SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

GONAPEPTYL DAILY 100 microgram/1 ml Solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each syringe with 1 ml solution contains 100 µg triptorelin acetate equivalent to 95,6 micrograms triptorelin free base.

GONAPEPTYL DAILY contains sodium chloride, glacial acetic acid and Water for injections.

For full list of excipients, see section 6.1

Sugar free.

3 PHARMACEUTICAL FORM

Solution for subcutaneous (s.c.) injection.

Appearance of the injection: Clear colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

GONAPEPTYL DAILY is indicated for down-regulation and prevention of premature luteinising hormone (LH) surges in women undergoing controlled ovarian hyperstimulation for assisted reproductive technologies (ART).

4.2 Posology and method of administration

The dosage regimen of GONAPEPTYL DAILY is 100 micrograms given once daily as a 1 ml subcutaneous injection into the lower abdominal wall. Treatment with GONAPEPTYL DAILY should be initiated under the supervision of a physician experienced in the treatment of infertility. 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.

Subsequent injections of GONAPEPTYL DAILY may be self-administered by the patient. In this instance the patient should first be instructed on appropriate self-injection technique and be made aware of the signs and symptoms that may indicate hypersensitivity, the consequences of such a reaction and the need for immediate medical intervention should such a reaction occur. For detailed information on how to inject GONAPEPTYL DAILY, the patient should refer to the "Patient Information Leaflet" provided with the product.

Treatment can be started in the early follicular phase (day 2 or 3 of the menstrual cycle) or in the mid-luteal phase (day 21-23 of the menstrual cycle or 5-7 days before expected start of menses). Controlled ovarian hyperstimulation with gonadotropins should be started after approximately 2-4 weeks of GONAPEPTYL DAILY treatment. Ovarian response should be monitored clinically (including ovarian ultrasound alone or preferably in combination with measurement of oestradiol levels) and the dose of gonadotropins adjusted accordingly.

When a suitable number of follicles have reached an appropriate size, treatment with GONAPEPTYL DAILY and gonadotropin is stopped and a single injection of human chorionic gonadotrophin (hCG) is administered to induce the final follicular maturation. If down-regulation is not confirmed after 4 weeks (determined by ultrasound documentation of a shedded endometrium alone or preferably in combination with measurement of oestradiol levels), discontinuation of GONAPEPTYL DAILY should be considered. The total duration of treatment is usually 4-7 weeks.

When using GONAPEPTYL DAILY, luteal phase support should be provided according to the reproductive medical centre's practice.

Special populations

No specific dose recommendations are given for subjects with renal or hepatic impairment. A clinical study indicated that the risk of accumulation of triptorelin in patients with severe liver and renal impairment is small (see Pharmacokinetics).

Method of administration

Subcutaneous Injection.

Injecting the medicine

1. Remove the protective foil and take the syringe out of the blister packaging
2. Keep the syringe upright with the grey protective cap facing up
3. Remove the grey protective cap
4. Gently push the plunger until the first drops of liquid appear at the needle tip
5. The medicine is to be injected under the skin of the lower abdomen. Clean the injection site with an antiseptic swab immediately prior to injection
6. Lift up a fold of skin between thumb and forefinger. With your free hand hold the syringe at a right angle to the skin like a dart and quickly insert the needle all the way into the skinfold. Press down slowly on the plunger to inject the contents of the syringe
7. Remove the syringe and needle from the skin and discard this immediately into a sharps disposal unit
8. For each dose, choose a different injection site along the lower abdomen.

4.3 Contraindications

GONAPEPTYL DAILY is contraindicated in cases of:

- Hypersensitivity to triptorelin or to any of the excipients in GONAPEPTYL DAILY
- Hypersensitivity to gonadotropin-releasing hormone (GnRH) or any other GnRH analogue
- Pregnancy and lactation
- Women of childbearing potential should be examined carefully before treatment to exclude pregnancy.

4.4 Special warnings and precautions for use

GONAPEPTYL DAILY is associated with an increased risk of multiple pregnancies, pregnancy loss, ectopic pregnancies and congenital malformations. These risks are also valid with usage of GONAPEPTYL DAILY as adjunct therapy in controlled ovarian hyperstimulation.

