PROFESSIONAL INFORMATION FOR HUMAN MEDICINES

SCHEDULING STATUS S4

1 NAME OF THE MEDICINE

TEMINTAS 5 mg hard gelatin capsule

TEMINTAS 20 mg hard gelatin capsule

TEMINTAS 100 mg hard gelatin capsule

TEMINTAS 250 mg hard gelatin capsule

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

TEMINTAS 5:

Each hard gelatin capsule contains 5 mg temozolomide.

Excipients with known effect:

Each hard gelatin capsule contains 168 mg of anhydrous lactose.

TEMINTAS 20:

Each hard gelatin capsule contains 20 mg temozolomide.

Excipients with known effect:

Each hard gelatin capsule contains 14.6 mg of anhydrous lactose.

TEMINTAS 100:

Each hard gelatin capsule contains 100 mg temozolomide.

Excipients with known effect:

Each hard gelatin capsule contains 73 mg of anhydrous lactose.

TEMINTAS 250:

Each hard gelatin capsule contains 250 mg temozolomide.

Excipients with known effect:

Each hard gelatin capsule contains 182.5 mg of anhydrous lactose.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Hard gelatin capsules

TEMINTAS 5:

Green/White, hard gelatin capsules size'3' imprinted with 'TMZ' on cap & '5' on body, containing white to light pink powder.

TEMINTAS 20:

Yellow/ white hard gelatin capsules, size '5' imprinted 'TMZ' on cap & '20' on body, containing white to light pink powder.

TEMINTAS 100:

Pink/White hard gelatin capsules, size '3' imprinted 'TMZ' on cap & '100' on body, containing white to light pink powder.

TEMINTAS 250:

White/White, hard gelatin capsules size'0' imprinted with 'TMZ' on cap & '250' on body, containing white to light pink powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

TEMINTAS is indicated for the following:

- adult patients with newly diagnosed glioblastoma multiforme after debulking surgery concomitantly with radiotherapy and then as adjuvant treatment.
- recurrent malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma after debulking surgery.
- advanced metastatic malignant melanoma.

4.2 Posology and method of administration

Adult patients with newly diagnosed glioblastoma multiforme:

TEMINTAS is administered in combination with focal radiotherapy (concomitant phase) followed by up to 6 cycles of temozolomide monotherapy (adjuvant phase).

Concomitant phase

TEMINTAS is administered orally at a dose of 75 mg/m^2 daily for 42 days concomitant with focal radiotherapy (60 Gy administered in 30 fractions). No dose reductions will be made, but delay or discontinuation of TEMINTAS administration will be decided weekly according to haematological and non-haematological toxicity criteria. The TEMINTAS dose can be continued throughout the 42 day concomitant period (up to 49 days) if all of the following conditions are met: absolute neutrophil count ≥ 1,5 x 10^9/litre, thrombocyte count ≥ 100 x 10^9/litre, Common Toxicity Criteria (CTC) non-haematological toxicity ≤ Grade 1 (except for alopecia, nausea and vomiting).

During treatment a complete blood count should be obtained weekly.

TEMINTAS administration should be interrupted or discontinued during concomitant phase according to the haematological and non-haematological toxicity criteria as noted in Table 1.

Table 1 TEMINTAS Dosing Interruption or Discontinuation during Concomitant Radiotherapy and TEMINTAS

Toxicity	**TEMINTAS Interruption[a]**	**TEMINTAS Discontinuation**
Absolute Neutrophil Count	≥ 0,5 and < 1,5 x 10^9/litre	< 0,5 x 10^9/litre
Thrombocyte Count	≥ 10 and < 100 x 10^9/litre	< 10 x 10^9/litre
CTC Non-hematological Toxicity (except for alopecia, nausea, vomiting)	CTC Grade 2	CTC Grade 3 or 4
a: Treatment with concomitant TEMINTAS could be continued when all of the following conditions are met: absolute neutrophil count ≥ 1,5 x 10^9/litre; thrombocyte count ≥ 100 x 10^9/litre; CTC non-hematological toxicity ≤ Grade 1 (except for alopecia, nausea, vomiting) CTC = Common Toxicity Criteria		

