PROFESSIONAL INFORMATION

PRODYNA XR RANGE

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

PRODYNA 150 mg XR extended release tablets

PRODYNA 300 mg XR extended release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each PRODYNA 150 mg XR tablet contains bupropion hydrochloride 150 mg.

Each PRODYNA 300 mg XR tablet contains bupropion hydrochloride 300 mg.

PRODYNA XR is sugar free.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Extended release tablets.

PRODYNA 150 mg XR: Off-white to pale yellow, round, biconvex, coated tablets, imprinted with “L015” in black ink on one side and plain on other side.

PRODYNA 300 mg XR: Off-white to pale yellow, round, biconvex, coated tablets, imprinted with “L016” in black ink on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PRODYNA XR is indicated for the treatment of depression as defined by DSM (diagnostic and statistical manual of mental disorders) IV Criteria. Following a satisfactory response, continuation with PRODYNA XR therapy is effective in preventing relapse and preventing recurrence of further depressive episodes.

4.2 Posology and method of administration

Therapy should be initiated by medical practitioners experienced in the treatment of depression.

Posology

Initial treatment:

The initial dose of PRODYNA XR is 150 mg taken as a single daily dose in the morning. Patients who are not responding adequately to a dose of 150 mg/day may benefit from an increase to the usual adult target dose of 300 mg/day, given once daily. There should be an interval of at least 24 hours between successive doses.

Insomnia is a very common adverse event which is often transient. Insomnia may be reduced by avoiding dosing at bedtime (provided there is at least 24 hours between doses) or, if clinically indicated, dose reduction.

Switching patients from sustained release tablets:

When switching patients from sustained release tablets to extended release tablets; give the same total daily dose when possible. Patients who are currently being treated with sustained release tablets at 300 mg/day (e.g. 150 mg twice daily) may be switched to extended release tablets 300 mg once daily.

Special populations

Elderly: Greater sensitivity of some elderly individuals to PRODYNA XR cannot be ruled out, hence a reduced frequency and/or dose may be required (see section 4.4).

Renal Impairment: Treatment of patients with renal impairment should be initiated at a reduced frequency and/or dose, as bupropion and its metabolites may accumulate in such patients to a greater extent than usual (see section 4.4).

Liver Impairment: PRODYNA XR should be used with caution in patients with mild liver impairment. Because of

increased variability in the pharmacokinetics in patients with mild hepatic cirrhosis, a reduced frequency of dosing should be considered (see sections 4.4 and 4.8). PRODYNA XR is contraindicated in patients with moderate to severe hepatic cirrhosis.

Paediatric population

PRODYNA XR is not indicated for use in children or adolescents aged less than 18 years (see section 4.3).

Method of administration

PRODYNA XR tablets should be swallowed whole. The tablets should not be cut, crushed or chewed as this may lead to an increased risk of adverse effects including seizures.

Missed dose

Medical practitioners should advise patients who forget to take PRODYNA XR to wait and take the next tablet at the usual time. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

PRODYNA XR is contraindicated in:

- hypersensitivity to bupropion or to any of the excipients listed in 6.1
- patients under 18 years
- PRODYNA XR is contraindicated in patients with a seizure disorder
- PRODYNA XR should not be administered to patients currently being treated with any other preparation containing bupropion, as the incidence of seizures is dose dependent
- PRODYNA XR is contraindicated in patients undergoing abrupt discontinuation of alcohol or sedatives
- PRODYNA XR is contraindicated in patients with a current or previous diagnosis of bulimia or anorexia nervosa as a higher incidence of seizures was seen in this patient population when bupropion was

administered

- concomitant administration of PRODYNA XR with monoamine oxidase inhibitors (MAOIs) is contraindicated. At least 14 days should elapse between the discontinuation of MAOIs and initiation of treatment with PRODYNA XR
- liver disease, Child-Pugh grades B and C, range 7 - 13.

4.4 Special warnings and precautions for use

Seizures:

The recommended dose of PRODYNA XR should not be exceeded, since bupropion is associated with a dose-related risk of seizure.

PRODYNA XR should be discontinued promptly if patients experience hypersensitivity reactions during treatment (see section 4.8). Medical practitioners should be aware that symptoms may persist beyond the discontinuation of PRODYNA XR and clinical management should be provided accordingly.

