1.4. Product Information

1.4.1. Summary of Product Characteristics (SmPC)

1. Name of the Finished Pharmaceutical Product

Triclofem Injection 150mg/ml (Medroxyprogesterone Acetate Injection 150 mg/ml)

2. Qualitative and Quantitaive Composition

Each mL of suspension contains: 150 mg Medroxyprogesterone Acetate EP

Name of excipients	Qty in mg/ ml
Methylparaben	1.351
Propylparaben	0.147
Polysorbate 80,	2.378
Polyethylene Glycol 3350/(PEG 3350)	28.577
Sodium Hydroxide 5%	q.s.
Sodium chloride	8.582
Hydrochloric acid 37%,	q.s
Water for Injection(WFI)	q.s. to 1 ml

3. Pharmaceutical Form

Sterile suspension for Injection

4. Clinical particulars

4.1 . Therapeutic Indication

Triclofem 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.

Triclofem may also be used for short-term contraception in the following circumstances:
(i) For partners of men undergoing vasectomy, for protection until the vasectomy becomes effective.
(ii) In women who are being immunised against rubella, to prevent pregnancy during the period of activity of the virus.
(iii) In women awaiting sterilisation.

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

Use in adolescents (12 – 18 years)
In adolescents, Triclofem 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 Triclofem.

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

4.2 . Posology and method of administration

Dosage
Each ml of suspension contains 150 mg medroxyprogesterone acetate. The sterile aqueous suspension of Triclofem should be vigorously shaken just before use to ensure that the dose being given represents a uniform suspension of Triclofem. Doses should be given by deep intramuscular injection into the buttock or arm.

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.

Administration
Adults
First injection: To provide contraceptive cover in the first cycle of use, an injection of 150 mg I.M. 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.

Postpartum: To increase assurance that the patient is not pregnant at the time of first administration, this injection should be given within 5 days postpartum if not breast-feeding.

There is evidence that women prescribed depot medroxyprogesterone acetate 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 postpartum 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 postpartum, 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.

Paediatric population (12-18 years): Triclofem is not indicated before menarche. Data in adolescent females (12-18 years) is available. Other than concerns about loss of BMD, the safety and effectiveness of Triclofem is expected to be the same for adolescents after menarche and adult females.

Switching from other methods of contraception: Triclofem 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 Triclofem within 7 days of taking their last active pill)

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

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

4.3 . Method of administration

Adults

First injection: To provide contraceptive cover in the first cycle of use, an injection of 150 mg I.M. 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.

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

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

4.4 Contra-indications

Triclofem is contraindicated in patients with a known sensitivity to medroxyprogesterone acetate or any ingredient of this medicine.
Triclofem should not be used during pregnancy, either for diagnosis or therapy.
Triclofem is contraindicated as a contraceptive at the above dosage in known or suspected hormone-dependent malignancy of breast or genital organs.
Triclofem 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 estrogen, Triclofem 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.

4.5 Special warnings and precautions for use

Warnings:

Loss of bone mineral density:
Use of Triclofem reduces serum estrogen levels and is associated with significant loss of BMD due to the known effect of estrogen deficiency on the bone remodelling system. Bone loss is greater with increasing duration of use; however BMD appears to increase after Triclofem is discontinued and ovarian estrogen 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 Triclofem 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 medroxyprogesteone acetate IM (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, Triclofem 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 Triclofem.

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

A retrospective cohort study using data from the General Practice Research Database (GPRD) reported that women using MPA injections (DMPA), have a higher risk of fracture compared with contraceptive users with no recorded use of DMPA (incident rate ratio 1.41, 95% CI 1.35-1.47 for the five year follow-up period); it is not known if this is due to DMPA, or to other related lifestyle factors which have a bearing on fracture rate. By contrast, in women using DMPA, the fracture risk before and after starting DMPA was not increased (relative risk 1.08, 95% CI 0.92-1.26). Importantly, this study could not determine whether use of DMPA has an effect on fracture rate later in life.

