chromosome aberration test, mouse micronucleus test). Cetrorelix acetate induced polyploidy in CHL-Chinese hamster lung fibroblasts, but not in V79-Chinese hamster lung fibroblasts, cultured peripheral human lymphocytes or in an in vitro micronucleus test in the CHL-cell line. Treatment with 0.46 mg/kg cetrorelix acetate for 4 weeks resulted in complete infertility in female rats which was reversed 8 weeks after cessation of treatment.	**Carcinogenesis, Mutagenesis, Impairment of Fertility** Long-term carcinogenicity studies in animals have not been performed with cetrorelix acetate. Cetrorelix acetate was not genotoxic in vitro (Ames test, HPRT test, chromosome aberration test) or in vivo (chromosome aberration test, mouse micronucleus test). Cetrorelix acetate induced polyploidy in CHL-Chinese hamster lung fibroblasts, but not in V79-Chinese hamster lung fibroblasts, cultured peripheral human lymphocytes or in an in vitro micronucleus test in the CHL-cell line. Treatment with 0.46 mg/kg cetrorelix acetate for 4 weeks resulted in complete infertility in female rats which was reversed 8 weeks after cessation of treatment.	

Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
Pregnancy (see CONTRAINDICATIONS) Cetrotide® is contraindicated in pregnant women. When administered to rats for the first seven days of pregnancy, cetrorelix acetate did not affect the development of the implanted conceptus at doses up to 38 µg/kg (approximately 1 times the recommended human therapeutic dose based on body surface area). However, a dose of 139 µg/kg (approximately 4 times the human dose) resulted in a resorption rate and a postimplantation loss of 100%. When administered from day 6 to near term to pregnant rats and rabbits, very early resorptions and total implantation losses were seen in rats at doses from 4.6 µg/kg (0.2 times the human dose) and in rabbits at doses from 6.8 µg/kg (0.4 times the human dose). In animals that maintained their pregnancy, there was no increase in the incidence of fetal abnormalities. The fetal resorption observed in animals is a logical consequence of the alteration in hormonal levels effected by the antigonadotrophic properties of Cetrotide®, which could result in fetal loss in humans as well. Therefore, this drug should not be used in pregnant women.	**Pregnancy** (see CONTRAINDICATIONS) Cetrorelix acetate injection is contraindicated in pregnant women. When administered to rats for the first seven days of pregnancy, cetrorelix acetate did not affect the development of the implanted conceptus at doses up to 38 µg/kg (approximately 1 times the recommended human therapeutic dose based on body surface area). However, a dose of 139 µg/kg (approximately 4 times the human dose) resulted in a resorption rate and a postimplantation loss of 100%. When administered from day 6 to near term to pregnant rats and rabbits, very early resorptions and total implantation losses were seen in rats at doses from 4.6 µg/kg (0.2 times the human dose) and in rabbits at doses from 6.8 µg/kg (0.4 times the human dose). In animals that maintained their pregnancy, there was no increase in the incidence of fetal abnormalities. The fetal resorption observed in animals is a logical consequence of the alteration in hormonal levels effected by the antigonadotrophic properties of Cetrorelix acetate injection, which could result in fetal loss in humans as well. Therefore, this drug should not be used in pregnant women.	RLD proprietary name replaced with prefilled syringe generic product name.
Nursing Mothers It is not known whether Cetrotide® is excreted in human milk. Because many drugs are excreted in human milk, and because the effects of Cetrotide® on lactation and/or the breast-fed child have not been determined, Cetrotide® should not be used by nursing mothers.	**Nursing Mothers** It is not known whether Cetrorelix acetate injection is excreted in human milk. Because many drugs are excreted in human milk, and because the effects of Cetrorelix acetate injection on lactation and/or the breast-fed child have not been determined, Cetrorelix acetate injection should not be used by nursing mothers.	RLD proprietary name replaced with prefilled syringe generic product name.
Geriatric Use Cetrotide® is not intended to be used in subjects aged 65 and over.	**Geriatric Use** Cetrorelix acetate injection is not intended to be used in subjects aged 65 and over.	
ADVERSE REACTIONS The safety of Cetrotide® in 949 patients undergoing controlled ovarian stimulation in clinical studies was evaluated. Women were between 19 and 40 years of age (mean: 32). 94.0% of them	**ADVERSE REACTIONS** The safety of Cetrorelix acetate injection in 949 patients undergoing controlled ovarian stimulation in clinical studies was	

Side by Side Comparison of Prescribing Information (RLD Vs Generic)

<table>
<tr><th>RLD (PI)</th><th>Generic (PI)</th><th>Justification</th></tr>
<tr>
<td>were Caucasian. Cetrotide® was given in doses ranging from 0.1 mg to 5 mg as either a single or multiple dose.

