SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ORENCIA ® 125 mg Solution for subcutaneous injection

This formulation is not suitable for IV injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe of ORENCIA 125 mg Solution for subcutaneous injection contains 125 mg abatacept.

ORENCIA 125 mg contains 171,19 mg sucrose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

ORENCIA 125 mg solution for subcutaneous injection is supplied as a sterile, preservative-free, ready-to-use solution for subcutaneous injection.

The solution for injection for subcutaneous administration is a clear, colourless to pale yellow, slightly opalescent solution, essentially free of particulate matter on visual inspection, with a pH of 6,8 to 7,4.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adult rheumatoid arthritis (RA)

ORENCIA is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with active rheumatoid arthritis. ORENCIA may be used as monotherapy or concomitantly with DMARDs (disease modifying anti-rheumatic drugs) other than tumour necrosis factor (TNF) blocking agents.

Paediatrics and Adolescents

The safety and efficacy of ORENCIA subcutaneous administration in children below 18 years of age have not been established. No data are available.

4.2 Posology and method of administration

Posology

Recommended dosage

ORENCIA 125 mg solution for subcutaneous injection should be administered weekly at a dose of 125 mg by subcutaneous injection regardless of weight and used with or without an IV loading dose (see section 5.2). For patients initiating therapy with an IV loading dose, ORENCIA should be initiated with a single intravenous infusion followed by the first 125 mg subcutaneous injection administered within a day of the IV infusion, and then by subcutaneous injection once a week thereafter (please refer to section 4.2 for use for IV loading dose in the Professional Information of ORENCIA 250 mg lyophilisate solution for infusion).

Patients switching from ORENCIA intravenous therapy to subcutaneous administration should administer the first subcutaneous dose instead of the next scheduled intravenous dose.

Special populations

Renal impairment, hepatic impairment

As ORENCIA has not been studied in these patients, no dose recommendations can be made.

Paediatric and adolescent

The safety and efficacy of ORENCIA subcutaneous administration in children below 18 years of age have not been established. No data are available.

Geriatric

No dose adjustment is required.

Concomitant therapy

MTX, other non-biologic DMARDs, corticosteroids, salicylates, nonsteroidal anti-inflammatory drugs (NSAIDs), or analgesics may be used during treatment with ORENCIA.

Preparation and administration instructions for subcutaneous administration

ORENCIA 125 mg solution for subcutaneous injection is not intended for IV infusion.

ORENCIA solution for subcutaneous injection is intended for use under the guidance of a medical practitioner or healthcare practitioner. After proper training in subcutaneous injection technique, a patient may self-inject with ORENCIA solution for subcutaneous injection if a doctor determines that it is appropriate.

Patients should be instructed to follow the detailed ***"Instructions for preparing and giving a subcutaneous injection of ORENCIA"*** provided at the end of the Patient Information Leaflet.

ORENCIA should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit.

Do not use ORENCIA prefilled syringes exhibiting particulate matter or discolouration.

ORENCIA solution for subcutaneous injection should be clear to slightly opalescent and colourless to pale yellow. Any leftover product remaining in the prefilled syringe should not be used.

Patients using ORENCIA solution for subcutaneous injection should be instructed to inject the full amount in the syringe (1,0 ml), which provides 125 mg of ORENCIA, according to the directions provided in the Patient Information Leaflet.

Injection sites should be rotated and injections should never be given into areas where the skin is tender, bruised, red or hard.

4.3 Contraindications

- ORENCIA should not be administered to patients with known hypersensitivity to ORENCIA or any of its

components.

- Active or dormant untreated tuberculosis.
- ORENCIA should NOT be used during pregnancy, or if a woman plans to become pregnant, or by mothers who are breastfeeding their infants (see section 4.6).

4.4 Special warnings and precautions for use

ORENCIA 125 mg Solution for subcutaneous injection is not indicated for juvenile idiopathic arthritis.

Combination with TNF blocking agents

ORENCIA should not be administered concomitantly with TNF blocking agents.

There is limited experience with the use of ORENCIA in combination with TNF blocking agents. In placebo-controlled clinical trials in patients with adult RA, patients receiving concomitant intravenous ORENCIA and TNF blocking agent therapy experienced more infections (24 %) and serious infections (2,2 %) compared to patients treated with only TNF blocking agents (19 % and 0,8 %, respectively). Concurrent therapy with ORENCIA and a TNF blocking agent is not recommended.