The overall incidence of seizure with bupropion hydrochloride in clinical trials was approximately 0,1 %.

There is an increased risk of seizures occurring with the use of PRODYNA XR in the presence of predisposing risk factors, which lower the seizure threshold. Therefore, PRODYNA XR should not be administered to patients with one or more conditions predisposing to a lowered seizure threshold, which include:

- history of head trauma
- central nervous system (CNS) tumour
- history of seizures
- concomitant administration of other medications known to lower the seizure threshold, excessive use of alcohol or sedatives (see section 4.3), diabetes treated with hypoglycaemics or insulin and use of stimulants or anorectic medicines.

PRODYNA XR should be discontinued and not recommenced in patients who experience a seizure while on

treatment.

Clinical worsening and suicide risk in adults associated with psychiatric disorders:

Patients with major depressive disorder, may experience worsening of their depression and or the emergence of suicidal ideation and behaviour, whether or not they are taking antidepressant medicines. This risk may persist until significant remission occurs. A causal role, however, for antidepressant medicine in inducing such behaviour has not been established. As improvement may occur during the first few weeks or more of treatment, patients being treated with PRODYNA XR should, nevertheless, be observed closely for clinical worsening (including development of new symptoms) and suicidality, especially at the beginning of a course of therapy or at any time of dose changes, either increases or decreases. Patients with a history of suicidal behaviour or thoughts, young adults and those patients exhibiting a significant degree of suicidal ideation prior to commencement of treatment are at a greater risk of suicidal thoughts or suicide attempts and should receive careful monitoring during treatment.

The following symptoms have been reported in patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and non-psychiatric: anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, and mania.

In addition, a meta-analysis of placebo controlled clinical trials of antidepressant medicines in adults with major depressive disorder and other psychiatric disorders showed an increased risk of suicidal thinking and behaviour associated with antidepressant use compared to placebo in patients less than 25 years old.

Patients (and caregivers of patients) should be alerted about the need to monitor for any worsening of their condition (including development of new symptoms) and/or the emergence of suicidal ideation/behaviour or thoughts of harming themselves and to seek medical advice immediately if these symptoms present. It should be recognised that the onset of neuropsychiatric symptoms could be related either to the underlying disease state or the medicine therapy and an appropriate patient assessment should be undertaken (see section 4.8).

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing PRODYNA XR, in patients who experience clinical worsening (including development of new symptoms) and/or the emergence of suicidal ideation/behaviour, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Although there is no need to taper PRODYNA XR upon discontinuation, the patient should be monitored for worsening of depressive symptoms following discontinuation.

Neuropsychiatric symptoms including mania and bipolar disorder:

Neuropsychiatric symptoms have been reported (see section 4.8). In particular, psychotic and manic symptomatology has been observed, mainly in patients with a known history of psychiatric illness. Aggression, rage and violent behaviour may occur. Additionally, a major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone can increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Limited clinical data on use of bupropion in combination with mood stabilisers in patients with a history of bipolar disorder suggests a low rate of switch to mania.

Prior to initiating treatment with PRODYNA XR, patients should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

Hepatic impairment:

Bupropion is extensively metabolised in the liver to active metabolites, which are further metabolised. No statistically significant differences in the pharmacokinetics of bupropion were observed in patients with mild hepatic cirrhosis compared with healthy volunteers, but bupropion plasma levels showed a higher variability between individual patients.

Therefore, PRODYNA XR should be used with caution in patients with mild hepatic impairment and reduced frequency of dosing should be considered (see sections 4.3 and 5.2).

Renal impairment and elderly patients:

Bupropion is extensively metabolised in the liver to active metabolites which are further metabolised and excreted by the kidneys. Therefore, treatment of patients with renal impairment should be initiated at reduced frequency and/or dose as bupropion and its metabolites may accumulate in such patients to a greater extent than usual. The patient should be closely monitored for possible adverse effects (e.g. insomnia, dry mouth, seizures) that could indicate high bupropion or metabolite levels, toxic effects of elevated blood and tissue levels of bupropion and metabolites.

Clinical experience with PRODYNA XR has not identified any differences in tolerability between elderly and other adult patients, However, greater sensitivity of some elderly individuals cannot be ruled out, hence a reduced frequency and/or dose may be required (see section 5.2).