Adjuvant (Monotherapy) Phase

Four weeks after completing the TEMINTAS + Radiotherapy phase, TEMINTAS is administered for up to 6 cycles of monotherapy treatment. Dosage in Cycle 1 (adjuvant/monotherapy) is 150 mg/m2 once daily for 5 days followed by 23 days without treatment. At the start of Cycle 2, the dose is escalated to 200 mg/m2 if the CTC non-haematological toxicity for Cycle I is Grade ≤ 2 (except for alopecia, nausea and vomiting), absolute neutrophil count (ANC) is ≥ 1,5 x 109/litre, and the thrombocyte count is ≥ 100 x 109/litre. If the dose was not escalated at Cycle 2, escalation should not be done in subsequent cycles. Once escalated, the dose remains at 200 mg/m2 per day for the first 5 days of each subsequent cycle except if toxicity occurs. Dose reductions and discontinuations during the adjuvant/monotherapy phase should be applied according to Tables 2 and 3.

During treatment a complete blood count should be obtained on Day 22 (21 days after the first dose of TEMINTAS). The TEMINTAS dose should be reduced or discontinued according to Table 3.

Table 2 TEMINTAS Dose Levels for Adjuvant Treatment

Dose Level	**Dose (mg/m^2/day)**	**Remarks**
-1	100	Reduction for prior toxicity
0	150	Dose during Cycle 1
1	200	Dose during Cycles 2 to 6 in absence of toxicity

Table 3 TEMINTAS Dose Reduction or Discontinuation during Adjuvant treatment

Toxicity	**Reduce TEMINTAS by 1 Dose Level[a]**	**Discontinue TEMINTAS**
Absolute Neutrophil Count	< 1,0 x 10^9/litre	See footnote b
Thrombocyte Count	< 50 x 10^9/litre	See footnote b
CTC Non-haematological Toxicity (except for alopecia, nausea, vomiting)	CTC Grade 3	CTC Grade 4[b]
a: TEMINTAS dose levels are listed in Table 2 b: TEMINTAS is to be discontinued if: • dose level -1 (100 mg/m^2) still results in unacceptable toxicity • the same Grade 3 non-haematological toxicity (except for alopecia, nausea, vomiting)		

recurs after dose reduction CTC = Common Toxicity Criteria

Adult patients:

In patients previously untreated with chemotherapy, TEMINTAS is administered orally at a dose of 200 mg/m^2 once daily for 5 days per 28-day cycle.

In patients previously treated with chemotherapy, the initial dose is 150 mg/m^2 once daily, to be increased in the second cycle to 200 mg/m^2 daily, provided that the absolute neutrophil count (ANC) is ≥ 1,5 x 10^9 /ℓ and the thrombocyte count is ≥ 100 x 10^9 /ℓ on day 1 of the next cycle.

Paediatric patients:

In patients 3 years of age and older, previously untreated with chemotherapy, TEMINTAS is administered orally at a dose of 200 mg/m^2, once daily for the first 5 days per 28-day cycle.

Paediatric patients previously treated with chemotherapy should receive an initial dose of 150 mg/m^2 once daily for 5 days, increased to 200 mg/m^2 once daily at the next cycle; provided there is no haematological toxicity.

Children under 3 years (see section 4.4):

- **For Glioblastoma multiforme:** TEMINTAS should not be used in children under the age of 3 years.
- **For Melanoma:** TEMINTAS should not be used in children under the age of 18 years.

TEMINTAS should be administered in the fasting state, at least one hour before a meal.

Anti-emetic therapy may be administered prior to or following administration.

If vomiting occurs after the dose is administered, a second dose should not be administered that day.

TEMINTAS capsules must not be opened or chewed, but are to be swallowed whole with a glass of water.

If a capsule becomes damaged, contact of the powder contents with skin or mucous membranes should be avoided.

Therapy with TEMINTAS can be continued until disease progression for a maximum of two years.

4.3 Contraindications

TEMINTAS is contra-indicated:

- in patients who have a history of hypersensitivity reaction to its components or to dacarbazine (DTIC)
- in patients with severe myelosuppression
- in patients who are pregnant or lactating (see section 4.6).