While transitioning from TNF blocking agent therapy to ORENCIA therapy, patients should be monitored for signs of infection.

Combination with other biologic agents

ORENCIA is not recommended for use concomitantly with other biologic rheumatoid arthritis therapy, such as anakinra.

Hypersensitivity

Hypersensitivity reactions including anaphylactic reactions have been reported with intravenous ORENCIA administration in clinical trials, where patients were not required to be pretreated to prevent hypersensitivity reactions.

Other events potentially associated with hypersensitivity, such as hypotension, urticaria, and dyspnoea that occurred within 24 hours of ORENCIA infusion, may occur.

Anaphylaxis or anaphylactoid reactions can occur after the first infusion and can be life-threatening. In postmarketing experience, a case of fatal anaphylaxis following the first infusion of ORENCIA has been reported. If an anaphylactic or other serious allergic reaction occurs, administration of ORENCIA should be stopped immediately with appropriate therapy instituted, and the use of ORENCIA should be permanently discontinued (see section 4.8).

Effects on the immune system

The possibility exists for ORENCIA to affect vaccination responses and host defences against infections and malignancies.

Infections

Serious infections, including sepsis and pneumonia, have been reported in patients receiving ORENCIA. Some of these infections have been fatal.

Medical practitioners should exercise caution when considering the use of ORENCIA in patients with a history of recurrent infections, underlying conditions which may predispose them to infections, or chronic, latent, or localised infections.

Patients who develop a new infection while undergoing treatment with ORENCIA should be monitored closely. **Administration of ORENCIA should be discontinued if a patient develops a serious infection.**

A higher rate of serious infections has been observed in adult RA patients treated with concurrent TNF blocking agents and ORENCIA.

When treating patients with therapies that modulate the immune system, it is appropriate to screen and monitor for tuberculosis infections. ORENCIA has not been studied in patients with a positive tuberculosis screen, and the safety of ORENCIA in individuals with latent tuberculosis is unknown (see section 4.3).

Before starting treatment with ORENCIA, all patients must be evaluated for both active and inactive ("latent") tuberculosis. This evaluation should include a detailed medical history with personal history of tuberculosis or possible previous contact with tuberculosis and previous and/or current immunosuppressive therapy. Appropriate screening tests, i.e., tuberculin skin test and chest x-ray should be performed in all patients (local

recommendations may apply).

Prescribers are reminded of the risk of false negative tuberculin skin test results especially in patients who are severely ill or immunocompromised. If active tuberculosis is diagnosed, ORENCIA treatment should not be initiated (see section 4.3).

If inactive ("latent") tuberculosis is diagnosed, prophylactic anti-tuberculosis therapy must be started before the initiation of ORENCIA, and in accordance with local recommendations.

In this situation, the benefit/risk balance of ORENCIA therapy should be carefully considered. Patients must be monitored closely for infections, including miliary tuberculosis, while on and after treatment with ORENCIA.

In clinical trials with ORENCIA, patients were not screened for HIV infection, however patients with known HIV infection were excluded from study.

Anti-rheumatic therapies have been associated with hepatitis B reactivation. Therefore, screening for viral hepatitis should be performed in accordance with guidelines before starting therapy with ORENCIA. In clinical studies with ORENCIA, patients who screened positive for hepatitis were excluded from study.

Progressive multifocal leukoencephalopathy (PML)

Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients receiving abatacept mostly in combination with other immunosuppressive medication. PML can be fatal and should be considered in the differential diagnosis in immunosuppressed patients with new onset or worsening neurological, psychiatric and cognitive symptoms. If symptoms suggestive of PML occur during ORENCIA therapy, treatment with ORENCIA should be discontinued and appropriate diagnostic measures initiated.

Malignancies

The potential role of long-term use (> 42 months) of ORENCIA in the development of malignancies in humans is unknown.

The frequencies of malignancies in the placebo-controlled clinical trials were similar for ORENCIA-treated and placebo-treated patients (1,2 % and 0,9 % respectively) (see section 4.8).

There have been reports of non-melanoma skin cancers in patients receiving abatacept. Periodic skin examinations are recommended for all patients, particularly those with risk factors for skin cancer.