Cardiovascular disease:

There is limited clinical experience of the use of PRODYNA XR to treat depression in patients with cardiovascular disease. A causal relationship between the use of PRODYNA XR and sudden death cannot be excluded. Care should be exercised if PRODYNA XR is used in these patients.

Brugada Syndrome

Cardiac conduction disorders-Bupropion may unmask cardiac conduction syndromes e.g. Brugada syndrome, a rare hereditary disease of the cardiac sodium channel with characteristic ECG changes (right bundle branch block and ST segment elevation in right precordial leads), which may lead to cardiac arrest and or sudden death. Caution is advised in patients with Brugada syndrome or family history of cardiac arrest or sudden death.

Paediatric Population:

The safety and efficacy with the treatment of PRODYNA XR tablets in patients under 18 years of age have not been established. Treatment with antidepressants is associated with an increased risk of suicidal thinking and

behaviour in children and adolescents with major depressive disorder and other psychiatric disorders (see section 4.3).

4.5 Interaction with other medicines and other forms of interaction

Medicines known to affect the CYP2B6 isoenzyme:

Bupropion is metabolised to its major active metabolite hydroxybupropion primarily by the cytochrome P450 IIB6 (CYP2B6) (see section 5.2).

Care should therefore be exercised when PRODYNA XR is co-administered with medicines known to affect the CYP2B6 isoenzyme (e.g. orphenadrine, cyclophosphamide, ifosfamide, ticlopidine, clopidogrel).

Medicines metabolized by CYP2D6:

Although bupropion is not metabolised by the CYP2D6 isoenzyme, *in vitro* human P450 studies have shown that bupropion and hydroxybupropion are inhibitors of the CYP2D6 pathway.

In a human pharmacokinetic study, administration of bupropion increased plasma levels of desipramine. This effect was present for at least 7 days after the last dose of bupropion. Concomitant therapy with medicines predominantly metabolised by this isoenzyme (such as certain beta blockers, antidysrhythmics, selective serotonin re-uptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), antipsychotics) should be initiated at the lower end of the dose range of the concomitant medicine. If PRODYNA XR is added to the treatment regimen of a patient already receiving a medication metabolised by CYP2D6, the need to decrease the dose of the original medication should be considered, particularly for those concomitant medications with a narrow therapeutic index (see section 5.2).

Citalopram:

Although citalopram is not primarily metabolised by CYP2D6, in one study, bupropion increased the C_{max} and area under the plasma concentration timed curve (AUC) of citalopram by 30 % and 40 %, respectively.

Medicines known to induce metabolism:

Since bupropion is extensively metabolised, the co-administration of medicines known to induce metabolism (e.g. carbamazepine, phenobarbitone, phenytoin) or inhibit metabolism may affect its clinical activity.

Ritonavir:

In a series of studies in healthy volunteers, ritonavir (100 mg twice daily or 600 mg twice daily) or ritonavir 100 mg plus lopinavir 400 mg twice daily, reduced the exposure of bupropion and its major metabolites in a dose dependent manner by approximately 20 - 80 %. This effect is thought to be due to the induction of bupropion metabolism. Patients receiving ritonavir may need increased doses of PRODYNA XR but the maximum recommended dose of PRODYNA XR should not be exceeded.

Alcohol:

There have been reports of adverse neuropsychiatric events or reduced alcohol tolerance in patients drinking alcohol during bupropion hydrochloride treatment. The consumption of alcohol during PRODYNA XR treatment should be minimised or avoided.

Levodopa or amantadine:

Limited clinical data suggest a higher incidence of adverse events in patients receiving concurrent administration of bupropion and levodopa. Administration of PRODYNA XR to patients receiving either levodopa or amantadine concurrently should be undertaken with caution.

Nicotine:

Concomitant use of PRODYNA XR and a nicotine transdermal system (NTS) may result in elevations of blood pressure.

Monoamine oxidase inhibitors (MAOIs):

Bupropion inhibits the reuptake of dopamine and noradrenaline (norepinephrine). Concomitant use of monoamine oxidase inhibitors (MAOIs) and bupropion is contraindicated because there is an increased risk of hypertensive reactions if bupropion is used concomitantly with MAOIs. At least 14 days should elapse between discontinuation of an MAOI intended to treat depression and initiation of treatment with PRODYNA XR. Conversely, at least 14 days should be allowed after stopping PRODYNA XR before starting a MAOI antidepressant.