4.4 Special warnings and precautions for use

It has been reported that patients who received concomitant TEMINTAS and radiotherapy for the prolonged 42 day schedule were shown to be at particular risk for developing Pneumocystis carinii pneumonia (PCP). Thus, prophylaxis against Pneumocystis carinii pneumonia is required for all patients receiving concomitant TEMINTAS and radiotherapy for the 42 day regimen (with a maximum of 49 days) regardless of lymphocyte count. If lymphopenia occurs, they are to continue the prophylaxis until recovery of lymphopenia to grade ≤ 1.

- **Paediatric use** (see section 4.2):

For Glioblastoma multiforme: Should not be used in children under the age of 3 years.

There is limited experience in children over the age of 3 years with glioma.

For Melanoma: Should not be used in children under the age of 18 years.

- **Elderly patients:**

Older patients (> 70 years of age) may be at an increased risk of developing neutropenia and thrombocytopenia.

- **Gastro-intestinal disturbances:**

Nausea and vomiting may occur frequently, may be mild to moderate in severity.

- **Myelosuppression:**

Grade 3 or Grade 4 thrombocytopenia and neutropenia may occur. This may lead to hospitalisation or discontinuation of therapy. Myelosuppression usually occurs within the first few cycles, with the nadir between day 21 and 28, and recovery usually within 1 to 2 weeks. Cumulative myelosuppression does not occur.

- **Vomiting:**

Nausea and vomiting are very commonly associated with TEMINTAS and guidelines are provided:

Patients with newly diagnosed glioblastoma multiforme:

- anti-emetic prophylaxis is recommended prior to the initial dose of concomitant TEMINTAS.
- anti-emetic prophylaxis is strongly recommended during the adjuvant phase.

Patients with recurrent or progressive glioma:

Patients who have severe vomiting (Grade 3 or 4) may require anti-emetic therapy before initiating TEMINTAS treatment.

- **Laboratory parameters:**

Prior to dosing, the following laboratory parameters must be met:

- ANC ≥ 1,5 x 10^9/ℓ and platelet count ≥ 100 x 10^9/ℓ.
- A complete blood count should be obtained on day 22 (21 days after the first dose) or within 48 hours of that day and weekly until ANC is above 1,5 x 10^9/ℓ and the platelet count exceeds 100 x 10^9/ℓ.
- If the ANC falls to < 1,0 x 10^9/ℓ or the platelet count is < 50 x 10^9/ℓ during any cycle, the next cycle should be reduced one dose level.
- Dose levels include 100 mg/m^2, 150 mg/m^2 and 200 mg/m^2.
- The lowest recommended dose is 100 mg/m^2.

- **Hepatic or renal dysfunction:**

The pharmacokinetics of temozolomide are comparable in patients with normal hepatic function and in those with mild or moderate hepatic dysfunction. No data is available on the administration of TEMINTAS in patients with severe hepatic dysfunction (Child's Class III) or with renal dysfunction. Based on the pharmacokinetic properties of TEMINTAS, dose reductions are not generally necessary in patients with severe hepatic dysfunction or renal dysfunction. However, caution should be exercised when administering TEMINTAS to these patients.

- **Lactose intolerance**

TEMINTAS contains lactose. Patients with rare hereditary problems of galactose intolerance, lapp lactase deficiency or glucose-galactose malabsorption should not take TEMINTAS.

4.5 Interactions with other medicines and other forms of interaction

The use of TEMINTAS in combination with other myelosuppressive agents may increase the likelihood of myelosuppression.

Administration with ranitidine or with food does not cause a clinically significant alteration in the extent of absorption of TEMINTAS.

Co-administration with dexamethasone, prochlorperazine, phenytoin, carbamazepine, ondansetron, H2-receptor antagonists or phenobarbital does not alter the clearance of TEMINTAS.

Co-administration with valproic acid is associated with decrease in the clearance of TEMINTAS.

4.6 Fertility, pregnancy and lactation

Safety of TEMINTAS during pregnancy and lactation has not been established.

TEMINTAS is contra-indicated for use during pregnancy and lactation (see section 4.3).

TEMINTAS is teratogenic or may cause foetal toxicity.

Women of childbearing potential should be advised not to fall pregnant while they are receiving TEMINTAS, or in the six months after discontinuation of TEMINTAS.

It is not known whether TEMINTAS is excreted in breast milk; therefore, it should not be used by women who are lactating.