Immunisations

Live vaccines should not be given concurrently with ORENCIA or within 3 months of its discontinuation. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving ORENCIA. No data are available on the effects of vaccinations in patients receiving ORENCIA. Medicines that affect the immune system, including ORENCIA, may blunt the effectiveness of some immunisations.

Patients treated with ORENCIA may receive concurrent non-live vaccines.

Responses to pneumococcal and inactivated influenza vaccines have been studied in subjects receiving ORENCIA. Pneumococcal vaccination with the standard 23-valent vaccine was studied in healthy subjects to assess the effect of ORENCIA on the antibody response to pneumococcal vaccine. This study suggested that ORENCIA may blunt the effectiveness of the immune response but did not significantly inhibit the ability of healthy subjects to develop a clinically significant or positive immune response (at least a 2-fold increase above baseline) to 23-valent pneumococcal vaccines. ORENCIA was evaluated in an open-label study in RA patients administered the 23-valent pneumococcal vaccine. After pneumococcal vaccination, a majority of ORENCIA-treated patients (62/112) were able to mount an adequate immune response of at least a 2-fold increase in antibody titers to pneumococcal polysaccharide vaccine.

ORENCIA was also evaluated in an open-label study in rheumatoid arthritis patients administered the seasonal influenza trivalent virus vaccine. After influenza vaccination, 73 of 119 ORENCIA-treated patients without protective antibody levels at baseline were able to mount an adequate immune response of at least a 4-fold increase in antibody titers to trivalent influenza vaccine.

Paediatrics and adolescents

The safety and efficacy of ORENCIA 125 mg solution for subcutaneous injection in children below 18 years of age have not been established. No data are available.

Sucrose

Contains sucrose, which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrose-isomaltase insufficiency should not receive ORENCIA.

4.5 Interaction with other medicines and other forms of interaction

Formal interaction studies have not been conducted with ORENCIA.

Concurrent administration of a TNF blocking agent with ORENCIA has been associated with an increased risk of serious infections. Concurrent therapy with ORENCIA and TNF blocking agents is not recommended.

There is insufficient experience to assess the safety and efficacy of ORENCIA administered concurrently with other biologic rheumatoid arthritis therapy, such as anakinra, and therefore such use is not recommended.

ORENCIA has not been studied in combination with agents which deplete lymphocyte count. Such combination therapy could potentiate the effects of ORENCIA on the immune system.

Effect of other medicines on abatacept

The majority of patients in the IV placebo-controlled clinical trials received concomitant DMARDs, NSAIDs, and/or corticosteroids. Most patients were taking MTX. Other less frequently used concomitant DMARDs included chloroquine/hydroxychloroquine, sulfasalazine and leflunomide. There is limited experience with abatacept in combination with other DMARDs such as azathioprine, gold and anakinra.

Population pharmacokinetic analyses revealed that MTX, NSAIDs, corticosteroids, and TNF blocking agents did not influence abatacept clearance.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no studies in pregnant women. ORENCIA should NOT be used during pregnancy, or if a woman is planning to become pregnant.

Abatacept may cross the placenta into the serum of infants born to women treated with abatacept during pregnancy. Consequently, these infants may be at increased risk for infection. The safety of administering live vaccines to infants exposed to abatacept *in utero* is unknown. Administration of live vaccines to infants exposed to abatacept *in utero* is not recommended for 10 weeks following the mother's last exposure to abatacept during pregnancy.

Breastfeeding

Abatacept has been shown to be present in rat milk. It is not known whether abatacept is excreted in human milk. Mothers should be instructed not to breastfeed if they are receiving ORENCIA.

4.7 Effects on ability to drive and use machines

Dizziness and reduced visual acuity have been reported as common and uncommon adverse reactions respectively, from patients treated with ORENCIA, therefore if a patient experiences such symptoms, driving and use of machines should be avoided.

4.8 Undesirable effects

The most frequently reported adverse drug reaction (ADRs) (≥ 5 %) among ORENCIA-treated patients in placebo-controlled clinical trials were headache and nausea.

Listed below are ADRs that occurred with greater frequency (difference > 0,2 %) in ORENCIA-treated patients than in placebo-treated patients. Also listed are ADRs from clinical trials at least possibly causally-related to ORENCIA displayed by system organ class and frequency.