Bupropion has been classified as possibly porphyrinogenic. It should be used only when no safe alternative is available, and precautions should be considered in vulnerable patients.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established.

Pregnancy

Epidemiological studies of pregnancy outcomes following maternal exposure to bupropion in the first trimester have reported an association with increased risk of some congenital cardiovascular malformations, including ventricular septal defects and left ventricular outflow tract defects. These findings are not consistent across studies.

Breastfeeding

As bupropion and its metabolites are excreted in human breast milk, mothers should be advised not to breastfeed while taking PRODYNA XR.

Fertility

There is no data on fertility with PRODYNA XR.

4.7 Effects on ability to drive and use machines

Patients should exercise caution before driving or use of machinery until they are reasonably certain PRODYNA XR tablets do not adversely affect their performance as dizziness, visual disturbances and hallucinations have been reported as occurring side effects.

4.8 Undesirable effects

Tabulated list of adverse effects

System Organ Class	**Frequency**	**Side effects**
Blood and lymphatic system disorders	Frequency unknown	Ecchymosis, anaemia, leukocytosis, leukopaenia, lymphadenopathy, pancytopaenia, and thrombocytopaenia, altered prothrombin time (PT) and/or international normalised ratio (INR), associated with haemorrhagic or thrombotic complications, when co-administered with warfarin

Immune system disorders	Frequent	Hypersensitivity reactions such as urticaria
	Less frequent	More severe hypersensitivity reactions including angioedema, dyspnoea/bronchospasm and anaphylactic shock, arthralgia, myalgia, fever, rash (symptoms resemble serum sickness)
Endocrine disorders	Frequency unknown	Hyperglycaemia, hypoglycaemia, syndrome of inappropriate antidiuretic hormone secretion
Metabolism and nutrition disorders	Frequent	Anorexia, weight loss
	Less frequent	Blood glucose disturbances
	Frequency unknown	Glycosuria

Psychiatric disorders	Frequent	Insomnia, agitation, anxiety
	Less frequent	Confusion, depression, aggression, hostility, irritability, restlessness, hallucinations, abnormal dreams, depersonalisation, delusions, paranoid ideation
	Frequency unknown	Suicide attempt

Nervous system disorders	Frequent	Headache, tremor, dizziness, taste disorders
	Less frequent	Concentration disturbances, seizures (see section 4.4), dystonia, ataxia, parkinsonism, incoordination, memory impairment, paraesthesia, syncope
	Frequency unknown	Emotional lability, derealisation, euphoria, abnormal coordination, hyperkinesia, hypertonia, hyperesthesia, vertigo, amnesia, abnormal electroencephalogram (EEG), akinesia, aphasia, coma, dysarthria, dyskinesia, extrapyramidal syndrome, hypokinesia, increased libido, neuralgia, neuropathy, unmasking tardive dyskinesia

Eye disorders	Frequent Frequency unknown	Visual disturbance Accommodation abnormality, dry eye, increased intraocular pressure angle-closure glaucoma, mydriasis
Ear and labyrinth disorders	Frequent Frequency unknown	Tinnitus Deafness
Cardiac disorders	Less frequent Frequency unknown	Tachycardia, palpitations complete atrioventricular block, extrasystoles, myocardial infarction
Vascular disorders	Frequent Less frequent Frequency unknown	Increased blood pressure (sometimes severe), flushing Vasodilation, postural hypotension Hypertension, stroke, phlebitis, pulmonary embolism

Respiratory, thoracic and mediastinal disorders	Frequency unknown	Bronchospasm, pneumonia
Gastrointestinal disorders	Frequent	Dry mouth, gastrointestinal disturbance including nausea and vomiting, abdominal pain, constipation
	Frequency unknown	Gastric reflux, stomatitis, thirst, colitis, esophagitis, gastrointestinal haemorrhage, intestinal perforation, stomach ulcer
Hepatobiliary disorders	Less frequent	Elevated liver enzymes, jaundice, hepatitis
	Frequency unknown	Abnormal liver function, liver damage, pancreatitis