Table 3 shows systemic adverse events, reported in clinical studies without regard to causality, from the beginning of Cetrotide® treatment until confirmation of pregnancy by ultrasound at an incidence ≥ 1% in Cetrotide® treated subjects undergoing COS.

Table 3: Adverse Events in ≥1%
<table>
<tr><td>(WHO preferred term)</td><td>Cetrotide® N=949 % (n)</td></tr>
<tr><td>Ovarian Hyperstimulation Syndrome*</td><td>3.5 (33)</td></tr>
<tr><td>Nausea</td><td>1.3 (12)</td></tr>
<tr><td>Headache</td><td>1.1 (10)</td></tr>
</table>
* Intensity moderate or severe, or WHO Grade II or III, respectively

Local site reactions (e.g. redness, erythema, bruising, itching, swelling, and pruritus) were reported. Usually, they were of a transient nature, mild intensity and short duration. During post-marketing surveillance, cases of mild to moderate Ovarian Hyperstimulation syndrome and cases of hypersensitivity reactions including anaphylactoid reactions have been reported. Two stillbirths were reported in Phase 3 studies of Cetrotide®.

Congenital Anomalies
Clinical follow-up studies of 316 newborns of women administered Cetrotide® were reviewed. One infant of a set of twin neonates was found to have anencephaly at birth and died after four days. The other twin was normal. Developmental findings from ongoing baby follow-up included a child with a ventricular septal defect and another child with bilateral congenital glaucoma.

Four pregnancies that resulted in therapeutic abortion in Phase 2 and Phase 3 controlled ovarian stimulation studies had major anomalies (diaphragmatic hernia, trisomy 21, Klinefelter</td>
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Congenital Anomalies
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Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
syndrome, polymalformation, and trisomy 18). In three of these four cases, intracytoplasmic sperm injection (ICSI) was the fertilization method employed; in the fourth case, in vitro fertilization (IVF) was the method employed. The minor congenital anomalies reported include: supernumerary nipple, bilateral strabismus, imperforate hymen, congenital nevi, hemangiomata, and QT syndrome. The causal relationship between the reported anomalies and Cetrotide® is unknown. Multiple factors, genetic and others (including, but not limited to ICSI, IVF, gonadotropins, and progesterone) make causal attribution difficult to study.	syndrome, polymalformation, and trisomy 18). In three of these four cases, intracytoplasmic sperm injection (ICSI) was the fertilization method employed; in the fourth case, in vitro fertilization (IVF) was the method employed. The minor congenital anomalies reported include: supernumerary nipple, bilateral strabismus, imperforate hymen, congenital nevi, hemangiomata, and QT syndrome. The causal relationship between the reported anomalies and Cetrorelix acetate injection is unknown. Multiple factors, genetic and others (including, but not limited to ICSI, IVF, gonadotropins, and progesterone) make causal attribution difficult to study.	RLD proprietary name replaced with prefilled syringe generic product name.
OVERDOSAGE There have been no reports of overdosage with Cetrotide® 0.25 mg or 3 mg in humans. Single doses up to 120 mg Cetrotide® have been well tolerated in patients treated for other indications without signs of overdosage.	**OVERDOSAGE** There have been no reports of overdosage with Cetrorelix acetate injection, 0.25 mg or 3 mg in humans. Single doses up to 120 mg Cetrorelix acetate injection have been well tolerated in patients treated for other indications without signs of overdosage.	
DOSAGE AND ADMINISTRATION Ovarian stimulation therapy with gonadotropins (FSH, hMG) is started on cycle Day 2 or 3. The dose of gonadotropins should be adjusted according to individual response. Cetrotide® 0.25 mg may be administered subcutaneously once daily during the early- to mid-follicular phase. Cetrotide® 0.25 mg is administered on either stimulation day 5 (morning or evening) or day 6 (morning) and continued daily until the day of hCG administration. When assessment by ultrasound shows a sufficient number of follicles of adequate size, hCG is administered to induce ovulation and final maturation of the oocytes. No hCG should be administered if the ovaries show an excessive response to the treatment with gonadotropins to reduce the chance of developing ovarian hyperstimulation syndrome (OHSS).	**DOSAGE AND ADMINISTRATION** Ovarian stimulation therapy with gonadotropins (FSH, hMG) is started on cycle Day 2 or 3. The dose of gonadotropins should be adjusted according to individual response. Cetrorelix acetate injection, 0.25 mg/mL may be administered subcutaneously once daily during the early- to mid-follicular phase. Cetrorelix acetate injection, 0.25 mg/mL is administered on either stimulation day 5 (morning or evening) or day 6 (morning) and continued daily until the day of hCG administration. When assessment by ultrasound shows a sufficient number of follicles of adequate size, hCG is administered to induce ovulation and final maturation of the oocytes. No hCG should be administered if the ovaries show an excessive response to the treatment with gonadotropins to reduce the chance of developing ovarian hyperstimulation syndrome (OHSS).	RLD proprietary name replaced with prefilled syringe generic product name.
Administration Cetrotide® 0.25 mg can be administered by the patient herself after appropriate instructions by her doctor.	**Administration** Cetrorelix acetate injection, 0.25 mg/mL can be administered by the patient herself after appropriate instructions by her doctor.	RLD proprietary name replaced with prefilled

Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
		syringe generic product name.
Directions for using Cetrotide® 0.25 mg with the enclosed needles and pre-filled syringe:	**Directions for using Cetrorelix acetate injection, 0.25 mg/mL Ready to Use prefilled syringe:**	
	Cetrorelix Acetate Injection, in a Ready to Use prefilled syringe is supplied in a single dose, sterile, prefilled syringe and is intended for SUBCUTANEOUS administration only. It is separately provided with a injection needle	The directions of use are tailored based on the prefilled syringe generic product.
1. Wash hands thoroughly with soap and water. 2. Flip off the plastic cover of the vial and wipe the aluminum ring and the rubber stopper with an alcohol swab. 3. Twist the injection needle with the yellow mark (20 gauge) on the pre-filled syringe. 4. Push the needle through the center of the rubber stopper of the vial and slowly inject the solvent into the vial. 5. Leaving the syringe in the vial, gently swirl the vial until the solution is clear and without residues. Avoid forming bubbles. 6. Draw the total contents of the vial into the syringe. If necessary, invert the vial and pull back the needle as far as needed to withdraw the entire contents of the vial. 7. Replace the needle with the yellow mark by the injection needle with the grey mark (27 gauge). 8. Invert the syringe and push the plunger until all air bubbles have been expelled. 9. Choose an injection site in the lower abdominal area, preferably around, but staying at least one inch away from the navel. Choose a different injection site each day to minimize local irritation. Use a second alcohol swab to clean the skin at the injection site and allow alcohol to dry. Gently pinch up the skin surrounding the site of injection. 10. Inject the prescribed dose as directed by your doctor, nurse or pharmacist. 11. Use the syringe and needles only once. Dispose of the syringe and needles properly after use. If available, use a medical waste container for disposal.	2. Wash hands thoroughly with soap and water. 3. Twist the injection needle on the pre-filled syringe. 4. Invert the syringe and push the plunger until all air bubbles have been expelled. 5. Choose an injection site in the lower abdominal area, preferably around, but staying at least one inch away from the navel. Choose a different injection site each day to minimize local irritation. Use a second alcohol swab to clean the skin at the injection site and allow alcohol to dry. Gently pinch up the skin surrounding the site of injection. 6. Inject the prescribed dose as directed by your doctor, nurse or pharmacist. 7. Use the syringe and needles only once. Dispose of the syringe and needles properly after use. If available, use a medical waste container for disposal. 8. Discard unused portion.	

