

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lutrate 1 month Depot 3.75mg Powder and Solvent for Prolonged-Release Suspension for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 3.75 mg of leuporelin acetate (equivalent to 3.57 mg leuporelin free base).
1 ml of reconstituted suspension contains 1.875 mg of leuporelin acetate.

Excipients with known effect:

Each vial contains from 1.3 to 2.2 mg (<1 mmol) of sodium (as carmellose sodium).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for prolonged-release suspension for injection.

Powder: white to off-white powder.

Solvent: clear transparent solution (pH 5.0 – 7.0).

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

- (i) Metastatic prostate cancer.
- (ii) Locally advanced prostate cancer, as an alternative to surgical castration.
- (iii) As an adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.
- (iv) As an adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression.
- (v) As neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.

4.2 Posology and method of administration

Posology

The usual recommended dose of Lutrate 1 month Depot is 3.75 mg presented as a one month depot injection and administered as a single intramuscular injection every month.

Lutrate 1 month Depot must be administered under the supervision of a physician or a qualified health practitioner.

The dose of Lutrate 1 month Depot allowing the continuous release of leuporelin acetate during one month is incorporated in a depot formulation. The lyophilized powder should be reconstituted and administered as a single intramuscular injection at monthly intervals. Intra-arterial or intravenous administration must be avoided. The vial of Lutrate 1 month Depot microsphere powder should be reconstituted immediately prior to administration by intramuscular injection. As with other drugs administered regularly by injection, the injection site should be varied periodically.

Lutrate 1 month Depot therapy should not be discontinued when remission or improvement occurs.

Response to Lutrate 1 month Depot therapy should be monitored measuring serum levels of testosterone as well as prostate-specific antigen (PSA) periodically. Clinical studies have shown that testosterone levels increased during the

first 4 days of treatment in the majority of non-orchietomised patients. They then decreased and reached castrate levels by 3-4 weeks. Once attained, castrate levels (defined as concentration of testosterone less than 0.5 ng/mL) were maintained as long as drug therapy continued.

If a patient's response appears to be sub-optimal, then it would be advisable to confirm that serum testosterone levels have reached or are remaining at castrate levels. Transient increases in acid phosphatase levels sometimes occur early in the treatment period but usually return to normal or near normal values by the 4th week of treatment.

Duration of treatment

Lutrate 1 month Depot should be administered as monthly intramuscular injections. As a rule, prostate cancer therapy with Lutrate 1 month Depot entails long-term treatment and therapy should not be discontinued when remission or improvement occurs.

Special populations

Paediatric population

The safety and efficacy of Lutrate 1 month Depot in the paediatric patients has not been established. Therefore, Lutrate 1 month Depot is not recommended in children or adolescents until safety and efficacy data become available.

Renal/hepatic impairment

The pharmacokinetics of Lutrate 1 month Depot in hepatically and renally impaired patients has not been determined.

Elderly

In the clinical trial for Lutrate 1 month Depot, the mean age of the subjects studied was 71.6±9.2 years. Therefore, the labelling reflects the pharmacokinetics, efficacy and safety of Lutrate 1 month Depot in this population.

Method of administration

Lutrate 1 month Depot must be administered via the intramuscular route only. Do not administer by any other route. If it is administered subcutaneously by mistake, the patient should be closely monitored since no data about other administration routes apart from intramuscular is available for Lutrate 1 month Depot. For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance, luteinising hormone releasing hormone (LHRH) analogues or to any of the excipients listed in section 6.1. Reports of anaphylactic reactions to synthetic LHRH or LHRH agonist analogues have been reported in the medical literature.

Previous orchiectomy.

Lutrate 1 month Depot must not be used as the only treatment in patients with prostate cancer and with evidence of spinal cord compression or spinal metastases.

Lutrate 1 month Depot is not indicated for use in women.

Lutrate 1 month Depot is not indicated for use in paediatric patients.