Follicular recruitment, induced by the use of GONAPEPTYL DAILY and gonadotropins, may be markedly increased in a minority of predisposed patients, particularly in case of Polycystic Ovarian Syndrome (PCOS).

Ovarian stimulation should be conducted under strict medical supervision.

Ovarian Hyperstimulation Syndrome

The use of GONAPEPTYL DAILY in controlled ovarian hyperstimulation may increase the risk of ovarian hyperstimulation syndrome (OHSS) and ovarian cysts. There have been reports of OHSS associated with the use of GONAPEPTYL DAILY in combination with gonadotropins.

OHSS is a medical event distinct from uncomplicated ovarian enlargement. OHSS is a syndrome that can manifest itself with increasing degrees of severity. It comprises marked ovarian enlargement, high serum sex steroids, and an increase in vascular permeability which can result in an accumulation of fluid in the peritoneal, pleural and, rarely, in the pericardial cavities.

The following symptoms may be observed in severe cases of OHSS: abdominal pain, abdominal distension, severe ovarian enlargement, weight gain, dyspnoea, oliguria and gastrointestinal symptoms including nausea, vomiting and diarrhoea. Clinical evaluation may reveal hypovolaemia, haemoconcentration, electrolyte imbalances, ascites, haemoperitoneum, pleural effusions, hydrothorax, acute pulmonary distress, and thromboembolic events.

Excessive ovarian response to GONAPEPTYL DAILY treatment seldom gives rise to OHSS unless hCG is administered to trigger ovulation. Therefore in cases of OHSS it is prudent to withhold hCG and advise the patient to refrain from coitus or to use barrier methods for at least 4 days. OHSS may progress rapidly (within 24 hours to several days) to become a serious medical event, therefore patients should be followed for at least two weeks after the hCG administration.

OHSS may be more severe and more protracted if pregnancy occurs. This syndrome occurs with higher incidence in patients with polycystic ovarian disease. Most often, OHSS occurs after hormonal treatment has been discontinued and reaches its maximum severity at about seven to ten days following treatment. Usually, OHSS resolves spontaneously with the onset of menses. If severe OHSS occurs, gonadotropin treatment should be stopped if still ongoing, the patient hospitalised and specific therapy for OHSS started e.g. with rest, intravenous infusion of electrolyte solutions or colloids and heparin.

The risk of OHSS might be higher with use of GONAPEPTYL DAILY in combination with gonadotropins than with use of gonadotropins alone. In two clinical studies (MFK/ IVF/0399E and FE999906 CS003), GnRH agonists, including GONAPEPTYL DAILY, were used in combination with gonadotropins, OHSS was reported in 6,5 % and 3,1 % of patients respectively.

Ovarian cysts

Ovarian cysts may occur during the initial phase of treatment with GONAPEPTYL DAILY. They are usually asymptomatic and non-functional.

Bone loss

Long term use of GONAPEPTYL DAILY may cause reduction in bone mineral density. Patients with known risk of osteopenia should discuss this with the treating physician.

Medicine/conditions affecting pituitary secretion

Treatment with GONAPEPTYL DAILY may reveal the presence of a previously unknown gonadotroph cell pituitary adenoma. These patients may present with a pituitary apoplexy characterised by sudden headache, vomiting, visual impairment and ophthalmoplegia. When GONAPEPTYL DAILY is co-administered with medicine affecting pituitary secretion of gonadotropins caution should be exercised and it is recommended that the patient’s hormonal status should be supervised.

Mood changes

Mood changes, including depression have been reported during long term use of GONAPEPTYL DAILY. Patients with known depression should be monitored closely during therapy.

Hepatic/renal impairment

In patients with renal or hepatic impairment, triptorelin has a mean terminal half-life of 7-8 hours compared to 3-5 hours in healthy subjects (see Pharmacokinetics). Despite this prolonged exposure, triptorelin contained in GONAPEPTYL DAILY is not expected to be present in circulation at the time of embryo transfer.

