Summary of Product Characteristics

MEDWIN

Pre-filled syringe

[Rx] Medroxyprogesterone Injection 150 mg/mL

1. Name of the medicinal product

1.1 Product Name: MEDWIN

1.2 Strength: Medroxyprogesterone 150 mg/mL

1.3 Pharmaceutical Dosage Form: Sterile Suspension for Injection

2. Qualitative and quantitative composition

2.1 Qualitative Declaration: Medroxyprogesterone acetate

INN Name: Medroxyprogesterone

2.2 Quantitative Declaration:

Active Ingredient: Each mL of suspension contains medroxyprogesterone acetate Ph.Eur 150 mg.

3. Pharmaceutical form

Sterile Suspension for Injection

4. Clinical particulars

4.1 Therapeutic indication

Progestogen: for contraception.

Medroxyprogesterone is a long-term contraceptive agent suitable for use in women who have been appropriately counselled concerning the likelihood of menstrual disturbance and the potential for a delay in return to full fertility.

Medroxyprogesterone may also be used for short-term contraception in the following circumstances:

1) For partners of men undergoing vasectomy, for protection until the vasectomy becomes effective.

2) In women who are being immunised against rubella, to prevent pregnancy during the period of activity of the virus.

3) In women awaiting sterilisation.

Since loss of bone mineral density (BMD) may occur in females of all ages who use Medroxyprogesterone Injection long-term (see section 4.4), a risk/benefit assessment, which also takes into consideration the decrease in BMD that occurs during pregnancy and/or lactation, should be considered before giving the Injection of Medroxyprogesterone.

Paediatric population (12-18 years)

In adolescents, medroxyprogesterone may be used, but only after other methods of contraception have been discussed with the patient and considered unsuitable or unacceptable.

It is of the greatest importance that adequate explanations of the long-term nature of the product, of its possible side- effects and of the impossibility of immediately reversing the effects of each Injection are given to potential users and that every effort is made to ensure that each patient receives such counselling as to enable her to fully understand these explanations. Patient information leaflets are supplied by the manufacturer. It is recommended that the doctor uses these leaflets to aid counselling of the patient before giving the Injection of Medroxyprogesterone.

Consistent with good clinical practice a general medical as well as gynaecological examination should be undertaken before administration of Medroxyprogesterone and at appropriate intervals thereafter.

4.2 Posology and method of administration

Posology

Adults:

First Injection: To provide contraceptive cover in the first cycle of use, an Injection of 150 mg IM should be given during the first five days of a normal menstrual cycle. If the Injection is carried out according to these instructions, no additional contraceptive cover is required.

Post Partum: To increase assurance that the patient is not pregnant at the time of first administration, this Injection should be given within 5 days post partum if not breast-feeding.

There is evidence that women prescribed medroxyprogesterone in the immediate puerperium can experience prolonged and heavy bleeding. Because of this, the drug should be used with caution in the puerperium. Women who are considering use of the product immediately following delivery or termination should be advised that the risk of heavy or prolonged bleeding may be increased. Doctors are reminded that in the non breast-feeding, post partum patient, ovulation may occur as early as week 4.

If the puerperal woman will be breast-feeding, the initial Injection should be given no sooner than six weeks post partum, when the infant's enzyme system is more fully developed. Further Injections should be given at 12 week intervals.

Further doses: These should be given at 12 week intervals, however, as long as the Injection is given no later than five days after this time, no additional contraceptive measures (e.g. barrier) are required. (N.B. For partners of men undergoing vasectomy, a second Injection of 150 mg I.M. 12 weeks after the first may be necessary in a small proportion of patients where the partner's sperm count has not fallen to zero.) If the interval from the preceding Injection is greater than 89 days (12 weeks and five days) for any reason, then pregnancy should be excluded before the next Injection is given and the patient should use additional contraceptive measures (e.g. barrier) for fourteen days after this subsequent Injection.

Elderly: Not appropriate.

Paediatric population: Medroxyprogesterone is not indicated before menarche (see section 4.1)

Data in adolescent females (12-18 years) is available (see section 4.4). Other than concerns about loss of BMD, the safety and effectiveness of Medroxyprogesterone is expected to be the same for adolescents after menarche and adult females.