Skin and subcutaneous tissue disorders	Frequent Less frequent Frequency unknown	Rash, pruritus, sweating Erythema multiforme and Stevens-Johnson syndrome Maculopapular rash, alopecia, angioedema, exfoliative dermatitis and hirsutism
Musculoskeletal, connective tissue and bone disorders	Less frequent Frequency unknown	Twitching Leg cramps, fever/rhabdomyolysis, and muscle weakness
Renal and urinary disorders	Less frequent Frequency unknown	Urinary frequency and/or retention Dysuria, urinary incontinence, cystitis
Reproductive system and breast disorders	Frequency unknown	Impotence, prostate disorder, abnormal ejaculation, dyspareunia, gynaecomastia, menopause, painful erection, salpingitis, vaginitis

General disorders and administrative site conditions	Frequent Frequency unknown	Fever, asthenia, chest pain Bruxism, gingivitis, glossitis, increased salivation, mouth ulcers, oedema of tongue, gum haemorrhage

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. Healthcare professionals are.

requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website. An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of PRODYNA XR.

4.9 Overdose

Signs and symptoms

Drowsiness, loss of consciousness and ECG changes such as conduction disturbances (including QRS prolongation) or dysrhythmias.

Acute ingestion of doses more than 10 times the maximum therapeutic dose has been reported.

Management of overdose

In the event of overdose, hospitalisation is advised.

ECG and vital signs should be monitored.

Ensure an adequate airway, oxygenation and ventilation. The use of activated charcoal is recommended. No specific antidote for bupropion is known.

Further management should be as clinically indicated or as recommended by the national poisons centre, where

available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antidepressants

ATC code: N06AX12

Pharmacological classification: A.1.2 Psychoanaleptics (antidepressants)

Bupropion is an inhibitor of the neuronal re-uptake of catecholamines (noradrenaline (norepinephrine) and dopamine) with minimal effect on the re-uptake of indolamines (serotonin) and does not inhibit monoamine oxidase. The mechanism of action of bupropion is unknown.

5.2 Pharmacokinetic properties

Absorption

Following oral administration of bupropion tablets to healthy volunteers, time to peak plasma concentrations for bupropion was approximately 5 hours. The absorption of bupropion is not significantly affected when taken with food. Bupropion and its metabolites exhibit linear kinetics following chronic administration of 150 - 300 mg per day.

Distribution

Bupropion is widely distributed with an apparent volume of distribution of approximately 2000 L. Bupropion and hydroxybupropion are moderately bound to plasma proteins (84 % and 77 %, respectively).

The extent of protein binding of the threohydrobupropion metabolite is about half that seen with bupropion.

Biotransformation

Bupropion is extensively metabolised in humans. Three pharmacologically active metabolites have been

identified in plasma: hydroxybupropion and the amino-alcohol isomers, threohydrobupropion and erythrohydrobupropion. These have clinical importance, as their plasma concentrations are as high as or higher than those of bupropion.

Peak plasma concentrations of hydroxybupropion occur approximately 7 hours following administration of bupropion.

Erythrohydrobupropion cannot be measured in the plasma after a single dose of bupropion. The active metabolites are further metabolised to inactive metabolites and excreted in the urine.

In vitro studies indicate that bupropion is metabolised to its major active metabolite hydroxybupropion primarily by CYP2B6, while cytochrome P450s are not involved in the formation of threohydrobupropion (see section 4.5).

Bupropion and hydroxybupropion are both relatively weak competitive inhibitors of the CYP2D6 isoenzyme with K_i values of 21 and 13,3 μM (micrometers), respectively. In human volunteers known to be extensive metabolisers of the CYP2D6 isoenzyme, co-administration of bupropion and desipramine has resulted in 2- and 5-fold increases in the C_{max} and AUC, respectively, of desipramine. This effect was present for at least 7 days after the last dose of bupropion. Since bupropion is not metabolised by the CYP2D6 pathway, desipramine is not anticipated to affect the pharmacokinetics of bupropion. Caution is advised when bupropion is administered with substrates for the CYP2D6 pathway (see section 4.5).

In humans, there is no evidence of enzyme induction of bupropion or hydroxybupropion in volunteers or patients receiving recommended doses of bupropion for 10 - 45 days.

Elimination

Following oral administration of 200 mg of $_{14}$C-bupropion in humans, 87 % and 10 % of the radioactive dose were recovered in the urine and faeces, respectively. The fraction of the dose of bupropion excreted unchanged was only 0,5 %, a finding consistent with the extensive metabolism of bupropion. Less than 10 % of this ^{14}C dose

was accounted for in the urine as active metabolites.