The list is presented by system organ class and frequency, using the following categories: very common (≥ 10 %); common (≥ 1 %; < 10 %); uncommon (≥ 0,1 %; < 1 %); rare (≥ 0,01 %; < 0,1 %).

Side Effects in Placebo-Controlled Trials

Infections and infestations	Very common	Upper respiratory tract infection (including tracheitis, nasopharyngitis, sinusitis)
	Common	Lower respiratory tract infection (including bronchitis), urinary tract infection, herpes infections (including herpes simplex, oral herpes, and herpes zoster, pneumonia
	Uncommon	Tooth infection, infected skin ulcer, onychomycosis, pelvic inflammatory disease, rhinitis, ear infection, pyelonephritis
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	Uncommon	Basal cell carcinoma
Blood and the lymphatic system disorders	Uncommon	Thrombocytopenia, leukopenia
Immune system disorders	Uncommon	Hypersensitivity
Psychiatric disorders	Uncommon	Depression, anxiety, sleep disorder (including insomnia)
Nervous system disorders	Common	Headache, dizziness
	Uncommon	Paraesthesia
Eye disorders	Uncommon	Conjunctivitis, reduced visual acuity
Ear and labyrinth disorders	Uncommon	Vertigo
Cardiac disorders	Uncommon	Tachycardia, bradycardia, palpitations
Vascular disorders	Common	Hypertension
	Uncommon	Hypotension, hot flush, flushing
Respiratory, thoracic and mediastinal disorders	Common	Cough
	Uncommon	Chronic obstructive pulmonary disease

		exacerbation
Gastrointestinal disorders	Common	Abdominal pain, diarrhoea, nausea, dyspepsia, mouth ulceration, aphthous stomatitis
	Uncommon	Gastritis
Skin and subcutaneous tissue disorders	Common	Rash (including dermatitis)
	Uncommon	Increased tendency to bruise, alopecia, dry skin, hyperhidrosis, erythema, acne
Musculoskeletal, connective tissue and bone disorders	Uncommon	Arthralgia, pain in extremity
Reproductive system and breast disorders	Uncommon	Amenorrhoea, menorrhagia
General disorders and administration site conditions	Common	Fatigue, asthenia, local injection site reactions
	Uncommon	Influenza-like illness
Investigations	Common	Increased blood pressure, abnormal liver function test (including increased transaminases)
	Uncommon	Decreased blood pressure, increased weight

Infections

In the placebo-controlled trials with durations of 6 to 14 months, infections at least possibly related to treatment were reported in 22,7 % of ORENCIA-treated patients and 20,5 % of placebo patients.

Serious infections at least possibly related to treatment were reported in 1,5 % of ORENCIA-treated patients and 1,1 % of placebo patients. The type and frequency of serious infections was similar between the ORENCIA and placebo treatment groups.

Malignancies

In placebo-controlled clinical trials with durations of up to 14 months, malignancies were reported in 1,2 % (31/2653) of ORENCIA-treated patients and in 0,9 % (14/1485) of placebo-treated patients.

In the cumulative period in 7044 patients treated with ORENCIA during 21011 patient-years the incidence rate of malignancy was 1,2 (1,1, 1,4) per 100 patient-years, and the annualised incidence rate remained stable.

The most frequently reported malignancy in the placebo-controlled clinical trials was non-melanoma skin cancer; 0,6 (0,3, 1,0) per 100 patient-years for abatacept-treated patients, 0,4 (0,1, 0,9) per 100 patient-years for placebo-treated patients, and 0,5 (0,4, 0,6) per 100 patient-years in the cumulative period.

The most frequently reported solid organ cancer in the placebo-controlled clinical trials was lung cancer (0,17 (0,05, 0,43) per 100 patient-years) for abatacept-treated patients, 0 for placebo-treated patients, and 0,12 (0,08, 0,17) per 100 patient-years in the cumulative period. The most common haematologic malignancy was lymphoma (0,04 (0, 0,24) per 100 patient-years) for abatacept-treated patients, 0 for placebo-treated patients, and 0,06 (0,03, 0,1) per 100 patient-years in the cumulative period.

Adverse medicine reactions in patients with chronic obstructive pulmonary disease (COPD)

In one study, there were 37 patients with COPD treated with ORENCIA and 17 treated with placebo. The adult COPD patients treated with ORENCIA developed adverse drug reactions more frequently than those treated with placebo (51,4 % vs. 47,1 %, respectively).

