SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

SOMNAPAM TABLET

1. Name of the medicinal product

Somnapam Tablets (Nitrazepam BP 5mg)

2. Qualitative and quantitative composition

Each tablet contains:

Nitrazepam BP	5mg

Excipients:

Nipagin (Methyl Paraben)	0.36mg
Nipasol (Propyl Paraben)	0.18mg
Dicalcium Phosphate	444.50mg
Corn Starch (Bulk)	113.10mg
Corn Starch (Paste)	55.00mg
Talcum	2.00mg
Magnesium Stearate	3.00mg
Purified Water	q.s

For the full list of excipients, see Section 6.1.

3. Pharmaceutical form

Tablets

White circular shaped tablet with ‘SOMNAPAM’ inscribed on one side and ‘O’ on the other side presented in a blister strips of 2 x 10 per pack. 10 of such packs are packed into a carton with insert

4. Clinical particulars

4.1 Therapeutic indications

Nitrazepam Tablets should be used for short term treatment of insomnia only when it is severe, disabling, or subjecting the individual to extreme distress, where daytime sedation is acceptable.

4.2 Posology and method of administration

Treatment should be as short as possible and should be started with the lowest effective dose. The maximum dose should not be exceeded. Generally the duration of treatment varies from a few days to two weeks, with a maximum of four weeks; including the tapering off process. Dosage should be adjusted on an individual basis. If possible, the treatment should be on an intermittent basis. Long-term chronic use is not recommended.

Adults: 5 mg before retiring. This dose may be increased, if necessary, to 10 mg.

Children below the age of 12 years: Do not use.

Elderly and debilitated patients: 2.5 – 5 mg before retiring, doses should not exceed half those normally recommended for adults.

In patients with chronic pulmonary insufficiency, and in patients with chronic renal or hepatic disease, dosage may need to be reduced.

Further details are given in Section 4.4 Special warnings and precautions for use, Duration of treatment.

Method of administration: For oral administration.

4.3 Contraindications

• Patients with known hypersensitivity to benzodiazepines or any of the excipients (see Section 6.1).

• Hypersensitivity reactions with benzodiazepines include rash, angioedema and hypertension been reported on rare occasions in susceptible patients.

• Acute pulmonary insufficiency, respiratory depression, as ventilatory failure may be exacerbated

• Acute Porphyria

• Myasthenia gravis, as the condition may be exacerbated

• Sleep apnoea syndrome, as the condition may be exacerbated

• Severe hepatic insufficiency (elimination half-life of nitrazepam may be prolonged).

• Phobic or obsessional states and chronic psychosis

• Use in children.

• Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 Special warnings and precautions for use

Nitrazepam tablets should not be used alone to treat depression or anxiety with depression, since suicide may be precipitated in such patients.

In patients with chronic pulmonary insufficiency, and in patients with chronic renal or hepatic disease, dosage may need to be reduced. Benzodiazepines are contraindicated in patients with severe hepatic insufficiency.

Benzodiazepines are not recommended for the primary treatment of psychotic illness. If the patient is awoken during the period of maximum drug activity, recall may be impaired.

In cases of loss or bereavement, psychological adjustment may be inhibited by benzodiazepines.

Insomnia

An underlying cause for insomnia should be sought before deciding upon the use of benzodiazepines for symptomatic relief.

Tolerance

Some loss of efficacy, due to the hypnotic effects of benzodiazepines, may develop after repeated use for a few weeks.

Dependence (including use with alcohol) and withdrawal

Use of benzodiazepines may lead to the development of physical and psychological dependence upon these products. The risk of dependence increases when high doses are used, especially when given over long periods. This is particularly so in patients with a history of alcoholism or drug abuse or in patients with marked personality disorders.

