SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

NIDASALL 200 (Tablets)

NIDASALL 400 (Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

NIDASALL 200: Each tablet contains metronidazole 200 mg

Contains sugar: Lactose 100 mg

NIDASALL 400: Each tablet contains metronidazole 400 mg

Contains sugar: Lactose 80 mg

3. PHARMACEUTICAL FORM:

NIDASALL 200: White, biconvexed, scored tablet.

NIDASALL 400: Yellow, biconvexed, scored tablet.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications

- Urogenital trichomoniasis
- non-specific vaginitis
- all forms of amoebiasis
- giardiasis
- acute ulcerative gingivitis (Vincent's)
- acute pericoronitis
- Treatment of infections in which anaerobic bacteria have been identified or are suspected as pathogens, particularly Bacteroides

fragilis and other species of Bacteroides and including other species for which metronidazole is bactericidal, such as fusobacteria, clostridia, eubacteria and anaerobic streptococci.

- **NIDASALL** has been used successfully for anaerobic infections in the following conditions: pelvic inflammatory disease and postoperative wound infections. Combined therapy is often indicated as there are usually mixed infections.
- Prevention of postoperative infections due to anaerobic bacteria:
    - Given before and after gynaecological surgery
    - Given before and after appendectomy
    - Given before and after colonic surgery

4.2 Posology and method of administration

The usual adult dose is:

Indication	**Duration in days**	**Adult dose**	**Children 7-10 years**	**Children 3-7 years***
UROGENITAL TRICHO-MONIASIS. Where re-infection is likely, in adults the consort should receive a similar course of treatment concurrently.	1	2 g as a single dose	-	
	7	200 mg three times daily or 400 mg twice daily	100 mg three times daily	100 mg twice daily

	2	800 mg in the morning and 1,2 g in the evening	-	
NON-SPECIFIC VAGINITIS	7	400 mg twice daily	-	
	Or 1	2 g as a single dose	-	
AMOEBIASIS a) Invasive intestinal disease in susceptible subjects.	5	800 mg three times daily	400 mg three times daily	200 mg four times daily
AMOEBIASIS b) Intestinal disease in less susceptible subjects and “chronic amoebic hepatitis”.	5 to 10	400 mg three times daily	200 mg three times daily	100 mg four times daily
AMOEBIASIS c) Amoebic liver abscess, also other forms of extra-intestinal amoebiasis.	5	400 mg three times daily	200 mg three times daily	100 mg four times daily
AMOEBIASIS (d) Symptomless cyst passers.	5 to 10	400 to 800 mg three times daily	200 to 400 mg three times daily	100 to 200 mg four

				times daily
GIARDIASIS A second course of treatment may be necessary for some patients two weeks after the end of the first course.	3	2 g once daily	1 g once daily	600 to 800 mg once daily
ACUTE ULCERATIVE GINGIVITIS	3	200 mg three times daily	100 mg three times daily	100 mg twice daily
ACUTE PERICORONITIS	3-7	200 mg three times daily	-	

*__NIDASALL__ is only recommended if the children in this age group can swallow tablets. Children who cannot swallow tablets should take Metronidazole suspension.

(__NIDASALL__ is not available in a suspension)

Anaerobic infections

a) Treatment:

__NIDASALL__ may be given alone or concurrently with other bacteriologically appropriate antibacterial agents. They should be given for 7 days or longer depending on clinical and bacteriological assessments of the patient's condition.

Adults: Initially, 800 mg followed by 400 mg by mouth every 8 hours.

Children: 7,5 mg/kg body mass by mouth every 8 hours.

b) Prevention:

Adults: Administered in doses similar to those used for the treatment of established infection. 400 mg may be given every 8 hours in the 24 hours before surgery followed postoperatively by intravenous or rectal administration until oral therapy is possible.

Children: as for treatment (a).

Method of administration

The tablets should be taken with or after food

4.3 Contraindications

- Hypersensitivity to metronidazole and other imidazoles.
- Co-administration with busulfan (see section 4.4).

4.4 Special warnings and precautions for use

- Patients should be advised not to take alcohol during **NIDASALL** therapy and for at least one to three days afterwards because of the possibility of a disulfiram-like reaction (see section 4.5).
- Co-administration with busulfan: As plasma levels of busulfan may be increased significantly, it may lead to severe busulfan toxicity and death.
- Pseudomembranous colitis has been reported with the use of **NIDASALL**.
- Studies have shown **NIDASALL** to be mutagenic in bacteria and carcinogenic in some animals.