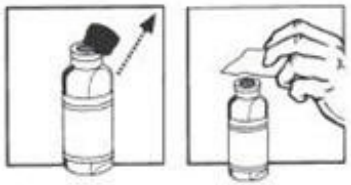
Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
HOW SUPPLIED Cetrotide® 0.25 mg is available in a carton of one packaged tray (NDC 44087-1225-1). Each packaged tray contains: one glass vial containing 0.26-0.27 mg cetrorelix acetate (corresponding to 0.25 mg cetrorelix), one pre-filled glass syringe with 1 mL of Sterile Water for Injection, USP (pH 5-8), one 20 gauge needle (yellow) and one 27 gauge needle (grey).	**HOW SUPPLIED** Cetrorelix Acetate Injection, 0.25 mg/mL is available in a carton of one packaged tray (NDC 70700-204-98) Each packaged tray contains disposable, ready to use, single dose, sterile prefilled 1 mL glass syringes containing 0.25 mg/mL aqueous solution of Cetrorelix Acetate closed with a rubber piston that does not contain latex. Each Cetrorelix Acetate sterile, prefilled syringe is provided with one 20 gauge needle (yellow) closed by a needle shield.	RLD proprietary name, NDC Number and packaging details are replaced with the PFS generic product.
Storage Store Cetrotide® 0.25 mg refrigerated, 2-8°C (36-46°F). Store the packaged tray in the outer carton in order to protect from light.	**Storage** Store Cetrorelix Acetate Injection, 0.25 mg/mL refrigerated, 2-8°C (36-46°F). Store the packaged tray in the outer carton in order to protect from light.	RLD proprietary name replaced with prefilled syringe generic product name.
Rx only	**Rx only**	
Manufactured for: EMD Serono, Inc, Rockland, MA 02370, USA	**Manufactured for:** [Manufacturer]. [Address] [Country of Origin]	Manufacturer Information is revised based on product specific information.
December 2023	**May 2024**	Revision date is updated for generic product.
PATIENT LEAFLET Cetrotide® 0.25 mg Active ingredient: cetrorelix acetate	**PATIENT LEAFLET** Cetrorelix Acetate Injection, Ready to Use Prefilled syringe, 0.25 mg/mL Active ingredient: cetrorelix acetate	RLD proprietary name replaced with prefilled syringe generic product name.
Summary Cetrotide® blocks the effects of a natural hormone, called gonadotropin-releasing hormone (GnRH). GnRH controls the secretion of another hormone, called luteinizing hormone (LH), which induces ovulation during the menstrual cycle. During hormone treatment for ovarian stimulation, premature ovulation may lead to eggs that are not suitable for fertilization. Cetrotide® blocks such undesirable premature ovulation.	**Summary** Cetrorelix acetate injection blocks the effects of a natural hormone, called gonadotropin-releasing hormone (GnRH). GnRH controls the secretion of another hormone, called luteinizing hormone (LH), which induces ovulation during the menstrual cycle. During hormone treatment for ovarian stimulation, premature ovulation may lead to eggs that are not suitable for fertilization. Cetrorelix acetate injection blocks such undesirable premature ovulation.	
Uses	**Uses**	

Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
Cetrotide® is used to prevent premature ovulation during controlled ovarian stimulation.	Cetrorelix acetate injection is used to prevent premature ovulation during controlled ovarian stimulation.	RLD proprietary name replaced with prefilled syringe generic product name.
General Cautions Do not use Cetrotide® if you • have kidney disease • are allergic to cetrorelix acetate, mannitol or exogenous peptide hormones (medicines similar to Cetrotide®) or • are pregnant, or think that you might be pregnant, or if you are breast-feeding. Consult your doctor before taking Cetrotide® if you have had severe allergic reactions.	**General Cautions** Do not use Cetrorelix Acetate Injection if you • have kidney disease • are allergic to cetrorelix acetate, mannitol or exogenous peptide hormones (medicines similar to Cetrorelix acetate injection) or • are pregnant, or think that you might be pregnant, or if you are breast-feeding. Consult your doctor before taking Cetrorelix acetate injection if you have had severe allergic reactions.	
Proper Use Ovarian stimulation therapy is started on cycle Day 2 or 3. Cetrotide® 0.25 mg is injected under the skin once daily, as directed by your physician. When an ultrasound examination shows that you are ready, another drug (hCG) is injected to induce ovulation.	**Proper Use** Ovarian stimulation therapy is started on cycle Day 2 or 3. Cetrorelix acetate injection, 0.25 mg/mL is injected under the skin once daily, as directed by your physician. When an ultrasound examination shows that you are ready, another drug (hCG) is injected to induce ovulation.	RLD proprietary name replaced with prefilled syringe generic product name.
How should you use Cetrotide®? You may self-inject Cetrotide® after special instruction from your doctor.	**How should you use Cetrorelix Acetate Injection?** You may self-inject Cetrorelix acetate injection after special instruction from your doctor.	
To fully benefit from Cetrotide®, please read carefully and follow the instructions given below, unless your doctor advises you otherwise.	To fully benefit from Cetrorelix acetate injection, please read carefully and follow the instructions given below, unless your doctor advises you otherwise.	RLD proprietary name replaced with prefilled syringe generic product name.
Cetrotide® is for injection under the skin of the lower abdominal area, preferably around, but staying at least one inch away from the belly button. Choose a different injection site each day to minimize local irritation.	Cetrorelix acetate injection is for injection under the skin of the lower abdominal area, preferably around, but staying at least one inch away from the belly button. Choose a different injection site each day to minimize local irritation.	
Dissolve Cetrotide® powder only with the water contained in the pre-filled syringe. Do not use a Cetrotide® solution if it contains particles or if it is not clear. Before you inject Cetrotide® yourself, please read the following instructions carefully:	Do not use a Cetrorelix acetate injection solution if it contains particles or if it is not clear. Before you inject Cetrorelix acetate injection yourself, please read the following instructions carefully:	The instruction is tailored as per PFS generic product, since the product is a ready to use pre filled syringe it doesn't require any dissolving.