Switching from other Methods of Contraception

Medroxyprogesterone should be given in a manner that ensures continuous contraceptive coverage. This should be based upon the mechanism of action of other methods, (e.g. patients switching from oral contraceptives should have their first Injection of Medroxyprogesterone within 7 days of taking their last active pill)

Hepatic Insufficiency

The effect of hepatic disease on the pharmacokinetics of Medroxyprogesterone is unknown. As Medroxyprogesterone largely undergoes hepatic elimination it may be poorly metabolised in patients with severe liver insufficiency (see section 4.3).

Renal Insufficiency

The effect of renal disease on the pharmacokinetics of Medroxyprogesterone is unknown. No dosage adjustment should be necessary in women with renal insufficiency, since Medroxyprogesterone is almost exclusively eliminated by hepatic metabolism.

Method of Administration

The sterile aqueous suspension of medroxyprogesterone should be vigorously shaken just before use to ensure that the dose being given represents a uniform suspension of Medroxyprogesterone.

Doses should be given by deep intramuscular Injection. Care should be taken to ensure that the depot Injection is given into the muscle tissue, preferably the gluteus maximus, but other muscle tissue such as the deltoid may be used.

The site of Injection should be cleansed using standard methods prior to administration of the Injection.

4.3 Contraindication

Hypersensitivity to medroxyprogesterone acetate or to any of excipients listed in section 6.1.
Medroxyprogesterone should not be used during pregnancy, either for diagnosis or therapy.

Medroxyprogesterone is contraindicated as a contraceptive at the above dosage in known or suspected hormone-dependent malignancy of breast or genital organs.

Medroxyprogesterone is contraindicated in patients with the presence or history of severe hepatic disease whose liver function tests have not returned to normal.

Whether administered alone or in combination with oestrogen, Medroxyprogesterone should not be employed in patients with abnormal uterine bleeding until a definite diagnosis has been established and the possibility of genital tract malignancy eliminated.

4.4 Special warning and precautions for use

Loss of Bone Mineral Density:

Use of medroxyprogesterone reduces serum oestrogen levels and is associated with significant loss of BMD due to the known effect of oestrogen deficiency on the bone remodelling system. Bone loss is greater with increasing duration of use; however BMD appears to increase after Medroxyprogesterone is discontinued and ovarian oestrogen production increases.

This loss of BMD is of particular concern during adolescence and early adulthood, a critical period of bone accretion. It is unknown if use of medroxyprogesterone by younger women will reduce peak bone mass and increase the risk for fracture in later life.

A study to assess the BMD effects of medroxyprogesterone acetate IM (Medroxyprogesterone, DMPA) in adolescent females showed that its use was associated with a significant decline in BMD from baseline. In the small number of women who were followed-up, mean BMD recovered to around baseline values by 1- 3 years after discontinuing treatment. In adolescents, Medroxyprogesterone may be used, but only after other methods of contraception have been discussed with the patients and considered to be unsuitable or unacceptable.

In women of all ages, careful re-evaluation of the risks and benefits of treatment should be carried out in those who wish to continue use for more than 2 years. In particular, in women with significant lifestyle and/or medical risk factors for osteoporosis, other methods of contraception should be considered prior to use of Medroxyprogesterone.

Significant risk factors for osteoporosis include:

- Alcohol abuse and/or tobacco use
- Chronic use of drugs that can reduce bone mass, e.g. anticonvulsants or corticosteroids
- Low body mass index or eating disorder, e.g. anorexia nervosa or bulimia
- Previous low trauma fracture
- Family history of osteoporosis

For further information on BMD changes in both adult and adolescent females, refer to section 5.1. Adequate intake of calcium and Vitamin D, whether from the diet or from supplements, is important for bone health in women of all ages.

Menstrual Irregularity: The administration of Medroxyprogesterone usually causes disruption of the normal menstrual cycle. Bleeding patterns include amenorrhoea (present in up to 30% of women during the first 3 months and increasing to 55% by month 12 and 68% by month 24); irregular bleeding and spotting; prolonged (>10 days) episodes of bleeding (up to 33% of women in the first 3 months of use decreasing to 12% by month 12). Rarely, heavy prolonged bleeding may occur. Evidence suggests that prolonged or heavy bleeding requiring treatment may occur in 0.5-4 occasions per 100 women years of use. If abnormal bleeding persists

or is severe, appropriate investigation should take place to rule out the possibility of organic pathology and appropriate treatment should be instituted when necessary. Excessive or prolonged bleeding can be controlled by the co-administration of oestrogen. This may be delivered either in the form of a low dose (30 micrograms oestrogen) combined oral contraceptive pill or in the form of oestrogen replacement therapy such as conjugated equine oestrogen (0.625-1.25 mg daily). Oestrogen therapy may need to be repeated for 1-2 cycles. Long-term co-administration of oestrogen is not recommended.