Regular monitoring in such patients is essential; routine repeat prescriptions should be avoided and treatment should be withdrawn gradually. Symptoms such as depression, headaches, muscle weakness, nervousness, extreme anxiety, tension, restlessness, confusion, mood changes, rebound insomnia, irritability, sweating, and diarrhoea have been reported following abrupt cessation of treatment in patients receiving even normal therapeutic doses for short periods of time.

When benzodiazepines with a long duration of action are being used it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact and hallucinations or epileptic seizures. In rare instances, withdrawal following excessive dosages may produce confusional states and psychotic manifestations and convulsions. Abuse of the benzodiazepines has been reported.

Rebound insomnia and anxiety

This is a transient syndrome that may occur on withdrawal of treatment whereby the symptoms that led to treatment with a benzodiazepine recur in an enhanced form. It may be accompanied by other reactions including mood changes, anxiety or sleep disturbances and restlessness. Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage is decreased gradually.

Duration of treatment

The duration of treatment should be as short as possible (see 4.2 Posology and method of administration) depending on the indication, but should not exceed 4 weeks for insomnia, including tapering off process. Extension beyond these periods should not take place without re-evaluation of the situation. Routine prescriptions should therefore be avoided.

It may be useful to inform the patient when treatment is started that it will be of limited duration and to explain precisely how the dosage will be progressively decreased. Moreover it is important that the patient should be aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms should they occur while the medicinal product is being discontinued.

There are indications that, in the case of benzodiazepines with a short duration of action, withdrawal phenomena can become manifest within the dosage interval, especially when the dosage is high.

When benzodiazepines with a long duration of action are being used it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

Amnesia

Benzodiazepines may induce anterograde amnesia. The condition occurs most often one to two hours after taking the product and may last several hours, therefore to reduce the risk patients should ensure that they will be able to have an uninterrupted sleep of 7-8 hours.

Psychiatric and paradoxical reactions

Extreme caution should be used in prescribing nitrazepam to patients with personality disorders.

Reactions like restlessness, agitation, irritability, aggressiveness, excitement, confusion, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects (such as the uncovering of depression with suicidal tendencies) are known to occur when using benzodiazepines. These reactions may be quite severe and are more likely to occur in the elderly and children. Should this occur, use of the medicinal product should be discontinued.

Specific patient groups

Due to the myorelaxant effect there is a risk of falls and consequently of hip fractures particularly for elderly patients when they get up at night.

Hypoalbuminaemia (may predispose patient to higher incidence of sedative side effects).

Care should be exercised in patients with epilepsy since there have been reports of rare paradoxical exacerbation of seizures in these patients (see Section 4.5).

Care should be taken in patients with chronic renal or hepatic disease as the elimination half-life of nitrazepam may be prolonged.

4.5 Interaction with other medicinal products and other forms of interaction

Not recommended: Concomitant intake with alcohol.

The sedative effects may be enhanced when the product is used in combination with alcohol. This adversely affects the ability to drive or use machines.

Antipsychotics (neuroleptics), tranquillisers, hypnotics, analgesics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anti-epileptic products, anaesthetics, sedative antihistamines, lofexidine, and nabilone: Concomitant use may lead to enhancement of the central depressive effect. The elderly require special supervision.

Narcotic analgesics: Enhancement of the euphoric effect may also occur, leading to an increase in psychological dependence.

Anti-epileptic drugs: When used in conjunction with nitrazepam, side effects and toxicity may be more evident, particularly with hydantoins or barbiturates or combinations which include them. This requires extra care in adjusting dosage in the initial stages of treatment.

Dopaminergics: Concurrent use with benzodiazepines may decrease the therapeutic effects of levodopa.

Caffeine and theophylline: Concurrent use may result in reduced sedative and anxiolytic effects of nitrazepam.

Cimetidine, oestrogen-containing contraceptives, disulfiram: These medicines may inhibit hepatic metabolism of nitrazepam.

Antibacterials: Rifampicin may increase the metabolism of nitrazepam. Isoniazid may inhibit the metabolism of benzodiazepines.