Use of TEMINTAS in male patients:

Effective contraception should also be used by male patients who are on therapy with TEMINTAS.

TEMINTAS can have genotoxic effects.

Men being treated with TEMINTAS should be advised not to father a child during therapy, or for up to 6 months after discontinuation of TEMINTAS, because of the possibility of irreversible infertility due to therapy with TEMINTAS, men should be counselled to seek medical advice on cryoconservation.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. The ability to drive and use machines may be impaired in patients treated with TEMINTAS due to fatigue and somnolence.

4.8 Undesirable effects

The following side-effects may occur with the use of TEMINTAS:

Table 4: Treatment emergent adverse events in patients with newly diagnosed glioblastoma multiforme during the concomitant and adjuvant phases of treatment.

System Organ	TEMINTAS + Concomitant	TEMINTAS Adjuvant Therapy

Class	Radiotherapy	
Infections and Infestations		
Frequent:	Oral candidiasis, Herpes simplex, infection, pharyngitis, wound infection	Oral candidiasis, infection
Less frequent:		Herpes simplex, Herpes zoster, influenza-like symptoms
Blood and the lymphatic system disorders		
Frequent:	Leukopenia, lymphopenia, neutropenia, thrombocytopenia	Anaemia, febrile neutropenia, leukopenia, thrombocytopenia
Less frequent:	Anaemia, febrile neutropenia	Lymphopenia, petechiae
Endocrine disorders		
Less frequent:	Cushingoid	Cushingoid
Metabolism and nutrition disorders		
Frequent:	Anorexia, hyperglycaemia, weight decreased	Anorexia, weight decreased
Less frequent:	Hypokalaemia, alkaline phosphatase increased, weight increased	Hyperglycaemia, weight increased
Psychiatric disorders		
Frequent:	Anxiety, emotional lability, insomnia	Anxiety, depression, emotional lability, insomnia
Less frequent:	Agitation, apathy, behaviour disorder, depression, hallucination	Hallucination, amnesia
Nervous system disorders		
Frequent:	Headache, dizziness, aphasia, impaired balance, impaired	Headache, convulsions, dizziness, aphasia, impaired balance, impaired

	concentration, confusion, decreased consciousness, convulsions, memory impairment, neuropathy, paraesthesia, somnolence, speech disorder, tremor	concentration, confusion, dysphasia, hemiparesis, memory impairment, neurological disorder (NOS), neuropathy, peripheral neuropathy, paraesthesia, somnolence, speech disorder, tremor
Less frequent:	Ataxia, impaired cognition, dysphasia, extrapyramidal disorder, abnormal gait, hemiparesis, hyperesthesia, hypoaesthesia, neurological disorder (NOS), peripheral neuropathy, status epilepticus	Ataxia, abnormal coordination, abnormal gait, hemiplegia, hyperaesthesia, sensory disturbance
Eye disorders		
Frequent:	Vision blurred	Vision blurred, diplopia, visual field defect
Less frequent:	Eye pain, hemianopia, vision disorder, reduced visual acuity, visual field defect	Eye pain, eyes dry, reduced visual acuity
Ear and labyrinth disorders		
Frequent:	Hearing impairment	Hearing impairment, tinnitus
Less frequent:	Earache, hyperacusis, tinnitus, otitis media	Deafness, earache, vertigo
Cardiac disorders		
Less frequent:	Palpitation	
Vascular disorders		
Frequent:	Oedema, leg oedema,	Leg oedema, haemorrhage, deep