Use in atopic patients

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

4.5 Interaction with other medicines and other forms of interaction

Interactions of GONAPEPTYL DAILY with other medicines have not been investigated for this indication.

4.6 Fertility, pregnancy and lactation

Pregnancy

GONAPEPTYL DAILY is contraindicated during pregnancy (see CONTRAINDICATIONS). Pregnancy must be excluded before initiation of fertilisation treatment. Non-hormonal methods of contraception should be employed during therapy until menses resume. If a patient becomes pregnant while receiving GONAPEPTYL DAILY, therapy should be discontinued.

Limited clinical data on the use of GONAPEPTYL DAILY during pregnancy does not indicate an increased risk of congenital malformations. Treatment of pregnant rats with triptorelin acetate at 10 micrograms/kg/day by subcutaneous administration during early pregnancy resulted in retardation of foetal development and treatment in mid-pregnancy resulted in inhibition of parturition with frequent stillbirths.

Administration of the medicine during the period of organogenesis revealed no evidence of teratogenicity in rats or rabbits at subcutaneous doses up to 10 and 50 micrograms/kg/day, respectively (0,9 and 9 times the clinical dose on a body surface area basis). Based on the pharmacological effects, disadvantageous influence on the pregnancy and the offspring cannot be excluded.

Lactation

GONAPEPTYL DAILY is contraindicated for use during lactation (see CONTRAINDICATIONS).

4.7 Effects on ability to drive and use machines

No studies on the effects of the ability to drive and use machines have been performed. However, due to its pharmacological profile GONAPEPTYL DAILY is likely to have no or negligible influence on the patient's ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The information presented in Table 1 is based on adverse events (AEs) and adverse drug reactions (ADRs), and their frequencies, reported in 7 clinical trials of GONAPEPTYL DAILY in down-regulation and prevention of premature LH surges (N=1329) combined with the post marketing experience (presented in the not known category).

The following criteria were used in the selection of AEs/ADRs that are presented throughout this section.

1. Clinical trials: Treatment-Emergent AEs reported by at least 1% of the ART subjects receiving GONAPEPTYL DAILY 100 micrograms daily.
2. Post-marketing safety surveillance: > 3 ADR reports of the ART subjects receiving GONAPEPTYL DAILY 100 micrograms daily.

The most frequent adverse events reported in clinical trials and from post-marketing use are headache (5 %), abortion (4 %), dysmenorrhoea (2%), ovarian hyperstimulation syndrome (2 %), injection site inflammation (1 %) and nausea.

No anaphylactic reactions have been seen in clinical trials, and only very few cases of hypersensitivity reactions have been reported from post-marketing use.

Table 1: Listing of AEs/ADRs reported in clinical trials and from post-marketing use, according to frequency, in patients who received GONAPEPTYL DAILY 100 micrograms daily.

MedDRA System organ class	**Common (≥1/100 to <1/10)**	**Uncommon (≥ 1/1 000 to ≤1/100)**	**Not known**
Infections and infestations		Upper respiratory tract infection, Pharyngitis	
Immune system disorders			Allergic reaction, Hypersensitivity
Nervous system disorders		Dizziness	
Vascular disorders		Hot flushes	
Gastrointestinal disorders		Abdominal pain, Nausea, Vomiting	
Musculoskeletal and connective tissue disorders		Back pain	
Pregnancy, puerperium and perinatal conditions	Abortion		
Reproductive system and breast disorders	Ovarian hyperstimulation syndrome,	Pelvic pain, Ovarian cyst	

	Dysmenorrhoea		
General disorders and administration site conditions	Injection site inflammation	Injection site pain, Injection site reaction, Fatigue	Medicine ineffective

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another medicine. Adverse drug reaction information from clinical trials is useful for identifying medicine-related adverse events and for approximating rates.

Studies MFK/IVF/0399E and FE999906 CS003 listed in Table 2 were not prospectively designed to test triptorelin and AEs reported during stimulation may not reflect events associated with triptorelin.

Table 2. Treatment-Emergent AEs reported by at least 1 % of the IVF/ICSI patients receiving GONAPEPTYL DAILY 100 micrograms daily in studies MFK/IVF/0399E and FE999906 CS003.