Return to Fertility: There is no evidence that medroxyprogesterone causes permanent infertility. Pregnancies have occurred as early as 14 weeks after a preceding Injection, however, in clinical trials, the mean time to return of ovulation was 5.3 months following the preceding Injection. Women should be counselled that there is a potential for delay in return to full fertility following use of the method, regardless of the duration of use, however, 83% of women may be expected to conceive within 12 months of the first "missed" Injection (i.e. 15 months after the last Injection administered). The median time to conception was 10 months (range 4-31) after the last Injection.

Cancer Risks: Long-term case-controlled surveillance of medroxyprogesterone users found no overall increased risk of ovarian, liver, or cervical cancer and a prolonged, protective effect of reducing the risk of endometrial cancer in the population of users.

Breast cancer is rare among women under 40 years of age whether or not they use hormonal contraceptives.

Results from some epidemiological studies suggest a small difference in risk of the disease in current and recent users compared with never-users. Any excess risk in current or recent DMPA users is small in relation to the overall risk of breast cancer, particularly in young women (see below), and is not apparent after 10 years since last use. Duration of use does not seem to be important.

Table 1: Possible number of additional cases of breast cancer diagnosed up to 10 years after stopping injectable progestogens*

Age at last use of DMPA	No of cases per 10,000 women who are never-users	Possible additional cases per 10,000 DMPA users
20	Less than 1	Much less than 1
30	44	2-3
40	160	10

*based on use for 5 years”

Weight Gain: There is a tendency for women to gain weight while on medroxyprogesterone therapy. Studies indicate that over the first 1-2 years of use, average weight gain was 5-8 lbs. Women completing 4-6 years of therapy gained an average of 14-16.5 lbs. There is evidence that weight is gained as a result of increased fat and is not secondary to an anabolic effect or fluid retention.

Anaphylaxis: Reports of anaphylactic responses (anaphylactic reactions, anaphylactic shock, anaphylactoid reactions) have been received.

Thrombo-embolic Disorders: Should the patient experience pulmonary embolism, cerebrovascular disease or retinal thrombosis while receiving medroxyprogesterone, the drug should not be re-administered.

Psychiatric Disorders: Patients with a history of endogenous depression should be carefully monitored. Some patients may complain of premenstrual-type depression while on medroxyprogesterone therapy.

Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use (see section 4.8). Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their physician in case of mood changes and depressive symptoms, including shortly after initiating the treatment.

Abscess formation: As with any intramuscular Injection, especially if not administered correctly, there is a risk of abscess formation at the site of Injection, which may require medical and/or surgical intervention.

Precautions:

History or emergence of the following conditions require careful consideration and appropriate investigation: migraine or unusually severe headaches, acute visual disturbances of any kind, pathological changes in liver function and hormone levels.

Patients with thromboembolic or coronary vascular disease should be carefully evaluated before using medroxyprogesterone.

A decrease in glucose tolerance has been observed in some patients treated with progestogens. The mechanism for this decrease is obscure. For this reason, diabetic patients should be carefully monitored while receiving progestogen therapy.

Rare cases of thrombo-embolism have been reported with use of medroxyprogesterone, but causality has not been established. The effects of medroxyprogesterone acetate on lipid metabolism have been studied with no clear impact demonstrated. Both increases and decreases in total cholesterol, triglycerides and low-density lipoprotein (LDL) cholesterol have been observed in studies.

The use of medroxyprogesterone appears to be associated with a 15-20% reduction in serum high density lipoprotein (HDL) cholesterol levels which may protect women from cardiovascular disease. The clinical consequences of this observation are unknown. The potential for an increased risk of coronary disease should be considered prior to use.

Doctors should carefully consider the use of medroxyprogesterone in patients with recent trophoblastic disease before levels of human chorionic gonadotrophin have returned to normal.

Physicians should be aware that pathologists should be informed of the patient's use of medroxyprogesterone if endometrial or endocervical tissue is submitted for examination.