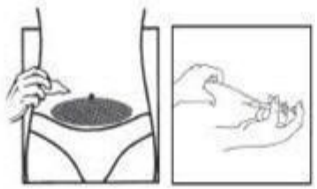
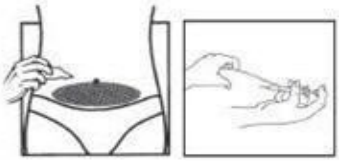
Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
Directions for using for Cetrotide® 0.25 mg with the enclosed needles and pre-filled syringe:	**Directions for using Cetrorelix Acetate Injection, 0.25 mg/ mL with the enclosed needles and pre-filled syringe:**	RLD proprietary name replaced with prefilled syringe generic product name.
1. Wash your hands thoroughly with soap and water. 	1. Wash your hands thoroughly with soap and water. 	
2. On a clean flat surface, lay out everything you need (One vial of powder, one pre-filled syringe, one injection needle with a yellow mark, and one injection needle with a grey mark). 	2. On a clean flat surface, lay out everything you need (one pre-filled syringe, one injection needle).	Instruction #2 in generic product is revised as prefilled syringe generic product contents.
3. Flip off the plastic cover of the vial. Wipe the aluminum ring and the rubber stopper with an alcohol swab. 		Instruction #3 in RLD does not apply to PFS generic product here
4. take the injection needle with the yellow mark and remove the wrapping. Take the pre-filled syringe and remove the cover. Twist the needle on the syringe and remove the cover of the needle. 	3. Take the injection needle and remove the wrapping. Take the pre-filled syringe and remove the cover. Twist the needle on the syringe and remove the cover of the needle.	Instruction #3 in PFS generic is updated as per prefilled syringe generic product contents.

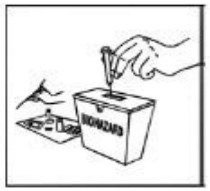
Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
		
5. Push the needle through the center of the rubber stopper of the vial. Inject the water into the vial by slowly pushing down on the plunger of the syringe.		Instruction #5 in RLD does not apply to PFS generic product here
		
6. Leave the syringe 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.		Instruction #6 in RLD does not apply to PFS generic product here
		
7. Draw the total contents of the vial into the syringe. If liquid is left in the vial, invert the vial, pull back the needle until the opening of the needle is just inside the stopper. If you look from the side through the gap in the stopper, you can control the movement of the needle and the liquid. It is important to withdraw the entire contents of the vial.		Instruction #7 in RLD does not apply to PFS generic product here
		

Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
8. Detach the syringe from the needle and lay down the syringe. Take the injection needle with the grey mark and remove its wrapping. Twist the needle on the syringe and remove the cover of the needle.  9. Invert the syringe and push the plunger until all air bubbles have been pushed out. Do not touch the needle or allow the needle to touch any surface.  10. Choose an injection site in the lower abdominal area, preferably around, but at least one inch away from the belly button. Choose a different injection site each day to minimize local irritation. Take a second alcohol swab and clean the skin at the injection site and allow alcohol to dry. Inject the prescribed dose as directed by your doctor, nurse or pharmacist. 	4. Invert the syringe and push the plunger until all air bubbles have been pushed out. Do not touch the needle or allow the needle to touch any surface.  5. Choose an injection site in the lower abdominal area, preferably around, but at least one inch away from the belly button. Choose a different injection site each day to minimize local irritation. Take a second alcohol swab and clean the skin at the injection site and allow alcohol to dry. Inject the prescribed dose as directed by your doctor, nurse or pharmacist. 	Instruction #8 in RLD does not apply to PFS generic product here

Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
11. Use the syringe and needles only once. Dispose of the syringe and needles immediately after use (put the covers on the needles to avoid injury). A medical waste container should be used for disposal. 	6. Use the syringe and needles only once. Dispose of the syringe and needles immediately after use (put the covers on the needles to avoid injury). A medical waste container should be used for disposal. 	
	7. Discard unused portion.	Instruction # 7 is added in Generic PI to be in compliance with Patient leaflet of Generic Vial Cetrorelix ANDA
SPECIAL ADVICE	**SPECIAL ADVICE**	
What do you do if you have used too much Cetrotide®? Contact your doctor in case of overdosage immediately to check whether an adjustment of the further ovarian stimulation procedure is required.	**What do you do if you have used too much Cetrorelix Acetate Injection?** Contact your doctor in case of overdosage immediately to check whether an adjustment of the further ovarian stimulation procedure is required.	RLD proprietary name replaced with prefilled syringe generic product name.
Possible Side Effects Mild and short lasting reactions may occur at the injection site like reddening, itching, and swelling. Nausea and headache have also been reported. Call your doctor if you have any side effect not mentioned in this leaflet or if you are unsure about the effect of this medicine.	**Possible Side Effects** Mild and short lasting reactions may occur at the injection site like reddening, itching, and swelling. Nausea and headache have also been reported. Call your doctor if you have any side effect not mentioned in this leaflet or if you are unsure about the effect of this medicine.	
Storage **How is Cetrotide® to be stored?** Store Cetrotide® in a cool dry place protected from excess moisture and heat.	**Storage** **How is Cetrorelix Acetate Injection to be stored?** Store Cetrorelix Acetate Injection in a cool dry place protected from excess moisture and heat.	RLD proprietary name replaced with prefilled syringe generic product name.
Store Cetrotide® 0.25 mg in the refrigerator at 2-8°C (36-46°F). Keep the packaged tray in the outer carton in order to protect it from light.	Store Cetrorelix Acetate Injection, 0.25 mg/mL in the refrigerator at 2-8°C (36-46°F). Keep the packaged tray in the outer carton in order to protect it from light.	RLD proprietary name replaced with prefilled syringe generic product name. also, the vial part

Side by Side Comparison of Prescribing Information (RLD Vs Generic)

RLD (PI)	Generic (PI)	Justification
How long may Cetrotide® be stored? Do not use the Cetrotide® powder or the pre-filled syringe after the expiration date, which is printed on the labels and on the carton and dispose of the vial and the syringe properly.	**How long may Cetrorelix Acetate Injection be stored?** Do not use the Cetrorelix Acetate Injection pre-filled syringe after the expiration date, which is printed on the labels and on the carton, and dispose of the syringe properly.	is removed in the Generic PI.
How long can you keep Cetrotide® after preparation of the solution? The solution should be used immediately after preparation.		This question does not apply to the Generic PFS since its already a ready to use solution, so no preparation is involved.
Store the medicine out of the reach of children.	***Store the medicine out of the reach of children.***	
If you suspect that you may have taken more than the prescribed dose of this medicine, contact your doctor immediately. This medicine was prescribed for your particular condition. Do not use it for another condition or give the drug to others.	If you suspect that you may have taken more than the prescribed dose of this medicine, contact your doctor immediately. This medicine was prescribed for your particular condition. Do not use it for another condition or give the drug to others.	
This leaflet provides a summary of the information about Cetrotide®. Medicines are sometimes prescribed for uses other than those listed in the Leaflet. If you have any questions or concerns, or want more information about Cetrotide®, contact your doctor or pharmacist.	This leaflet provides a summary of the information about Cetrorelix acetate injection. Medicines are sometimes prescribed for uses other than those listed in the Leaflet. If you have any questions or concerns, or want more information about Cetrorelix acetate injection, contact your doctor or pharmacist.	RLD proprietary name replaced with prefilled syringe generic product name.
This Leaflet has been approved by the U.S. Food and Drug Administration.	Manufactured for: [Manufacturer]. [Address] [Country of Origin]	Removed the highlighted sentence and replaced it with manufacturing information.
December 2023	**May 2024**	Revision date updated for generic product.