MedDRA Preferred term	**MFK/IVF/0399E n (%)**		**FE999906 CS003 n (%)**	
	Onset During Down-regulation with triptorelin N=113	**Onset During Stimulation N=113**	**Onset During Down-regulation with triptorelin N=781**	**Onset During Stimulation N=731**
Headache	30 (27 %)	31 (27 %)	29 (4 %)	36 (5 %)
Dizziness	5 (4 %)	6 (5 %)		
Dysmenorrhoea	7 (6 %)	2 (2 %)	20 (3 %)	

Vaginal Haemorrhage		2 (2 %)		176 (24 %)
Pelvic Pain				43 (6 %)
Leucorrhoea		2 (2%)		
Application site disorders All events Inj. site inflammation Inj. site pain Inj. site bruising Inj. site reaction	 16 (14 %) 13 (12 %) 5 (4 %) -- 2 (2 %)	 20 (18 %) 11 (10 %) 8 (7 %) 3 (3 %) 3 (3 %)		
Abdominal pain	10 (9 %)	17 (15 %)		
Abdominal distension				18 (2 %)
Nausea	6 (5 %)	11 (10 %)		20 (3 %)
Vomiting	3 (3 %)			
Diarrhoea		2 (2 %)		
Ovarian cyst			10 (1 %)	8 (1 %)
Abortion spontaneous				48 (7 %)
Abortion missed				15 (2 %)
OHSS				23 (3 %)
Adnexa Uteri Pain				12 (2 %)
Upper respiratory tract infection	4 (4 %)	4 (4 %)		
Dyspnoea	2 (2 %)			
Influence-like		3 (3 %)		

symptoms				
Pharyngitis		3 (3 %)		
Rhinitis		2 (2 %)		
Fatigue	3 (3 %)	4 (4 %)		
Hot flushes	2 (2 %)			
Malaise		2 (2 %)		
Back pain	3 (3 %)	3 (3 %)		
Flushing	4 (4 %)			
Post procedural pain				26 (4 %)
Post-operative pain		3 (3 %)		

Post-marketing experience

This post-marketing safety summary provides information on the daily dosing of triptorelin, formulation for ART indication, covering the period 1 January 1989 to 31 December 2020.

A total of 91 adverse drug reaction cases have been reported to Ferring in this period. Out of 91 cases, 45 were reported as serious (14 unlisted and 29 listed) and 46 cases non-serious.

Among the serious unlisted cases reported, there were two cases of OHSS reported in which other serious unlisted events were also reported (cerebral artery thrombosis, and ovarian haemorrhage). Also two serious unlisted cases each comprising ectopic pregnancy and paraesthesia were reported. In the remaining 10 serious unlisted cases, the following preferred terms were reported: pulmonary oedema, medicine ineffective, pelvic inflammatory disease, exposure during pregnancy, genital pain, bundle branch block, hyperemesis gravidarum, cerebellar syndrome, thrombocytopenia, and blood pressure increased.

In three cases the subjects were exposed to daily dosing of triptorelin during the pregnancy. In two of these cases, the outcome of the pregnancy was a normal healthy baby was delivered.

One case was confounded by the co-suspected medicine clomipramine, used for obsessive compulsive disorder during pregnancy. The baby was discovered to have Down’s syndrome and an abortion was chosen.

In general, injection site reactions (inflammation and pain) were reported as non-serious, mild and reversible.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of GONAPEPTYL DAILY is important. It allows continued monitoring of the benefit/risk balance of GONAPEPTYL DAILY. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Overdose in humans may result in a prolonged duration of action. In case of overdose, GONAPEPTYL DAILY treatment should be (temporarily) discontinued. Patients should be advised to immediately contact their doctor if they are concerned that they have given themselves too much GONAPEPTYL DAILY.
No adverse reaction has been reported as a consequence of overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gonadotropin releasing hormone analogues, ATC code: L02AE04

Mechanism of action

Triptorelin, a gonadotropin releasing hormone (GnRH) agonist, inhibits gonadotropin secretion when given continuously and in therapeutic doses. After the administration of triptorelin there is an initial and transient increase in circulating follicle-stimulating hormone (FSH) and luteinising hormone (LH) levels (flare-up). Continued administration of triptorelin then results in decreased FSH and LH secretion with a consequent marked reduction in gonadal hormone production.