- **NIDASALL** should be administered with caution to patients with hepatic encephalopathy.
- **NIDASALL should be used with great care in patients with blood dyscrasias or with active or chronic disease of the central and peripheral nervous system.**
- All patients receiving **NIDASALL** for more than 10 days should be monitored and treatment discontinued if signs of peripheral neuropathy or central nervous system toxicity develop. Doses should be reduced in patients with severe liver disease.
- **NIDASALL** has anti-treponemal activity and may mask the immunological response seen in untreated early syphilis; contacts of syphilis receiving **NIDASALL** should probably be screened for an additional 4 to 8 weeks.
- Patients should be warned that **NIDASALL** may darken urine (due to metronidazole metabolite).

NIDASALL film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose -galactose malabsorption should not take **NIDASALL**.

4.5 Interaction with other medicines and other forms of interaction

Disulfiram:

Acute psychoses or confusion have been associated with the concomitant use of **NIDASALL** and disulfiram.

Alcohol:

When given in conjunction with alcohol, **NIDASALL** may provoke a disulfiram-like reaction in some individuals (effects include intense vasodilation and flushing of the face and neck, restlessness, anxiety, tachycardia, tachypnoea, headache, nausea, vomiting, hyperpnoea, chest pains, sweating, pallour and hypotension); reactions have occurred after the administration of pharmaceutical preparations formulated with alcohol, including injections, as well as after drinking alcohol.

Alcoholic beverages and medicine containing alcohol should not be consumed during therapy and for at least 1 to 3 days afterwards (see section 4.4).

Oral anticoagulant therapy (warfarin type):

Potentiation of the anticoagulant effect and increased haemorrhagic risk. In case of co-administration with warfarin, prothrombin time/INR should be more frequently monitored and warfarin therapy/dose adjusted during treatment with **NIDASALL**.

Lithium:

Plasma levels of lithium may be increased by **NIDASALL**. Plasma concentrations of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive **NIDASALL**.

Ciclosporin:

Risk of elevation of ciclosporin serum levels. Serum ciclosporin and serum creatinine should be closely monitored when co-administration is necessary.

Phenytoin or phenobarbital:

There is evidence that phenytoin might accelerate the metabolism of **NIDASALL**.

Plasma concentrations of **NIDASALL** are decreased by the concomitant administration of phenobarbital, with a consequent reduction in the effectiveness of **NIDASALL**.

5-Fluorouracil:

Reduced clearance of 5-fluorouracil resulting in increased toxicity of 5-fluorouracil may occur.

Busulfan:

Plasma levels of busulfan may be increased by **NIDASALL**, which may lead to severe busulfan toxicity and death (see section 4.3 and 4.4).

Cimetidine:

Hepatic metabolism may be decreased when **NIDASALL** and cimetidine are used concurrently, possibly resulting in delayed elimination and increased serum metronidazole concentrations with an increased risk of neurological side effects.

4.6 Fertility, pregnancy, and lactation

Pregnancy

Safety in pregnancy and lactation has not been established.

Breastfeeding

NIDASALL crosses the placental barrier and is excreted in breast milk.

Women using **NIDASALL** should not breastfeed their infants.

4.7 Effects on the ability to drive and use machines

Patients should be warned about the potential for confusion, dizziness, hallucinations, convulsions or eye disorders (see section 4.8), and advised not to drive or operate machinery if these symptoms occur.

4.8 Undesirable effects

Blood and the lymphatic system disorders:

Less frequent: Agranulocytosis, neutropenia and thrombocytopenia

Frequency unknown: Leucopenia

Immune system disorders:

Less frequent: Anaphylaxis

Frequency unknown: Angioedema, urticaria

Metabolism and nutrition disorders:

Frequency unknown: Anorexia

Psychiatric disorders:

Less frequent: Psychotic disorders including confusion, irritability and hallucinations, changes in mood or mental state such as depression or confusion

Nervous system disorders:

Less frequent: Weakness, dizziness, drowsiness, insomnia, cases of encephalopathy (e.g. confusion) and subacute cerebellar syndrome (e.g. ataxia dysathria, gait impairment, nystagmus and tremor), which may resolve with discontinuation of the medicine

Frequency unknown: Peripheral neuropathy, usually presenting as numbness or tingling in the extremities, and epileptiform seizures are serious

adverse effects on the nervous system that have been associated especially with high doses of **NIDASALL** or prolonged treatment

Eye disorders:

Less frequent: The occurrence of transient vision disorders such as diplopia and myopia may follow the use of **NIDASALL**.