	haemorrhage	venous thrombosis
Less frequent:	Hypertension, cerebral haemorrhage	Oedema, peripheral oedema, pulmonary embolism
Respiratory, thoracic and mediastinal disorders		
Frequent:	Coughing, dyspnoea	Coughing, dyspnoea
Less frequent:	Pneumonia, upper respiratory infection, nasal congestion	Pneumonia, sinusitis, upper respiratory infection, bronchitis
Gastrointestinal disorders		
Frequent:	Constipation, nausea, vomiting, abdominal pain, diarrhoea, dyspepsia, dysphagia, stomatitis	Constipation, nausea, vomiting, diarrhoea, dyspepsia, dysphagia, dry mouth, stomatitis
Less frequent:		Abdominal distension, faecal incontinence, gastrointestinal disorder (NOS), gastroenteritis, haemorrhoids
Skin and subcutaneous tissue disorders		
Frequent:	Alopecia, rash, Dermatitis, dry skin, erythema, pruritus	Alopecia, rash, dry skin, pruritus
Less frequent:	Photosensitivity reaction, abnormal pigmentation, skin exfoliation	Erythema, abnormal pigmentation, increased sweating
Musculoskeletal and connective tissue disorders		
Frequent:	Arthralgia, muscle weakness	Arthralgia, musculoskeletal pain, myalgia, muscle weakness
Less frequent:	Back pain, musculoskeletal pain, myalgia, myopathy	Back pain, myopathy
Renal and urinary disorders		
Frequent:	Frequent micturition, urinary incontinence	Urinary incontinence

Less frequent:		Dysuria
Reproductive system and breast disorders		
Less frequent:	Impotence	Amenorrhoea, breast pain, menorrhagia, vaginal haemorrhage, vaginitis
General disorders and administration site conditions		
Frequent:	Fatigue, fever, pain, allergic reaction, radiation injury, facial oedema, taste perversion	Fatigue, Fever, pain, allergic reaction, radiation injury, taste perversion
Less frequent:	Flushing, hot flushes, asthenia, condition aggravated, rigors, tongue discoloration, parosmia, thirst	Asthenia, condition aggravated, pain, rigors, tooth disorder, face oedema, taste perversion
Investigation		
Frequent:	ALT increased	ALT increased
Less frequent:	Gamma GT increased, hepatic enzymes increased, AST increased	

Laboratory results:

Myelosuppression (neutropenia and thrombocytopenia), which is known dose-limiting toxicity for most cytotoxic medicines, including TEMINTAS, has been observed. It has been reported that when laboratory abnormalities and adverse events were combined across concomitant and monotherapy treatment phases, Grade 3 or Grade 4 neutrophil abnormalities including neutropenic events were observed in 8 % of the patients. Grade 3 or Grade 4 thrombocyte abnormalities, including thrombocytopenic events were observed in 14 % of the patients who received TEMINTAS.

Table 5: Adverse reactions in patients with recurrent anaplastic astrocytoma, glioblastoma multiforme or malignant melanoma:

Nervous system disorders	
Frequent:	Fatigue, headache, somnolence, asthenia, dizziness and paraesthesia
Gastro-intestinal disorders:	
Frequent:	Nausea, vomiting, constipation, anorexia, diarrhoea, abdominal pain, dyspepsia
Blood and lymphatic system disorders	
Frequent:	Thrombocytopenia, neutropenia, anaemia, leucopenia and lymphopenia
Frequency unknown:	Pancytopenia, secondary malignancies including myeloid leukaemia
Skin and subcutaneous tissue disorders	
Frequent:	Rash, alopecia, pruritus, petechiae
Less frequent:	Erythema multiforme
Respiratory, thoracic and mediastinal disorders	
Frequent:	Dyspnoea
Infections and infestations	
Less frequent:	Opportunistic infections including Pneumocystis jiroveci pneumonia (PCP)
Immune system disorders	
Less frequent:	Anaphylaxis
Frequency unknown:	Allergic reactions
General	
Frequent:	Fever, pain, malaise, weight decrease, rigors
Less frequent:	Myelodysplastic syndrome (MDS)

Laboratory results

It has been reported that Grade 3 or 4 thrombocytopenia and neutropenia occurred in 19 % and 17 % respectively, of patients treated for glioma and 20 % and 22 %, respectively of patients with metastatic melanoma. This led to hospitalisation and/or discontinuation of Temozolomide in 8 % and 4 %, respectively, of patients with glioma and 3 % and 1,3 %, respectively, of those with melanoma. Myelosuppression was predictable (usually within the first few cycles, with the nadir between Day 21 and 28), and recovery was usually within 1 to 2 weeks. No evidence of cumulative myelosuppression was observed.

Post-Marketing Experience

Allergic reactions including anaphylaxis have been reported Cases of erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome have also been observed. There have been reported cases of hepatotoxicity including elevations of liver enzymes, hyperbilirubinaemia, cholestasis and hepatitis.