Pharmacodynamic effects

Triptorelin-induced down-regulation of the pituitary can prevent the LH surge and thereby prevent premature ovulation and/or follicular luteinisation. The adoption of a down-regulation agent is intended to reduce the cycle cancellation rate and improve the pregnancy rate in assisted reproductive technology (ART) cycles.

5.2 Pharmacokinetic properties

Absorption:

Pharmacokinetic data suggest that after s.c. administration of the product, the systemic bioavailability of triptorelin is close to 100 %. Following a single dose of triptorelin 250 micrograms s.c. in healthy male subjects (n=4), the mean maximum plasma concentration of triptorelin was 5,68 (range: 4,76 to 7,14) ng/ml (n=4). Maximum plasma concentrations were reached approximately 45 minutes after s.c. administration.

Distribution:

Following an intravenous (i.v.) bolus injection of 500 micrograms triptorelin to 19 female subjects, the medicine is distributed and eliminated according to a 3-compartment model and the corresponding half-lives are 3,2 (range: 1,4 to 10,9) minutes, 46,1 (range: 20,2 to 138,1) minutes and 5,1 (range: 2,5 to 13,8) hours. The estimated volume of distribution at steady-state of triptorelin was 28,9 (range: 13,1 to 78,6) L. Protein binding has not been investigated.

Biotransformation:

Metabolites of triptorelin have not been determined in humans. However, human pharmacokinetic data suggest that C-terminal fragments produced by tissue degradation are either completely degraded within tissues or are rapidly further degraded in plasma, or cleared by the kidneys.

Elimination:

Triptorelin is either completely degraded within tissue or rapidly further degraded in plasma, or cleared by the kidneys. Following i.v. bolus injection of 500 micrograms triptorelin to 19 female subjects the medicine was distributed and eliminated according to a 3-compartment model. The mean terminal half-life was 5,1 (range: 2,5 to 13,8) hours. Average total clearance was estimated to 107 (range: 89 to 188) ml/min. Urinary excretion was investigated in 8 of the female subjects. Renal clearance over 24 hours was on average 25,3 (range: 5,3 to 45,4) ml/min. The mean percentage of the dose recovered in urine over the 24 hours was 16,7 (range: 3,4 to 34,6) %.

Special patient populations:

Hepatic and Renal impairment:

Patients with renal and liver impairment have also been studied after i.v. administration. This pharmacokinetic data is only available in male volunteers. Compared to young healthy adult males, mean triptorelin clearance was reduced by 43% in subjects with moderate renal impairment (mean creatinine clearance 40 mL/min), by 58% in subjects with severe renal impairment (mean creatinine clearance 8.9 mL/min) and by 73% in subjects with combined hepatic impairment (Child Pugh score 5-9) and a lower mean creatinine clearance (90 mL/min) than that of young healthy adult males.

These clinical studies indicate a risk of accumulation of triptorelin in patients with severe liver and renal impairment. However, the risk of accumulation appears to be small, given that the triptorelin terminal half-life is approximately 8 hours in these patients.

The effects of age and race on triptorelin pharmacokinetics have not been systematically studied.

Clinical trials

MFK/IVF/0399E and FE999906 CS003 were large randomised, multi-centre studies comparing highly purified-human menopausal gonadotrophin (HP-hMG) and recombinant follicle stimulating hormone (rFSH) in patients (18-38 years) undergoing controlled ovarian hyperstimulation for in-vitro fertilisation/intracytoplasmic sperm injection (IVF/ICSI) following the long GnRH agonist protocol starting

in the mid-luteal phase (refer to Table 3). These clinical studies were not prospectively designed to test the efficacy of triptorelin.

In MFK/IVF/0399E, several GnRH agonists were used for down-regulation. A total of 117 were given GONAPEPTYL DAILY 100 micrograms. Adequate down-regulation was established by serum estradiol < 200 pmol/L (56 pg/ml) and no ovarian cysts.