4.4 Special warnings and precautions for use

In the initial stages of Lutrate 1 month Depot treatment, as occurs during treatment with other LHRH agonists, a transient rise in levels of testosterone may occur. In some cases, this may be associated with a "flare" or exacerbation of the tumour growth resulting in temporary worsening of prostate cancer symptoms. These symptoms usually subside on continuation of therapy (see **section 4.8**). "Flare" may manifest itself as systemic or neurological symptoms in some cases (i.e. bone pain...). Also, cases of orchiatrophy and gynecomastia have been described with other LHRH agonists.

Treatment should be discontinued immediately if the patient develops any signs or symptoms suggestive of anaphylaxis/anaphylactic reaction (dyspnoea, asthma, rhinitis, angioneurotic oedema or glottis, hypotension, urticaria, rash, pruritus or interstitial pneumonitis). Patients should be informed before starting treatment, warning them to discontinue it and consult their doctor if any of the above mentioned symptoms occur. Patients who have experienced a hypersensitivity reaction to leuporelin should be closely monitored and should not be rechallenged with Lutrate 1 month Depot.

In patients treated with leuporelin acetate, isolated cases of urethral obstruction (with or without haematuria) and spinal cord compression or metastatic vertebral lesions have been observed, which may contribute to paralysis with or without fatal complications. Patients at risk of urethral obstruction, spinal cord compression or metastatic vertebral lesions should be considered carefully and closely supervised in the first few weeks of treatment. These patients should be considered for prophylactic treatment with anti-androgens.

Should urological/neurological complications occur, these should be treated by appropriate specific measures.

There is an increased risk of incident depression (which may be severe) in patients undergoing treatment with GnRH agonists, such as leuporelin acetate. Patients should be informed accordingly and treated as appropriate if symptoms occur.

Decreased bone density has been reported in the medical literature in men who have had orchiectomy or who have been treated with an LHRH agonist. Adding anti-androgenic therapy to the treatment regimen reduces bone loss, but increases the risk of other adverse effects such as clotting problems and oedema. If an anti-androgen is used over a prolonged period, due attention should be paid to the contraindications and precautions associated with its extended use. Patients at risk or with a medical history of osteoporosis should be considered carefully and closely supervised during treatment with leuporelin acetate (see **section 4.8**).

Hepatic dysfunction and jaundice with elevated liver enzyme levels have been reported with the use of leuporelin acetate. Therefore, close observation should be made and appropriate measures taken if necessary.

Response to Lutrate 1 month Depot therapy should be monitored by clinical parameters and by measuring testosterone and PSA serum levels periodically.

Patients may experience metabolic changes (e.g. glucose intolerance or worsening of existing diabetes), hypertension, weight changes and cardiovascular disorders. As would be expected with this class of drug, development or aggravation of diabetes may occur, therefore diabetic patients may require more frequent monitoring of blood glucose during treatment with Lutrate 1 month Depot. Patients at high risk for metabolic or cardiovascular diseases should be carefully assessed before commencing treatment and adequately monitored during androgen deprivation therapy. Therapy with leuporelin acetate results in suppression of the pituitary-gonadal system. Results of diagnostic tests of pituitary gonadotropic and gonadal functions conducted during and after leuporelin acetate therapy may be affected. Increased prothrombin time has been reported in patients under treatment with leuporelin acetate.

Seizures have been reported with the administration of leuporelin acetate. These cases were observed in patients with a history of seizures, epilepsy, cerebrovascular disorders, anomalies or central nervous system tumours and in patients with concomitant medications that have been associated with seizures for example bupropion and selective inhibitors of serotonin reuptake (SSRIs). Seizures in patients in the absence of the any medical conditions mentioned above have also been reported.

Leuporelin acetate should be used with precautions in the presence of, cardiovascular disease (including congestive heart failure condition), thromboembolism, oedema, depression and pituitary adenomas.

Leuporelin acetate should be used with caution in patients with known bleeding disorders, thrombocytopenia or on treatment with anticoagulants. Sportsmen should take precaution as Lutrate 1 month Depot contains an ingredient which may give a positive test result in doping controls.

This medicinal product contains less than 1 mmol sodium (23 mg) per vial. It is essentially 'sodium- free'.

Androgen deprivation therapy may prolong the QT interval.

In patients with a history of or risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval (see section 4.5) physicians should assess the benefit risk ratio including the potential for Torsade de pointes prior to initiating Lutrate 1 month Depot.