Respiratory disorders occurred more frequently in ORENCIA-treated patients than in placebo-treated patients (10,8 % vs. 5,9 %, respectively); these included COPD exacerbation and dyspnoea.

A greater percentage of ORENCIA-treated than placebo-treated patients with COPD developed a serious adverse reaction (5,4 % vs. 0 %), including COPD exacerbation (1 of 37 patients [2,7 %]) and bronchitis (1 of 37 patients [2,7 %]).

Auto-immune processes

ORENCIA therapy did not lead to increased formation of antinuclear or anti-double stranded DNA antibodies compared with placebo.

The incidence rate of autoimmune disorders in abatacept-treated patients during the double-blind period was 8,8 (7,6, 10,1) per 100 patient-years of exposure and for placebo-treated patients was 9,6 (7,9, 11,5) per 100

patient-years of exposure. The incidence rate in abatacept-treated patients was 3,8 per 100 patient-years in the cumulative period.

The most frequently reported autoimmune-related disorder other than the indication being studied during the cumulative period were psoriasis, rheumatoid nodule, and Sjogren's syndrome.

Injection site reactions

The overall frequency of injection site reactions was 2,6 % (19/736) in patients using ORENCIA 125 mg solution for subcutaneous injection.

Immunogenicity

Across seven studies in rheumatoid arthritis patients treated for up to 8 years with subcutaneous or intravenous administration of ORENCIA, 4,8 % (187/3877) developed anti-abatacept antibodies while on treatment. Samples from 22 of 48 of these patients with binding activity to CTLA-4 showed significant neutralising activity.

A subsequent study compared the immunogenicity to ORENCIA following subcutaneous vs intravenous administration. The overall immunogenicity frequency to ORENCIA was 1,1 % (8/725) and 2,3 % (16/710) for the subcutaneous and intravenous groups, respectively. These rates are consistent with previous experience, and there was no effect of immunogenicity on pharmacokinetics, safety or efficacy.

Laboratory findings

Based on the results of clinical studies, no special laboratory evaluations are necessary in addition to careful medical management and supervision of patients.

Geriatric use

A total of 404 patients 65 years of age and older, including 67 patients 75 years and older, received ORENCIA in placebo-controlled clinical studies.

Similar efficacy was observed in these patients and younger patients. The frequency of serious infection and

malignancy among ORENCIA-treated patients over age 65 was higher than for those under age 65. Because there is a higher incidence of infections and malignancies in the elderly population in general, caution should be used when treating the elderly.

The relative frequency of serious infection among ORENCIA-treated patients age 65 and over (18/323 (5,6 %) ORENCIA vs. 4/148 (2,7 %) placebo) was higher than for those under age 65 (40/1 632 (2,5 %) ORENCIA vs. 15/841 (1,8 %) placebo). The relative frequency of malignancy among ORENCIA-treated patients age 65 and over (18/323 (5,6 %) ORENCIA vs. 4/148 (2,7 %) placebo) was higher than for those under age 65 (9/1 632 (0,6 %) ORENCIA vs. 7/841 (0,8 %) placebo). Among patients aged 65 and over, non-melanoma skin cancers accounted for 11 of the 18 malignancy cases in ORENCIA-treated patients, and all 4 of the placebo cases.

Because there is a higher incidence of infections and malignancies in the elderly population in general, caution should be used when treating the elderly.

Postmarketing experience

Adverse reactions have been reported during the post-approval use of ORENCIA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to ORENCIA. Postmarketing reports of systemic injection reactions (eg, pruritus, throat tightness, dyspnoea) have been received following the use of ORENCIA 125 mg solution for subcutaneous injection.

In the post-marketing setting, cases of non-melanoma skin cancer (including basal cell carcinoma and squamous cell carcinoma) have been reported in patients treated with abatacept. A risk for the development of non-melanoma skin cancer in patients treated with abatacept cannot be excluded.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any

suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who.umc.org) found on SAHRPA website.

For reporting of adverse reactions directly to the Holder of Certificate of Registration, email: pharmacovigilance@equitypharma.co.za

4.9 Overdose

Doses up to 50 mg/kg have been administered intravenously without apparent toxic effect. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment instituted.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti Rheumatics (anti-inflammatory agents).