The results of certain laboratory tests may be affected by the use of medroxyprogesterone. These include gonadotrophin levels (decreased), plasma progesterone levels (decreased), urinary pregnanediol levels (decreased), plasma oestrogen levels (decreased), plasma cortisol levels (decreased), glucose tolerance test, metyrapone test, liver function tests (may increase), thyroid function tests (protein bound iodine levels may

increase and T3 uptake levels may decrease). Coagulation test values for prothrombin (Factor II), and Factors VII, VIII, IX and X may increase.

Women should be counselled that Medroxyprogesterone does not protect against sexually transmitted infections (STIs) including HIV infection (AIDS). Safer sex practices including correct and consistent use of condoms reduce the transmission of STIs through sexual contact, including HIV.

The benefits of contraceptive options and their risks must be evaluated individually for each woman.

4.5 Interaction with other medicinal products and other forms of interactions

Aminoglutethimide administered concurrently with medroxyprogesterone may significantly depress the bioavailability of Medroxyprogesterone.

Interactions with other medicinal treatments (including oral anticoagulants) have rarely been reported, but causality has not been determined. The possibility of interaction should be borne in mind in patients receiving medroxyprogesterone with other drugs.

The clearance of medroxyprogesterone acetate is approximately equal to the rate of hepatic blood flow. Because of this fact, it is unlikely that drugs which induce hepatic enzymes will significantly affect the kinetics of medroxyprogesterone acetate. Therefore, no dose adjustment is recommended in patients receiving drugs known to affect hepatic metabolising enzymes.

Medroxyprogesterone acetate (MPA) is metabolized in-vitro primarily by hydroxylation via the CYP3A4. Specific drug- drug interaction studies evaluating the clinical effects with CYP3A4 inducers or inhibitors on MPA have not been conducted and therefore the clinical effects of CYP3A4 inducers or inhibitors are unknown.

4.6 Pregnancy and lactation

Doctors should check that patients are not pregnant before initial Injection of medroxyprogesterone, and also if administration of any subsequent Injection is delayed beyond 89 days (12 weeks and five days).

Infants from accidental pregnancies that occur 1-2 months after Injection of Medroxyprogesterone may be at an increased risk of low birth weight, which in turn is associated with an increased risk of neonatal death. The attributable risk is low because such pregnancies are uncommon.

Children exposed to medroxyprogesterone acetate *in utero* and followed to adolescence, showed no evidence of any adverse effects on their health including their physical, intellectual, sexual or social development.

Medroxyprogesterone acetate and/or its metabolites are secreted in breast milk, but there is no evidence to suggest that this presents any hazard to the child. Infants exposed to medroxyprogesterone acetate via breast milk have been studied for developmental and behavioural effects to puberty. No adverse effects have been noted.

4.7 Effects on ability to drive and use machine

Medroxyprogesterone may cause headaches and dizziness. Patients should be advised not to drive or

operate machinery if affected.

4.8 Undesirable effects

The table below provides a listing of adverse drug reactions with frequency based on all-causality data from clinical studies that enrolled more than 4200 women who received DMPA for contraception for up to 7 years. Those most frequently (>5%) reported adverse drug reactions were weight increased (69%), weight decreased (25%), headache (16%), nervousness (11%), abdominal pain or discomfort (11%), dizziness (6%), and decrease in libido (6%).

The following lists of adverse reactions are listed within the organ system classes, under headings of frequency (number of patients expected to experience the reaction), using the following categories:

Very common (≥1/10)

Common (≥1/100 to <1/10);

Uncommon (≥1/1000 to <1/100);

Rare (≥1/10,000 to <1/1000);

Very rare (<1/10,000);

Not known (cannot be estimated from the available data)

Table 2: Adverse reactions are listed within the organ system classes

System Organ Class	Very Common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Rare ≥ 1/10,000 to < 1/1000
Neoplasms Benign, Malignant and Unspecified (Incl. Cysts and Polyps)				Breast cancer
Blood and lymphatic system disorders				Anaemia, Blood disorder
Immune system disorders			Drug hypersensitivity	Anaphylactic reaction, Anaphylactoid reaction, Angioedema
Metabolism & Nutrition Disorder			Increased appetite, decreased appetite	
Psychiatric disorders	Nervousness	Depression, Libido decreased	Insomnia	Anorgasmia, Emotional disturbance, Effective