Cases of opportunistic infections including Pneumocystis carinii pneumonia (PCP) have been reported. Cases of herpes simplex encephalitis, including cases of fatal outcomes, have also been reported. Cases of interstitial pneumonitis/pneumonitis and pulmonary fibrosis have been reported.

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 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

Dose-limiting toxicity is haematological, which is more severe at higher doses.

Overdose may cause pancytopenia, pyrexia, multi-organ failure, bone marrow suppression, with or without infection which can become severe and prolonged and resulting in death.

In the event of an overdose, a haematological evaluation is needed. Supportive measures should be provided as necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 26 Cytostatic Agents.

Mechanism of action:

Temozolomide is an imidazotetrazene alkylating agent with antitumour activity. Alkylating agents disturb DNA synthesis and cell division and induce cell death in rapidly proliferating tissues. Temozolomide undergoes rapid chemical conversion in the systemic circulation at physiologic pH to the active compound MTIC (monomethyl-triazeno- imidazole-carboxamide). The cytotoxicity of MTIC is thought to be due primarily to alkylation at the O6 position of guanine with additional alkylation also occurring at the N7 position.Cytotoxic lesions that develop subsequently are thought to involve aberrant repair of the methyl adduct.

5.2 Pharmacokinetic properties

Absorption:

After oral administration, temozolomide is rapidly absorbed with peak plasma concentrations reached as early as 20 minutes post-dose (mean times between 0,5 and 1,5 hours). Plasma concentrations

increase in a dose-related manner. Bioavailabilty approaches 100%. Plasma clearance, volume of distribution and half-life are independent of dose.

Distribution:

Temozolomide crosses the blood-brain barrier and is present in the cerebrospinal fluid.

Temozolomide has low protein binding (10 % to 20 %).

Metabolism:

Temozolomide undergoes rapid chemical conversion in the systemic circulation at physiologic pH to the active metabolite MTIC (monomethyl-triazeno-imidazole-carboxamide).

Elimination:

Temozolomide is excreted mainly via the faecal route (80 %).

Following oral administration, little intact medicine is recovered in the urine and the remainder of the medicine is excreted as the inactive 4-amino-5-imidazole-carboxamide hydrochloride (AIC) or other unidentified polar metabolites.

Population-based pharmacokinetics of temozolomide:

Plasma temozolomide clearance is independent of age, renal function, hepatic function or tobacco use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous lactose

Colloidal anhydrous silica

Sodium starch glycolate (Type A)

Tartaric acid

Stearic acid

Gelatin

Iron oxide yellow (E172)

Titanium dioxide (E171)

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a cool, dry place, at or below 25 °C.

Store in unit carton until before use.

6.5 Nature and contents of container

- TEMINTAS 5:

Hard gelatin capsules are packed in amber glass bottles of 5 capsules and 20 capsules per bottle, which are packed with a white cotton coil and desiccant disc, and a white opaque polypropylene child resistant closure, in a unit carton.

- TEMINTAS 20:

Hard gelatin capsules are packed in amber glass bottles of 5 capsules and 20 capsules per bottle, which are packed with a white cotton coil and desiccant disc, and a white opaque polypropylene child resistant closure, in a unit carton.

- TEMINTAS 100:

Hard gelatin capsules are packed in amber glass bottles of 5 capsules and 20 capsules per bottle, which are packed with a white cotton coil and desiccant disc, and a white opaque polypropylene child resistant closure, in a unit carton.

- TEMINTAS 250:

Hard gelatin capsules are packed in amber glass bottles of 5 capsules and 20 capsules per bottle, which are packed with a white cotton coil and desiccant disc, and a white opaque polypropylene child resistant closure, in a unit carton.

6.6 Special precautions for disposal

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

Eurolab (Pty) Ltd.

Woodmead Office Park

3 Stirrup Lane, Van Reenans Avenue

Woodmead

Gauteng

South Africa

8 REGISTRATION NUMBER

TEMINTAS 5: 44/26/0964

TEMINTAS 20: 44/26/0965

TEMINTAS 100: 44/26/0966

TEMINTAS 250: 44/26/0967

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26 October 2012

10 DATE OF REVISION OF THE TEXT

08 October 2024