For further information on BMD changes in both adult and adolescent females, as reported in recent clinical studies, refer to section 5.1 of the SPC. 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 Triclofem 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 estrogen. This may be delivered either in the form of a low dose (30 micrograms estrogen) combined oral contraceptive pill or in the form of estrogen replacement therapy such as conjugated equine (0.625-1.25 mg daily). Estrogen therapy may need to be repeated for 1-2 cycles.
Long-term co-administration of estrogen is not recommended.
Return to fertility: There is no evidence that Triclofem 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 DMPA 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.
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 Triclofem 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.

Thromboembolic disorders: Should the patient experience pulmonary embolism, cerebrovascular disease or retinal thrombosis while receiving Triclofem, 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 Triclofem therapy.

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 Triclofem.

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 DMPA, 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 DMPA 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 Triclofem 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 Triclofem if endometrial or endocervical tissue is submitted for examination.

The results of certain laboratory tests may be affected by the use of Triclofem. These include gonadotrophin levels (decreased), plasma progesterone levels (decreased), urinary pregnanediol levels (decreased), plasma estrogen 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.

4.6 Paediatric population

Triclofem is not indicated before menarche. Data in adolescent females (12-18 years) is available. Other than concerns about loss of BMD, the safety and effectiveness of Triclofem is expected to be the same for adolescents after menarche and adult females.

4.7 Interaction with other medicinal products and other forms of interaction

Aminoglutethimide administered concurrently with Triclofem may significantly depress the bioavailability of Triclofem.

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 concurrent treatment 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.

4.8 Additional information on special populations

Hepatic insufficiency: The effect of hepatic disease on the pharmacokinetics of Triclofem is unknown. As Triclofem largely undergoes hepatic elimination it may be poorly metabolized in patients with severe liver insufficiency (see Contraindications).

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

4.9 Fertility, pregnancy and lactation

Doctors should check that patients are not pregnant before initial injection of Triclofem,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 Triclofem 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 behavioral effects to puberty. No adverse effects have been noted.

4.10 Effects on ability to drive and use machines

Triclofem may cause headaches and dizziness. Patients should be advised not to drive or operate machinery if affected.

4.11 Undesirable effects

In a large clinical trial of over 3900 women, who were treated with DMPA for up to 7 years, the following adverse events were reported.

The following adverse events were commonly (by more than 5% of subjects) reported: menstrual irregularities (bleeding and/or amenorrhoea), weight changes, headache, nervousness, abdominal pain or discomfort, dizziness, asthenia (weakness or fatigue).

Adverse events reported by 1% to 5% of subjects using DMPA were: decreased libido or anorgasmia, backache, leg cramps, depression, nausea, insomnia, leucorrhoea, acne, vaginitis, pelvic pain, breast pain, no hair growth or alopecia, bloating, rash, oedema, hot flushes.

Adverse reactions are listed according to the following categories:
Very Common>10%, Common≥1% and <10%, Uncommon>0.1% and <1%, Rare<0.1%, Not known (frequency cannot be estimated from the available data)

Ear and Labyrinth Disorders: Uncommon: Vertigo
Gastrointestinal Disorders: Very common: Abdominal pain or discomfort. Common: Bloating, nausea. Uncommon: Abdominal distension, gastrointestinal disturbances
Rare: Rectal bleeding.
Infection & Infestations: Common: Vaginitis
Metabolism & Nutrition Disorders: Common: Appetite decrease, appetite increase. Uncommon: Weight increase, weight decrease, fluid retention.