The mean apparent clearance following oral administration of bupropion is approximately 200 L/hr and the mean elimination half-life of bupropion is approximately 20 hours.

The elimination half-life of hydroxybupropion is approximately 20 hours and its area under the plasma drug concentration versus time curve (AUC) at steady state is approximately 17 times that of bupropion. The elimination half-lives for threohydrobupropion and erythrohydrobupropion are longer (37 and 33 hours, respectively) and steady-state AUC values are 8 and 1,6 times higher than that of bupropion, respectively. Steady-state for bupropion and its metabolites is reached within 8 days.

Pharmacokinetics in special patient groups

Elderly

Pharmacokinetic studies in the elderly have shown variable results. A single dose study showed that the pharmacokinetics of bupropion and its metabolites in the elderly do not differ from those in the younger adults. Another pharmacokinetic study, single and multiple doses, has suggested that accumulation of bupropion and its metabolites may occur to a greater extent in the elderly. Clinical experience has not identified differences in tolerability between elderly and younger patients, but greater sensitivity in older patients cannot be ruled out.

Patients with renal impairment

The elimination of bupropion and its major metabolites may be reduced by impaired renal function (see section 4.4).

Patients with hepatic impairment

The pharmacokinetics of bupropion and its active metabolites were not statistically significantly different in patients with mild cirrhosis (Child-Pugh grade A, range 5 - 6) when compared to healthy volunteers, although more variability was observed between individual patients. For patients with moderate to severe hepatic cirrhosis (Child-Pugh grades B and C, range 7 - 13), a single dose of bupropion produced a C_{max} and AUC that were

substantially increased (mean difference approximately 70 % and 3-fold, respectively) and more variable when compared to the values in healthy volunteers; the mean half-life was also longer (by approximately 40 %). For the metabolites, the mean C_{max} was lower (by approximately 30% - 70 %), the mean AUC tended to be higher (by approximately 30% - 50 %), the median T_{max} was later (by approximately 20 hrs), and the mean half-lives were longer (by approximately 2 to 4-fold) than in healthy volunteers (see section 4.3).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cores:

Glyceryl behenate

Hydrophobic colloidal silica

L-cysteine hydrochloride monohydrate

Polyvinyl alcohol

Coating:

Colloidal silicon dioxide

Dibutyl sebacate

Ethyl cellulose

Hydroxypropyl cellulose

Methacrylic acid copolymer dispersion

Povidone

Triethyl citrate

Imprinting ink – Opacode black:

Ammonium hydroxide

Iron oxide black

Isopropyl alcohol

N-butyl alcohol

Propylene glycol

Shellac glaze

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

150 mg:

30's: White opaque 100 mL HDPE bottle containing 30 tablets along with one molecular sieve 1 g sachet, one activated carbon 1 g sachet and one StabilOx® strip form sachet closed with white child resistant closure.

90's: White opaque 150 mL HDPE bottle containing 90 tablets along with one molecular sieve 1 g sachet, one activated carbon 1 g sachet and one StabilOx® strip form sachet closed with white child resistant closure.

500's: White opaque 500 mL HDPE bottle containing 500 tablets along with one molecular sieve 5 g sachet, one activated carbon 5 g sachet and one StabilOx® strip form sachet closed with white non child resistant closure.

300 mg:

30's: White opaque 100 mL HDPE bottle containing 30 tablets along with one molecular sieve 1 g sachet, one

activated carbon 1 g sachet and one StabilOx® strip form sachet closed with white child resistant closure.

90's: White opaque 250 mL HDPE bottle containing 90 tablets along with one molecular sieve 1 g sachet, one activated carbon 1 g sachet and one StabilOx® strip form sachet closed with white child resistant closure.

500's: White opaque 500 mL HDPE bottle containing 500 tablets along with one molecular sieve 5 g sachet, one activated carbon 5 g sachet and one StabilOx® strip form sachet closed with white non child resistant closure.

*Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

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8. REGISTRATION NUMBER(S)

PRODYNA 150 mg XR: A54/1.2/0181

PRODYNA 300 mg XR: A54/1.2/0182

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27 June 2023

10. DATE OF REVISION OF THE TEXT

15 November 2024