4.5 Interaction with other medicinal products and other forms of interaction

No pharmacokinetic-based drug-drug interaction studies have been conducted with leuporelin acetate. However, because leuporelin acetate is a peptide that is primarily degraded by peptidase and not by Cytochrome P-450 enzymes as noted in specific studies, and the drug is only about 46% bound to plasma proteins, pharmacokinetic drug interactions would not be expected to occur.

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of Lutrate 1 month Depot with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as class IA (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc. should be carefully evaluated (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy:

Lutrate 1 month Depot is not indicated for use in pregnant women.

Leuporelin acetate injection may cause foetal harm when administered to a pregnant woman.

Therefore, the possibility exists that spontaneous abortion may occur if the drug is administered during pregnancy.

Breast-feeding:

Lutrate 1 month Depot should not be used in women who are breast-feeding.

Fertility:

Studies in animals have shown reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

No specific studies on the effects of Lutrate 1 month Depot on the ability to drive and use machines have been performed. However, the ability to drive and use machines may be impaired due to visual disturbances and dizziness.

4.8 Undesirable effects

Unless otherwise specified, the following safety profile of Lutrate 1 month Depot is based on the results of a phase III clinical trial in which prostate cancer patients were treated with six intramuscular monthly doses of Lutrate 1 month Depot and followed up for total a period of 26 weeks. Most of the treatment-related AEs reported were the usual ones associated with testosterone suppressing therapy.

The most commonly reported adverse reactions with Lutrate 1 month Depot are hot flushes, injection site pain, injection site irritation, night sweats and headache.

The following adverse reactions from clinical investigations were listed below by system organ class and in order of decreasing incidence (very common: $\geq 1/10$; common: $\geq 1/100$ to $< 1/10$; uncommon: $\geq 1/1,000$ to $< 1/100$).

Table 1. Number and frequency of ADRs during Lutrate 1 month Depot 3.75 mg therapy.

Category

SOC Frequency: Preferred Term
Metabolism and nutrition disorders Common: Decreased appetite Uncommon: hypercholesterolaemia, hyperlipidaemia
Psychiatric disorders Uncommon: Sleep disorders, insomnia, libido decreased, mood changes, anorexia and depression*
Nervous system disorders Common: Headache Uncommon: Somnolence
Ear and labyrinth disorders Uncommon: Vertigo
Vascular disorder Very common: Hot flush
Gastrointestinal disorders Uncommon: Abdominal pain lower, diarrhoea, nausea, vomiting
Hepatobiliary disorders Uncommon: Hyperbilirubinaemia
Skin and subcutaneous tissue disorders Common: Hyperhidrosis, night sweats, cold sweats Uncommon: Periorbital edema, urticaria, pruritus,
Musculoskeletal and connective tissue disorders Common: Back pain Uncommon: Arthralgia, muscle spasms, pain in extremity
Renal and urinary disorders Uncommon: Urinary retention, urinary incontinence, pollakiuria
Reproductive system and breast disorders Common: Erectile dysfunction Uncommon: Breast swelling, breast tenderness, ejaculation failure
General disorders and administration site conditions Common: Fatigue, asthenia, pyrexia, local adverse reactions (see table 2) Uncommon: Weakness, feeling hot and cold, feeling jittery
Investigations Common: Weight gain Uncommon: Increased AST, increased ALT, bilirubin increased, gamma glutamyltransferase increased, electrocardiogram QT prolonged (see sections 4.4 and 4.5).

* In a post-marketing study the frequency of mood changes and depression in long term users was common.

In terms of severity, 98% of all treatment-related AEs were mild or moderate. Eighty-nine percentage (89%) of the hot flushes were reported as mild and nine percentage (9%) as moderate. Two cases of hot flushes (0.2%) were reported as severe.

A total of 35 local adverse reactions (LAR) at the injection site were reported by 29 patients (18.1%) during the study.