Musculoskeletal, Connective Tissue & Bone Disorders:Common: Back pain. Uncommon: Arthralgia, muscle cramps, pain in limbs. Not known: Osteoporosis including osteoporotic fractures, loss of bone mineral density, axillary swelling.
Nervous System Disorders: Very common: Headaches. Common: Dizziness. Uncommon: Somnolence, migraine, convulsions. Rare: Paralysis. Not known: Syncope.
Reproductive System & Breast Disorders:Common: Amenorrhoea, breast pain/tenderness, intermenstrual bleeding, menometrorrhagia, menorrhagia, pelvic pain, leucorrhoea. Uncommon: Vaginal discharge, vulvovaginal dryness, dysmenorrhea, change in breast size, dyspareunia, ovarian cyst, premenstrual syndrome, genitourinary infection, uterine hyperplasia. Rare: Breast lumps or nipple bleeding. Not known: Abnormal uterine bleeding (irregular, increase, decrease), galactorrhoea, vaginal cysts, prevention of lactation, sensation of pregnancy, lack of return to fertility
Vascular Disorders:Common: Hot flushes. Uncommon: Hypertension, varicose veins, thrombophlebitis, pulmonary embolism. Not known: Thromboembolic disorders, deep vein thrombosis.
Cardiovascular Disorders: Rare: Tachycardia.
Immune System Disorders: Uncommon: Hypersensitivity reactions (e.g. anaphylaxis &anaphylactoid reactions, angioedema).
Hepatobiliary disorders: Uncommon: Abnormal liver enzymes, jaundice. Not known: disturbed liver function.
Skin & Subcutaneous Tissue Disorders: Common: Acne, alopecia, rash. Uncommon: Chloasma, dermatitis, ecchymosis, hirsutism, pruritus, melasma, urticaria, oedema. Not known: Skin striae, scleroderma.
General Disorders and Administration Site Conditions:Common: Fatigue, injection site reactions (such as pain or abscess), asthenia, paraesthesia. Uncommon: Chest pain, pyrexia. Rare: Thirst, hoarseness, paralysis. Not known: Facial palsy.
Investigations:Uncommon: Cervical smear abnormal Rare: Decreased glucose tolerance.
Psychiatric Disorders: Common: Anorgasmia, depression, nervousness, emotional disturbance, libido decreased, mood disorder, irritability, insomnia. Uncommon: Anxiety.
Neoplasms Benign, Malignant and Unspecified (Incl. Cysts and Polyps): Rare: Breast cancer.
Blood and lymphatic system disorders: Rare: Anaemia. Not known: Blood dyscrasia.
Respiratory, thoracic, and mediastinal disorders: Uncommon: Dyspnoea.
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.

4.12 Overdose – Antidote

No positive action is required other than cessation of therapy.

5. Pharmacological Properties

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Progestogens, ATC code: G03AC06
Medroxyprogesterone acetate exerts anti-estrogenic, 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:
In a 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 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: 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

Time in Study	Spine		Total Hip		Femoral Neck	
	DMPA	Control	DMPA	Control	DMPA	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 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

None stated

6. Pharmaceutical Particulars

6.1 List of excipients

Methylparaben, Polyethylene glycol 3350, Polysorbate 80, Propylparaben, Sodium chloride Hydrochloric Acid, Sodium hydroxide, Water for Injections

6.2 Incompatibilities

None reported

6.3 Shelf life

60 months

6.4 Special precautions for storage

Do not store above 30^{O}C and keep the glass vial in the provided carton to protect from the light. Do not frezee. Vials MUST be stored upright .Avoid excursions over 30^{O}C.

Keep out of reach of children. Do not mix with other agents. Discard any remaining contents after use. Do not use Triclofem after the expiry date stated on the vial label and the carton. The expiry date is the last day of that month.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

2 ml clear glass vial closed with a red bromo butyl rubber stopper and a purple flip cap aluminium seal.

6.6 Special precautions for disposal <and other handling>

Discard any unused contents in accordance with local requirement.

7. Marketing authorization holder and manufacturing site addresses

Marketing Authorization holder
Missionpharma A/S
Vassingeroedvej 9, DK-3540 Lynge
Denmark, Europe

Manufacturer
PT TUNGGAL IDAMAN ABDI
JI. Jenderal,
Ahmad Yani No.7,
Rawamangun,
Jakatra Timur,
Indonesia – 13230

8. Marketing authorization number

Rwanda FDA-HMP-MA-0040

9. Date of first registration/renewal of the registration

18/01/2021

10. Date of revision of the text

11. Dosimetry (if applicable)

Not applicable

12. Instructions for preparation of Radiopharmaceuticals (if applicable)

Not applicable

13. Document Revision History

Date of Revision	Revision Number	Document Number	Change Made
25/06/2021	Rev_1		