In FE999906 CS003, patients (21-37 years) diagnosed with tubal or unexplained infertility, including endometriosis stage III/IV and mild male factor eligible for IVF, were enrolled. In this study, 781 patients started down-regulation and all received GONAPEPTYL DAILY 100 micrograms s.c. daily. Confirmation of down-regulation prior to randomisation to HP-hMG or rFSH was defined as menstrual bleeding and transvaginal ultrasound showing a shedded endometrium with a thickness of < 5 mm and no ovarian cysts or serum estradiol (E2) < 50 pg/mL and no ovarian cysts.

A total of 898 patients were exposed to GONAPEPTYL DAILY 100 micrograms s.c. in these two studies. The primary endpoint in MFK/IVF/0399E and FE999906 CS003 was ongoing pregnancy rates (defined as at least one viable foetus at 10-11 weeks after embryo transfer) after one cycle. In FE999906 CS003, a strict protocol and treatment approach were implemented to minimize sources of variation in the study, including harmonisation of concomitant fertility treatments, a pre-specified stimulation goal and homogeneity of other major pre- and post-randomisation interventions. The treatment outcome associated with different types of GnRH agonists can be derived from MFK/ IVF/00399E. Comparative data with respect to ongoing pregnancy rate are shown in Table 4.

Among the 113 patients who were down-regulated with GONAPEPTYL DAILY 100 micrograms and underwent COH, the ongoing pregnancy rate was 24 % (27/113). By comparison, the ongoing pregnancy rate was 21 % for patients down-regulated with GONAPEPTYL DAILY Depot 3,75 mg, and 25 % for those who had used other GnRH agonists (daily or depot). Although this study was not designed to draw comparisons between different down-regulation agents, these results suggest that the ongoing pregnancy rate when GONAPEPTYL DAILY 100 micrograms s.c. daily was used is not different from the rates observed with the use of other GnRH agonists.

Table 4: Comparative data with respect to ongoing pregnancy rate.

Ongoing pregnancy rate by GnRH agonist (MFK/IV/0399E)			
	Gonapeptyl Daily 100 micrograms	Gonapeptyl Depot 3.75 mg	Other GnRH agonists [1)]
Ongoing pregnancy rate	24 % (27/113)	21 % (96/466)	25 % (37/148)

[1)] buserelin, leuprolide, goserelin, nafarelin

5.3 Preclinical safety data

Genotoxicity

In vitro tests for gene mutations in bacterial and mammalian cells and for chromosomal damage *in vitro* and *in vivo* (mouse micronucleus test) revealed no genotoxic activity for triptorelin.

Carcinogenicity

Carcinogenicity studies were conducted in mice (18 months) and rats (up to 23 months) with microparticles containing triptorelin, administered once monthly by intramuscular injection. No carcinogenic effect was observed in mice with treatment at up to 6 000 micrograms/kg/month (equivalent to 214 micrograms/kg/day), estimated to yield almost 4 times the clinical exposure at the maximum recommended human dose. In rats, pituitary adenomas and carcinomas were increased with treatment at all dose levels tested (≥120 micrograms/kg/month; equivalent to 4.3 micrograms/ kg/day, and estimated to yield less than a sixth of clinical exposure at the maximum recommended human dose). Rats are recognised to be particularly sensitive to such effects of luteinising hormone-releasing hormone (LHRH) analogues compared with other species. The clinical relevance of the finding is unknown, but considered likely to be low.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients

Sodium chloride

Glacial acetic acid

Water for injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze.

Store in the original package, to protect from light.

6.5 Nature and contents of container

1 ml solution in a pre-filled syringe (glass) with plunger stopper (chlorobutyl rubber), plunger rod (polystyrene), integrated needle and rigid needle shield.

Pack sizes of 7.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Ferring (Pty) Ltd.

6 Regency Drive, Route 21 Corporate Park

Nellmapius Drive, Irene, Pretoria

8 REGISTRATION NUMBER

46/21.10/0169

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11 August 2020

10 DATE OF REVISION OF THE TEXT

31 August 2023