Local adverse reactions after Lutrate 1 month Depot 3.75mg are those typically reported with other similar products administered via intramuscular injection. Injection site pain, injection site irritation, injection site discomfort, injection site bruising and erythema were the most commonly reported. Uncommonly reported reactions were injection site reaction, swelling, injury and haemorrhage (Table 2)

Table 2. Frequency of patients with local adverse reactions during Lutrate 1 month Depot therapy.

Primary SOC*	Patients with related LAR
PT: General disorders and administration site conditions	%
Common	
Injection site pain	8.1
Injection site irritation	4.4
Injection site discomfort	1.9
Injection site erythema	1.3
Injection site bruising	1.3
Uncommon	
Injection site reaction	0.6
Injection site swelling	0.6
Injection site injury	0.6
Injection site haemorrhage	0.6

*Subjects may fall into more than one category; LAR: local adverse reaction; SOC: System Organ Class.

In the presence of repeated administrations of Lutrate 1 month Depot, swelling (0.6%), pain (0.6%), bruising (0.6%) and irritation (0.6%) were reported as recurrent local adverse reactions. These events were all reported as not serious and mild. No patient discontinued therapy due to local adverse events.

In a phase I clinical trial (CRO-02-43) carried out in healthy subjects with Leuprolide Depot GP-Pharm 7.5 mg administered at single dose, one case of injection site induration was reported.

Other adverse events which have been reported to occur with leuprorelin acetate treatment include impotence, decrease in libido (both pharmacological consequences of testosterone deprivation), peripheral oedema, pulmonary embolism, palpitations, myalgia, muscle weakness, chills, dyspnoea, peripheral vertigo, rash, amnesia, visual disturbances and skin sensation. Infarction of pre-existing pituitary adenomas has been reported rarely after administration of both short and long acting LHRH agonists. There have been rare reports of thrombocytopenia and leucopenia. Changes in glucose tolerance have been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: <http://www.hpra.ie/> ; E-mail: medsafety@hpra.ie

4.9 Overdose

There is no clinical experience with the effects of an acute overdose of Lutrate 1 month Depot or leuprorelin acetate. In clinical trials using daily subcutaneous leuprorelin acetate in patients with prostate cancer, doses as high as 20 mg/day for up to two years caused no AEs differing from those observed with the 1 mg/day dose.

In animal studies, doses of up to 500 times the recommended human dose resulted in dyspnoea, decreased activity and local irritation at the injection site. In cases of overdosage, the patient should be monitored closely and management should be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Endocrine therapy. Hormones and related agents. Gonadotropin-releasing hormones analogues; ATC code: L02AE02.

Mechanism of action

The chemical name of Leuporelin acetate is 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-L-prolyl-ethylamide.

Leuporelin acetate is inactive when given orally due to poor membrane permeability and an almost complete inactivation by intestinal proteolytic enzymes.

Leuporelin acetate has potent LHRH agonist properties when given during short-term and intermittent therapy, however, when administered in a continuous, nonpulsatile manner, LHRH analogs induce inhibition of gonadotropin secretion and suppression of testicular steroidogenesis.