				disorder, Irritability, Anxiety
Nervous system disorders	Headache	Dizziness	Seizure, Somnolence, Paraesthesia	Migraine, Paralysis, Syncope
Ear and Labyrinth Disorder				Vertigo
Cardiac disorder				Tachycardia
Vascular disorders			Hot flush	Embolism and thrombosis, Deep vein thrombosis, Thrombophlebitis, Hypertension, Varicose veins
Respiratory, thoracic, and mediastinal disorders			Dyspnoea	Pulmonary embolism
Gastrointestinal disorders	Abdominal pain, Abdominal Discomfort	Nausea, Abdominal Distension		Rectal haemorrhage, Gastrointestinal disorder
Hepatobiliary disorders			Hepatic function Abnormal	Jaundice, Hepatic enzyme abnormal
Skin and subcutaneous tissue disorders		Alopecia, Acne, Rash	Hirsutism, Urticaria, Pruritus, Chloasma	Lipodystrophy acquired*, Dermatitis, Ecchymosis, Scleroderma, Skin striae
Musculoskeletal and connective tissue disorders		Back pain, Pain in extremity		Arthralgia, Muscle spasms, Osteoporosis, Osteoporotic fractures
Reproductive system and breast disorders		Vaginal discharge, Breast tenderness, Dysmenorrhea, Genitourinary tract infection	Dysfunctional uterine bleeding (irregular, increase, decrease, spotting, Galactorrhoea Pelvic pain, Dyspareunia, Suppressed Lactation	Vaginitis, Amenorrhoea, Breast pain, Metrorrhagia, Menometrorrhagia, Menorrhagia,Vulvovaginal dryness, Breast atropy, Ovarian cyst, Premenstrual syndrome, Endometrial hyperplasia, Breast mass, Nipple exudate bloody, Vaginal cyst, Breast enlargement, Lack of return

				to fertility, Sensation of pregnancy
General disorders and administration site conditions		Odema/Fluid retention, Asthenia	Chest pain	Pyrexia, Fatigue, Injection site reaction*, Injection site persistent atrophy/ indentation/dimpling*, Injection site nodule/ lump*, Injection site pain/ tenderness* Thirst, Dysphonia, VIIth nerve paralysis, Axillary swelling
Investigation	Weight increased, Weight Decreased			Bone density decreased, Glucose Tolerance decreased, Cervical smear abnormal

*ADR identified post-marketing

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 Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Cessation of therapy.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Progestogens, ATC code: G03AC06

Medroxyprogesterone acetate exerts anti-oestrogenic, anti-androgenic and antigonadotrophic effects.

Mechanism of action

DMPA, when administered parenterally at the recommended dose to women, inhibits the secretion of gonadotropins which, in turn, prevents follicular maturation and ovulation and causes thickening of cervical mucus which inhibits sperm entry into the uterus

BMD Changes in Adult Women

A study comparing changes in BMD in women using medroxyprogesterone with women using medroxyprogesterone acetate Injection (150 mg IM) showed no significant differences in BMD loss between the two groups after two years of treatment. Mean percent changes in BMD in the medroxyprogesterone

group are listed in Table 3.

Table 3. Mean percent change from baseline in BMD in women using Depo-Provera by Skeletal Site

Time on Treatment	Lumbar Spine		Total Hip		Femoral Neck	
	N	Mean% Change (95% CI)	N	Mean % Change (95% CI)	N	Mean % Change (95% CI)
1 year	166	-2.7 (-3.1 to -2.3)	166	-1.7 (-2.1 to -1.3)	166	-1.9 (-2.5 to -1.4)
2 year	106	- 4.1 (-4.6 to -3.5)	106	-3.5 (-4.2 to -2.7)	106	-3.5 (-4.3 to -2.6)

In another controlled, clinical study adult women using medroxyprogesterone acetate Injection (150 mg IM) for up to 5 years showed spine and hip mean BMD decreases of 5-6%, compared to no significant change in BMD in the control group. The decline in BMD was more pronounced during the first two years of use, with smaller declines in subsequent years. Mean changes in lumbar spine BMD of –2.86%, -4.11%, -4.89%, -4.93% and –5.38% after 1, 2, 3, 4 and 5 years, respectively, were observed. Mean decreases in BMD of the total hip and femoral neck were similar. Please refer to Table 2 below for further details.

After stopping use of medroxyprogesterone acetate Injection (150 mg IM), BMD increased towards baseline values during the post-therapy period. A longer duration of treatment was associated with a slower rate of BMD recovery.