Respiratory, thoracic and mediastinal disorders:

Frequency unknown: Nasal congestion

Gastrointestinal disorders:

Frequent: Gastrointestinal disturbances, especially nausea and taste disorders; nausea is sometimes accompanied by headache, and vomiting. Diarrhoea, dry mouth, a furred tongue, oral mucositis and stomatitis

Less frequent: Pseudomembranous colitis

Hepato-biliary disorders:

Less frequent: Increase in liver enzymes (AST, ALT, alkaline phosphatase) and cholestatic hepatitis sometimes with jaundice

Frequency unknown: Pancreatitis and raised liver enzyme values

Skin and subcutaneous tissue disorders:

Less frequent: Pustular eruptions, mild erythematous eruptions with fleeting joint pains resembling serum sickness

Frequency unknown: Skin rashes, flushing, and pruritus

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown: Myalgia and arthralgia

Renal and urinary disorders:

Less frequent: Urethral discomfort and darkening of the urine

General disorders and administration site conditions:

Frequency unknown: Fever

Post marketing experience:

The adverse effects listed below are based on data from post-marketing experience:

Nervous system disorders:

- Headache, aseptic meningitis

Eye disorders:

- Transient vision disorders such as blurred vision, decreased visual acuity, changes in colour vision
- Optic neuropathy/neuritis

Gastrointestinal disorders:

- Epigastric pain

Hepato-biliary disorders

- Mixed hepatitis and hepatocellular liver injury
- Cases of liver failure requiring liver transplant have been reported in patients treated with **NIDASALL** in combination with other antibiotic medication

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 drug reactions to SAHPRA

via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Innovata Pharmaceuticals Contact Details: regulatory@innovata.co.za

HOTLINE for reporting of side effects directly to Innovata Pharmaceuticals (Pty) Ltd: 086 999 0912

4.9 Overdose

Treatment is symptomatic and supportive.

5. Pharmacological properties

5.1 Pharmacodynamic properties

A 20.2.6 - Medicines against protozoa

Metronidazole has antiprotozoal activity against Trichomonas vaginalis and other protozoa, including Entamoeba histolytica and Giardia lamblia. It does not affect the acidophilic flora of the vagina and it has no effect on Candida species. Metronidazole has bactericidal activity against obligate anaerobic bacteria, whether they are Gram-positive or -negative and bacilli or cocci. It has no antibacterial activity against aerobic and facultative anaerobic bacteria. Metronidazole does not interfere with the activity of antibacterial agents which are active against a variety of aerobes and facultative anaerobes.

The following has been proposed as the mode of action of metronidazole: The parent compound penetrates the cell membrane unchanged, but once inside the cell the nitro group is reduced in the redox conditions prevalent in the anaerobic cell.

The reduced product is known to damage DNA causing eventual death of the organism.

5.2 Pharmacokinetic properties

Metronidazole is absorbed from the gastrointestinal tract and widely distributed in body tissues. Approximately 30-40 % of a dose is metabolised in the liver and excreted in the urine, together with the unchanged compound. Metronidazole is able to pass the blood-brain barrier. It reaches therapeutic concentrations in most other body fluids, i.e. saliva, bile, urine, amniotic fluid, breast milk and in abscess cavities.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose, maize starch, magnesium stearate, pregelatinised maize starch, purified talc, quinoline yellow.

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months from manufacture.

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light and moisture.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Nidasall 400: Securitainer containing 100 or 500 tablets.

"Ziploc' patient ready L.D.P.E. plastic bags of different pack sizes (5, 14 or 21 tablets).

Nidasall 200: Securitainer containing 250 tablets.

"Ziploc' patient ready L.D.P.E. plastic bags of different pack sizes (21 or 28 tablets).

6.6 Special precautions for disposal and other handling

7. Holder of certificate of registration

Innovata Pharmaceuticals

Crownwood Office Park

100 Northern Parkway

Ormonde

Johannesburg

2091

South Africa

8. Registration numbers

400 mg Tablets: 28/20.2.6/0037

200 mg Tablets: 28/20.2.6/0036

9. Date of first authorization/Renewal of the authorization

October 2020

10. Date of revision of the text

22/10/2025