Pharmacodynamic effects

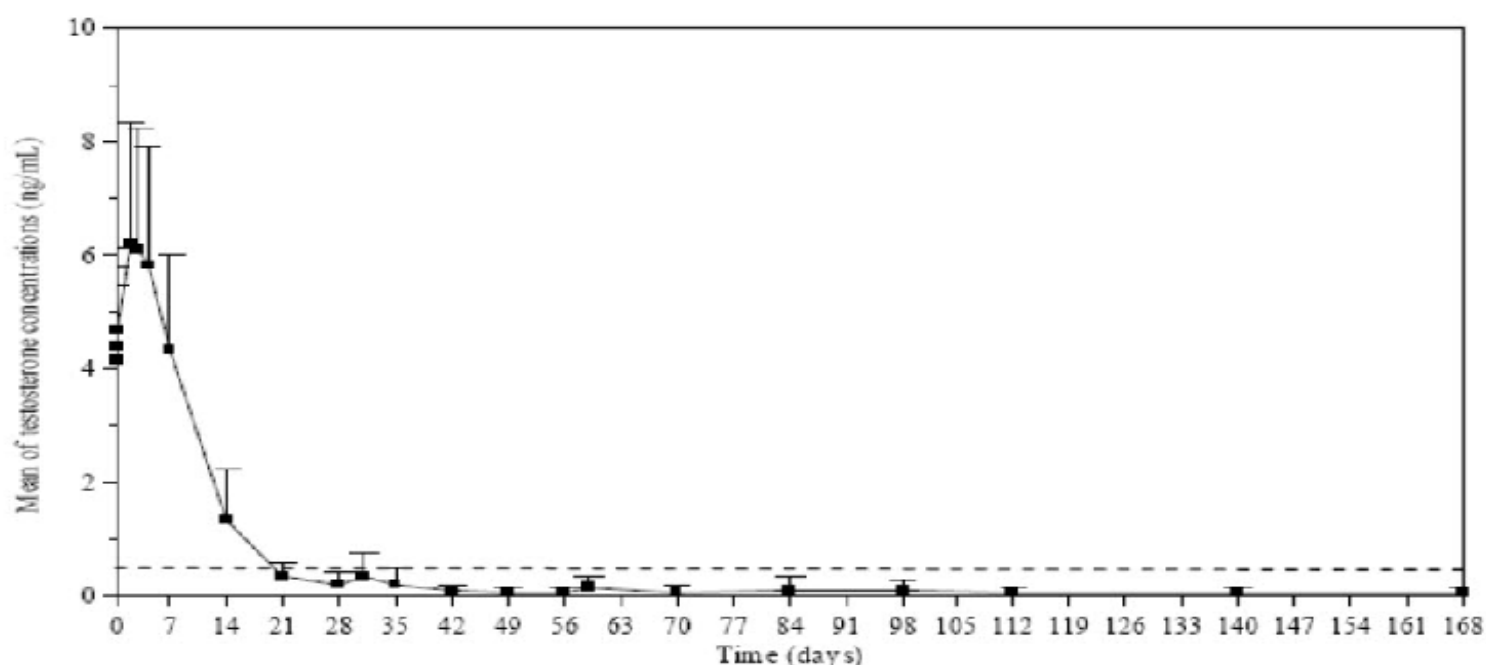
Upon binding to pituitary LHRH receptors, leuporelin acetate produces an initial increase in circulating levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH), leading to an acute rise in levels of testosterone and dihydrotestosterone. However, within five to eight days after drug administration, LHRH analogs produce desensitization of the LHRH receptor complex and/or downregulation of the anterior pituitary gland. Due to the fact that there are fewer receptors on the cell surface, cellular stimulation is decreased, and less gonadotropin is synthesized and secreted. Eventually, after several weeks of LHRH agonist therapy, LH and FSH secretion is suppressed. As a result, Leydig cells in the testes cease to produce testosterone, and the serum testosterone concentration declines to a castration level (less than 0.5 ng/mL) in about two to four weeks after initiation of treatment.

Clinical efficacy and safety

In an open-label, multicenter, multiple dose clinical study of Lutrate 1 month Depot, 160 patients with prostate cancer and no previous systemic cancer therapy, hormonal therapy for the treatment of prostate cancer, previous prostatic surgery neither previous orchiectomy, were enrolled. The objectives were to determine the efficacy and safety of Lutrate 1 month Depot when given to prostate cancer patients who could benefit from androgen deprivation therapy. Lutrate 1 month Depot was administered intramuscularly in 6 monthly doses.

Testosterone levels were monitored at different days during 168 days. As expected, after the first injection the mean testosterone levels rapidly increased from baseline levels (4.119 ± 1.341 ng/mL), reaching peak levels (C_{max}) of 6.598 ± 2.249 ng/mL at the third day. After peaking, testosterone levels fell, and by day 21, 78.7% of the evaluable patients had achieved medical castration (defined as testosterone less than 0.5 ng/mL). By Day 28, 96.8% of the patients had achieved castrate levels, and 73.1% had reached levels of ≤ 0.2 ng/mL (Figure 1).