Table 4. Mean percent change from baseline in BMD in adults by Skeletal Site and cohort after 5 Years of therapy with medroxyprogesterone acetate 150 mg IM and after 2 years post-therapy or 7 years of observation (control)

Time Study	Spine		Total Hip		Femoral Neck	
	Medroxyprogesterone acetate	Control	Medroxyprogesterone acetate	Control	Medroxyprogesterone acetate	Control
5 years*	n=33 -5.38%	n=105 0.43%	n=21 -5.16%	n=65 0.19%	n=34 -6.12%	n=106 -0.27%
7 years**	n=12 -3.13%	n=60 0.53%	n=7 -1.34%	n=39 0.94%	n=13 -5.38%	n=63 -0.11%

*The treatment group consisted of women who received medroxyprogesterone acetate Injection (150 mg IM) for 5 years and the control group consisted of women who did not use hormonal contraception for this time period.

** The treatment group consisted of women who received medroxyprogesterone acetate Injection (150 mg IM) for 5 years and were then followed up for 2 years post-use and the control group consisted of women

who did not use hormonal contraceptive for 7 years.

BMD Changes in Adolescent Females (12-18 years)

Results from an open-label, non-randomised, clinical study of Medroxyprogesterone acetate Injection (150 mg IM every 12 weeks for up to 240 weeks (4.6 years), followed by post–treatment measurements) in adolescent females (12-18 years) also showed that medroxyprogesterone acetate IM use was associated with a significant decline in BMD from baseline. Among subjects who received ≥ 4 Injections/60-week period, the mean decrease in lumbar spine BMD was -2.1 % after 240 weeks (4.6 years); mean decreases for the total hip and femoral neck were -6.4 % and -5.4 %, respectively.

Post-treatment follow-up showed that, based on mean values, lumbar spine BMD recovered to baseline levels approximately 1 year after treatment was discontinued and that hip BMD recovered to baseline levels approximately 3 years after treatment was discontinued. However, it is important to note that a large number of subjects discontinued from the study, therefore these results are based on a small number of subjects (n=71 at 60 weeks and n=25 at 240 weeks after treatment discontinuation). In contrast, a non-comparable cohort of unmatched, untreated subjects, with different baseline bone parameters from the DMPA users, showed mean BMD increases at 240 weeks of 6.4%, 1.7% and 1.9% for lumbar spine, total hip and femoral neck, respectively.

5.2 Pharmacokinetic Properties

Parenteral Medroxyprogesterone acetate (MPA) is a long acting progestational steroid. The long duration of action results from its slow absorption from the Injection site. Immediately after Injection of 150 mg/ml MPA, plasma levels were 1.7 ± 0.3 nmol/l. Two weeks later, levels were 6.8 ± 0.8 nmol/l. Concentrations fell to the initial levels by the end of 12 weeks. At lower doses, plasma levels of MPA appear directly related to the dose administered. Serum accumulation over time was not demonstrated. MPA is eliminated via faecal and urinary excretion. Plasma half-life is about six weeks after a single intramuscular Injection. At least 11 metabolites have been reported. All are excreted in the urine, some, but not all, conjugated.

5.3 Preclinical Safety data

No data held.

6. Pharmaceutical Particulars

6.1 List of excipients

Macrogol 3350

Polysorbate 80

Sodium chloride

Methyl parahydroxybenzoate

Propyl parahydroxybenzoate

Sodium hydroxide

Hydrochloric acid

Water for Injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C. Do not freeze.

6.5 Nature and contents of container

1 ml suspension for injection in 2.25 ml glass barrel with plastic rigid tip cap with luer lock adapter stoppered with black chlorobutyl plunger rubber stopper along with white plunger rod, pack size of 1, 6, & 24's Pre-filled syringes along with needles.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7. Marketing Authorization Holder

Imported by:

APL Pharma Thai Ltd

438 Phattanakarn 30, Phattanakarn Road,

Suanluang Subdistrict, Suanluang District,

Bangkok, Thailand 10250

Manufactured by:

Eugia Pharma Specialities Limited,

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Shameerpet Mandal,

Medchal-Malkajgiri District,

Telangana, India.

8. Marketing Authorization Number: 1C……/…….

9. Date of authorization: ……..

10. Date of revision of the text: December 12, 2022