Antivirals: Retonavir may inhibit benzodiazepine hepatic metabolism.

Antihypertensives: Enhanced hypotensive effects. Enhances sedative effect with alpha blockers or moxonidine.

4.6 Fertility, pregnancy and lactation

An increased risk of congenital malformations in humans has been associated with its use, particularly in the first and second trimesters.

If the product is prescribed to a woman of childbearing potential, she should be warned to contact her physician regarding discontinuance of the product if she intends to become or suspects that she is pregnant.

If, for compelling medical reasons, the product is administered during the late phase of pregnancy, or during labour at high doses, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected, due tothe pharmacological action of the compound. Irregularities to foetal heart and poor sucking in the neonate have also been reported.

Moreover, infants born to mothers who took benzodiazepines chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk for developing withdrawal symptoms in the postnatal period.

Since benzodiazepines are found in the breast milk, benzodiazepines should not be given to breast feeding mothers.

4.7 Effects on ability to drive and use machines

Patients should be advised that, like all medicines of this type, Nitrazepam tablets may modify patients' performance at skilled tasks. Sedation, amnesia, impaired concentration and impaired muscular function may adversely affect the ability to drive or to use machinery. If insufficient sleep duration occurs, the likelihood ofimpaired alertness may be increased (see Section 4.5). Patients should further be advised that alcohol may intensify any impairment, and should, therefore, be avoided during treatment.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

• This medicine is likely to affect how you drive

• Do not drive until you know how the medicine affects you

• It is an offence to drive while under the influence of this medicine

• However, you would not be committing an offence (called 'statutory defence') if:

o The medicine has been prescribed to treat a medical or dental problem and

o You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and

o It was not affecting your ability to drive safely

4.8 Undesirable effects

The following undesirable effects have been divided into the following categories: Very common: ≥1/10, Common: ≥1/100 to <1/10, Uncommon: ≥1/1,000 to <1/100 Rare: ≥1/10,000 to <1/1,000, Very rare: <1/10,000, Not known (cannot be estimatedfrom the available data).

Blood and the lymphatic system disorders	
Rare	Blood dyscrasias
Immune system disorders	

Very rare	Hypersensitivity reactions (anaphylaxis and angioedema)
Psychiatric disorders	
Uncommon	Confusion, sleeping disorders, including insomnia
Rare	Psychiatric and paradoxical reactions (1). Muscular cramps, libido fluctuations
Not known	Dependence and abuse of benzodiazepines, amnesia (2), symptoms (4)depression (3), withdrawal
Nervous system disorders	
Common	Dizziness, sedation, unsteadiness, ataxia, drowsiness, numbed emotions, reduced alertness, fatigue
Uncommon	Disturbances in attention, tremor
Rare	Dystonia, headache
Not known	Dysarthria
Eye disorders	
Rare	Visual disturbances
Not known	Double vision
Ear and labyrinth disorders	
Rare	Vertigo
Vascular disorders	
Rare	Hypotension
Respiratory, thoracic and mediastinal disorders	Respiratory depression
Rare	
Gastrointestinal disorders	
Rare	Nausea, gastrointestinal upsets
Hepato-biliary disorders	
Rare	Jaundice
Skin and subcutaneous tissue disorders	
Rare	Rash and other allergic skin reactions in the form of urticaria, pruritus, dermatitis, erythema multiforme, Stevens-Johnson syndrome
Renal and urinary disorders	
Rare	Urinary retention
Musculoskeletal, connective	

tissue and bone disorders	
Uncommon	Muscular weakness

1. Reactions such as restlessness, excitation, irritability, aggressiveness, delusions, rage, nightmares, hallucinations, psychoses, inappropriate behaviour and other behavioural side effects may occur during benzodiazepine treatment. They can be very serious with this product. These side effects are observed more frequently in elderly patients.