Figure 1. Mean (\pm SD) testosterone plasma levels during treatment with six monthly IM injections of Lutrate 1 month Depot 3.75 mg



Secondary efficacy endpoints included determination of serum LH, FSH and PSA concentrations. By day 14 and day 4 after the first Lutrate 1 month Depot injection, mean LH and FSH serum levels had decreased below the baseline concentrations. Concentrations remained well below baseline values from day 28 until the end of the study. During the treatment, mean PSA serum levels gradually decreased (first month) and then remained constantly below baseline level until the end of the study. However, a wide inter-individual variation in PSA concentrations was observed throughout the study.

The frequency of the acute on chronic response was 10.5 % and the frequency of testosterone breakthrough response was 11.8 %. No drug-related adverse events suggestive of a clinical testosterone flare (urinary retention, spinal cord compression, or exacerbation of bone pain) were reported in any of the patients showing a testosterone breakthrough effect.

5.2 Pharmacokinetic properties

Absorption

Following three once-monthly injections of Lutrate 1 month Depot in a sample of prostate cancer patients (N=12), maximal leuporelin acetate plasma concentration was similar among the three cycles. After first administration (Days 0-28), C_{\max} was $13,145.6 \pm 3,070.6$ pg/ml. Median time to achieve C_{\max} (T_{\max}) was 0.04 days, corresponding to 0.96 h (range 0.96 – 4.08 h).

Distribution

No drug distribution study was conducted with Lutrate 1 month Depot. However, in healthy male volunteers, the mean steady-state volume of distribution of leuporelin acetate following bolus intravenous (IV) 1.0 mg dose was 27 L. *In vitro* binding to human plasma proteins ranged from 43% to 49%.

Elimination

No drug metabolism or excretion study was conducted with Lutrate 1 month Depot.

Leuporelin is expected to be metabolised to smaller inactive peptides that may be excreted or further catabolised.

In healthy male volunteers, a 1.0 mg bolus of leuporelin acetate administered IV revealed that the mean systemic clearance was 7.6 L/h, with a terminal elimination half-life of approximately 3 hours based on a two compartment

model.

Following administration of leuporelin acetate to 3 patients, less than 5% of the dose was recovered as parent and M-I metabolite in the urine.

Special Populations

Renal/hepatic impairment

The pharmacokinetics of the drug in hepatically and renally impaired patients has not been determined.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity conducted with leuporelin acetate.

As expected from its known pharmacological properties, non-clinical studies showed effects on the reproductive systems, which were reversible. In the reproductive toxicity studies, leuporelin acetate did not show teratogenicity. However, embryotoxicity/lethality was observed in rabbits.

Carcinogenicity studies performed in rats with leuporelin acetate administered subcutaneously (0.6 to 4 mg/kg/day), showed a dose-related increase in pituitary adenomas. Furthermore a significant but not dose-related increase of pancreatic islet-cell adenomas in females and of testicular interstitial cell adenomas in males was observed. The highest incidence was in the low dose group. Administration of leuporelin acetate resulted in inhibition of the growth of certain hormone dependent tumours (prostatic tumours in Noble and Dunning male rats and DMBA-induced mammary tumours in female rats). No such effects were observed in carcinogenicity studies performed in mice. No carcinogenicity studies have been conducted with Lutrate 1 month Depot.

Studies with leuporelin acetate showed that the product was not mutagenic in a set of in vitro and in vivo assays. No mutagenicity studies have been conducted with Lutrate 1 month Depot.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients of the lyophilizate (vial):

Polysorbate 80
Mannitol (E-421)
Carmellose sodium (E-466)
Triethyl citrate
Poly(DL-lactide-co-glycolide) (PLGA)

Excipients of the solvent (prefilled syringe):

Mannitol (E-421)
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

No other solvent other than the sterile solvent provided for Lutrate 1 month Depot can be used for the reconstitution of Lutrate 1 month Depot powder.

6.3 Shelf life

3 years unopened.

Once reconstituted with the solvent the suspension should be administered immediately.

6.4 Special precautions for storage

Do not store above 25° C. Do not freeze.