Abatacept, a selective costimulation modulator, is a soluble fusion protein that consists of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the modified Fc (hinge, CH2, and CH3 domains) portion of human immunoglobulin G1.

Abatacept is produced by recombinant DNA technology in a mammalian cell expression system.

The apparent molecular weight of abatacept is 92 kilodaltons.

By specifically binding to CD80 and CD86 on antigen presenting cells, abatacept selectively modulates a key costimulatory signal required for full activation of T lymphocytes expressing CD28.

Studies indicate that naïve T lymphocyte responses are more affected by abatacept than memory T lymphocyte responses.

Studies in vitro and in animal models demonstrate that abatacept attenuates T lymphocyte dependent antibody responses and inflammation. In vitro, abatacept attenuates T lymphocyte activation as measured by decreased proliferation and cytokine production in human lymphocytes. Abatacept decreases antigen specific TNFα, interferon-γ, and interleukin-2 production by T lymphocytes.

In a rat collagen-induced arthritis model, abatacept suppresses inflammation, decreases anti-collagen antibody production and reduces antigen specific production of interferon-γ.

5.2 Pharmacokinetic properties

Abatacept exhibited linear pharmacokinetics following subcutaneous administration.

The mean (range) for Cmin and Cmax at steady state observed after 85 days of weekly treatment with 125 mg, was 32,5 µg/ml (6,6 to 113,8 µg/ml) and 48,1 µg/ml (9,8 to 132,4 µg/ml), respectively. The bioavailability of abatacept following subcutaneous administration relative to intravenous administration is 78,6 %. Mean estimates for systemic clearance (0,28 ml/h/kg), volume of distribution (0,11 l/kg), and terminal half-life (14,3 days) were comparable between SC and IV administration.

A single study was conducted to determine the effect of monotherapy use of abatacept in immunogenicity following subcutaneous administration without an IV load. When the IV loading dose was not administered, a mean trough concentration of 12,6 µg/ml was achieved after 2 weeks of dosing. The efficacy response over time in this study appeared consistent with studies that included an IV loading dose, however, the effect of no IV load on the onset of efficacy has not been formally studied.

Consistent with the IV data, population pharmacokinetic analyses for SC abatacept in RA patients revealed that there was a trend toward higher clearance of abatacept with increasing body weight. Age and gender (when corrected for body weight) did not affect apparent clearance. Concomitant methotrexate (MTX), non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and TNF (tumour necrosis factor) blocking agents did not influence abatacept apparent clearance.

Biotransformation and elimination

There are no studies to evaluate the metabolism or elimination of abatacept in humans. Owing to stearic and hydrophilic considerations, abatacept would not be metabolised by liver cytochrome P450 enzymes. Because of its large molecular weight abatacept is not expected to undergo renal elimination.

Special populations

No formal studies were conducted to examine the effects of either renal or hepatic impairment on the pharmacokinetics of abatacept.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose

Poloxamer 188

Sodium phosphate dibasic, anhydrous

Sodium phosphate monobasic, monohydrate

Water for injection

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months.

6.4 Special precautions for storage

ORENCIA 125 mg solution for subcutaneous injection: pre-filled syringes must be protected from light by storing in the original package until time of use. ORENCIA solution for subcutaneous injection must be refrigerated at 2 °C to 8 °C. Do not freeze the pre-filled syringes.

6.5 Nature and contents of container

ORENCIA solution for subcutaneous injection is supplied as a sterile, preservative-free, ready-to-use solution for subcutaneous injection. The ORENCIA solution for subcutaneous injection is supplied in a single-dose disposable prefilled glass syringe with a passive needle safety guard and flange extenders.

The Type I glass syringe has a coated stopper and fixed stainless steel needle (5 bevel, 29-gauge thin wall, ½-

inch needle) covered with a rigid needle shield. A sufficient excess of abatacept is incorporated into each syringe to account for needle-syringe losses so that 1,0 ml of solution containing 125 mg abatacept can be dispensed for subcutaneous injection.

Each carton contains four pre-filled syringes.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Equity Pharmaceuticals (Pty) Ltd*

100 Sovereign Drive

Route 21 Corporate Park

Nellmapius Drive

Irene

Pretoria, 0157

8. REGISTRATION NUMBER(S)

47/3.1/0467

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21 April 2016

10. DATE OF REVISION OF THE TEXT

24 March 2026

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