2. Anterograde amnesia may occur during the use of therapeutic doses since the risk is increased at higher doses. Amnesia may be combined with behavioural problems (see Section 4.4 Special warnings and precautions for use).

3. Existing depression may be revealed during the use of benzodiazepines (see also see Section 4.4 Special warnings and precautions for use).

4. Withdrawal effects on abrupt cessation of treatment – Depression, headaches, muscle weakness, nervousness, extreme anxiety, tension, restlessness, confusion, mood changes, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment. In rare cases, withdrawal following excessive dosages may produce confusional states, psychotic manifestations and convulsions.

   As with all benzodiazepines, withdrawal may be associated with physiological and psychological symptoms including depression.

   Reporting of suspected adverse reactions

   Reporting of 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 suspected adverse reactions via Yellow Card Scheme: www.mhra.gov.uk/yellowcard.

4.9 Overdose

As with other benzodiazepines, overdose should not present a threat to life unless combined with other CNS depressants (including alcohol).

In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken.

Symptoms

Overdose of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion, dysarthria and lethargy, in more serious cases, symptoms

may include ataxia, hypotonia, hypotension, respiratory depression, rarely coma and very rarely death.

Management

Vomiting should be induced (within one hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given in adults or children who have taken more than 1 mg/kg within one hour to reduce absorption provided they are not too drowsy.

Special attention should be paid to respiratory and cardiovascular functions in intensive care.

The value of dialysis has not been determined. Flumazenil, a benzodiazepine antagonist, may be useful as an antidote in emergency situations. Patients requiring such intervention should be monitored closely in hospital. Flumazenil is not indicatedin patients with epilepsy who have been treated with benzodiazepines. Antagonism of the benzodiazepine effect in such patients may trigger seizures.

If excitation occurs, barbiturates should not be used.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Hypnotics and Sedatives, Benzodiazepine derivatives,

ATC Code: N05CD02

Nitrazepam is a benzodiazepine compound with sedative properties. It acts in 30 to 60 minutes to produce sleep lasting six to eight hours.

5.2 Pharmacokinetic properties

Nitrazepam is well absorbed with peak blood levels being achieved within two hours after administration. Two hours after administration, the concentration of nitrazepam in the cerebrospinal fluid is about 8% and after 36 hours approximately 16% of the concentration in the plasma. The cerebrospinal fluid concentration thus corresponds to the non-protein-bound fraction of active ingredient in the plasma.

The half-life of Nitrazepam is on average 24 hours. Steady-state levels are achieved within five days. Nitrazepam undergoes biotransformation to a number of metabolites none of which possesses significant clinical activity.

About 5 % of metabolites are excreted unchanged in the urine together with less than 10% each of the 7-amino and 7-acetylamino metabolites in the first 48 hours. In younger persons the volume of distribution is 2L/kg, in elderly patients the volume of distribution is greater and the mean elimination half-life rises to 40 hours.

5.3 Preclinical safety data

There is no pre-clinical data of relevance to a prescriber, which is additional to that already included in other sections of the Summary of Product Characteristics.

6. Pharmaceutical particulars

6.1 List of excipients

Nipagin (Methyl Paraben)	0.36mg
Nipasol (Propyl Paraben)	0.18mg
Dicalcium Phosphate	444.50mg
Corn Starch (Bulk)	113.10mg
Corn Starch (Paste)	55.00mg
Talcum	2.00mg
Magnesium Stearate	3.00mg
Purified Water	q.s

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months in Blister strips

6.4 Special precautions for storage

Store below 30^{o}C. Protect from light.

6.5 Nature and contents of container

The product is available in blister packs of 2 x 10 tablets.10 of such packs packed in outer carton with insert.

6.6 Special precautions for disposal and other handling

No special instruction necessary.

7. Applicant / Manufacturer:

Vitabiotics Nigeria Limited

35, Mobolaji Johnson Avenue,

Oregun Industrial Estate,

Ikeja, Lagos,

Nigeria.