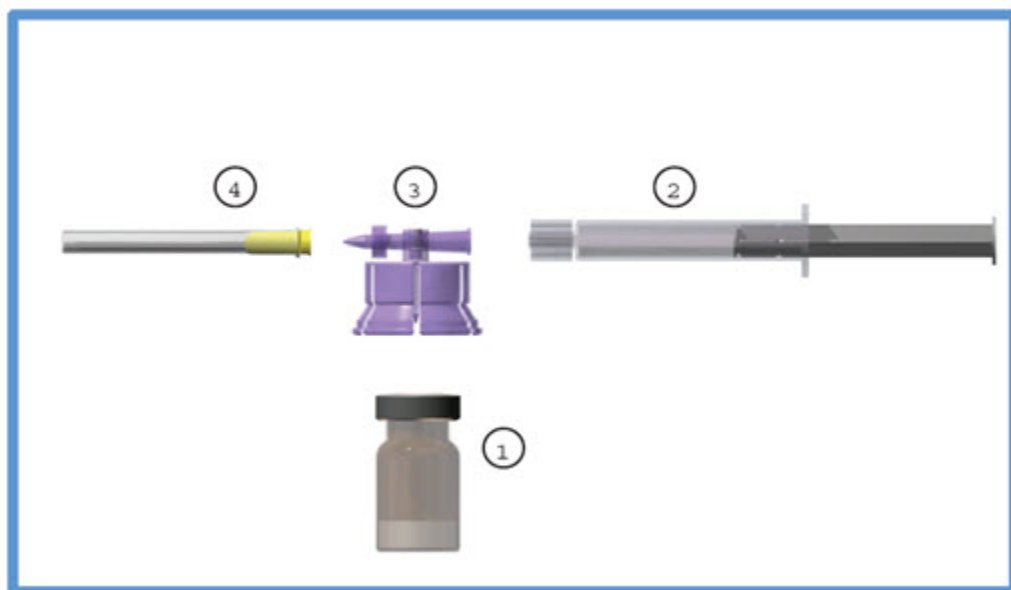
Store in the original package in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

The commercial kit includes:

1. One (1) type I glass vial containing 3.75 mg of leuporelin acetate as a freeze-dried powder, sealed with a bromobutyl stopper and an aluminium flip-off cap.
2. One (1) type I glass prefilled syringe containing 2 ml of solvent sealed with an elastomer cap.
3. One (1) polycarbonate / HDPE adaptor system including one (1) sterile 20 gauge needle.



6.6 Special precautions for disposal and other handling

Method of administration

The vial of Lutrate 1 month Depot microsphere powder should be reconstituted immediately prior to administration by intramuscular injection. Make sure an aseptic technique is followed.

The reconstituted product is a suspension of milky, white colour appearance.

No other solvent can be used for reconstitution of Lutrate 1 month Depot.

Reconstitute Lutrate 1 month Depot according to the following instructions:

<p>1</p>  <p>Remove blue cap from the vial</p>	<p>2</p>  <p>Attach the adaptor system (in purple) to vial until a 'clicking' sound is heard</p>	<p>3</p>  <p>Affix the white finger-grip to the diluents-containing syringe Remove the rubber cap from the syringe and attach it to the adaptor system</p>
<p>4</p>  <p>While keeping the syringe and vial securely coupled in an upright position, slowly push the plunger in order to transfer all the diluents into the vial</p>	<p>5</p>  <p>With the syringe still coupled to the vial, shake the vial gently for approximately one minute until a uniform milky-white suspension is obtained</p>	<p>6</p>  <p>Turn the system upside down, and carefully pull out the plunger to draw up the resuspended drug from the vial into the syringe</p>
<p>7</p>  <p>Detach the syringe and needle from the adaptor system by twisting the upper piece of the adaptor counter-clockwise. The drug is ready to be used.</p>	<p>8</p>  <p>Clean the injection area with an alcohol swab and let the skin dry. Inject the suspension intramuscularly into the upper outer quadrant of the gluteus</p>	

Some product may cake or clump at the vial wall. This is considered normal. During product manufacture the vial is filled with excess product in order to make sure that a final dose of 3.75 mg of leuporelin acetate is administered.

The product is meant for a single injection. Any remaining suspension must be discarded.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Limited
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85 King William Street,
London EC4N 7BL,
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0899/044/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th July 2015

10 DATE OF REVISION OF THE TEXT

June 2017