

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

AMODIS SUSPENSION 200mg/5ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of suspension contains Metronidazole Benzoate equivalent to Metronidazole 200 mg.

Excipient(s) with known effect:

Sucrose: 1500mg/5ml

Liquid Sorbitol (Non-crystallizing): 500mg/5ml

Propylene Glycol: 100mg/5ml

Methyl Hydroxybenzoate: 4mg/5ml

Propyl Hydroxybenzoate: 1mg/5ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

A white to creamy white orange flavored suspension having sweet and slight bitter after taste, filled and sealed in amber PET bottle with "SQUARE" printed white cap. Free from any visible foreign particles

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amodis Suspension is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria have been identified or are suspected as the pathogen.

Amodis Suspension is active against a wide range of pathogenic micro-organisms, notably *Trichomonas vaginalis*, *Entamoeba histolytica*, *Giardia lamblia*, *Balantidium coli* and other species of bacteroides, fusobacteria, eubacteria, clostridia, gardnerella vaginalis and anaerobic cocci.

It is indicated in

Adults, children and new-borns with a gestation age of over 40 weeks for:

- The treatment of septicaemia, bacteraemia, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis, peritonitis and post-operative wound infections from which one or more pathogenic anaerobes have been isolated.
- The prevention of post-operative infections caused by anaerobic bacteria particularly species of bacteroides and anaerobic streptococci.

Adults and children over 10 years only for:

- Bacterial vaginosis (also known as non-specific vaginitis, anaerobic vaginitis or Gardnerella vaginitis).
- Acute dental infections (e.g. acute pericoronitis and acute apical infections).
- Anaerobically infected leg ulcers and pressure sores.

Adults and children for:

- The treatment of urogenital trichomoniasis in the female (trichomonal vaginitis) and in the male.
- All forms of amoebiasis (intestinal and extra-intestinal disease and that of symptomless cyst passers)
- Giardiasis
- Acute ulcerative gingivitis.

Children for

- Eradication of *Helicobacter pylori*

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

A: **Prophylaxis:** against anaerobic infection- chiefly in the context of abdominal (especially colorectal) and gynaecological surgery.

Dosage: 400mg at 8 hourly intervals during the 24 hours preceding the operation followed by postoperative intravenous or rectal administration until the patient is able to take Amodis Suspension by mouth.

Children < 12 years: 20 – 30mg/kg as a single dose given 1 – 2 hours before surgery. New-borns with a gestation age <40 weeks: 10mg/kg body weight as a single dose before operation.

Elderly: Caution is advised in the elderly, particularly at high doses, although there is limited information available on modification of drug.

Anaerobic infections: The duration of a course of Metronidazole treatment is about 7 days but it will depend upon the seriousness of the patient's condition as assessed clinically and bacteriologically.

B: Treatment of established anaerobic infection:

800mg followed by 400mg at 8 hourly intervals.

Children > 8 weeks to 12 years of age: The usual daily dose is 20 – 30mg/kg/day as a single dose or divided into 7.5mg/kg every 8 hours. The daily dose may be increased to 40mg/kg, depending on the severity of the infection. Duration of treatment is usually 7 days.

Children < 8 weeks of age: 15mg/kg as a single dose daily or divided into 7.5mg/kg every 12 hours.

In new-borns with a gestation age <40 weeks, accumulation of metronidazole can occur during the first week of life, which is why the concentrations of metronidazole in serum should preferably be monitored after a few days therapy.

C: Treatment of Protozoal and Other Infections:

(See Table).

	Duration of dosage in days	Adults and children over 10 years**	Children*		
			7-10 years	3-7 years	1-3 years
Urogenital Trichomoniasis Where re-infection is likely, in adults the consort should receive a similar course of treatment concurrently	7	200mg three times daily	40mg/kg orally as a single dose or 15 – 30mg/kg/day divided in 2 – 3 doses not to exceed 2000mg/dose		
	or				
	5-7	400mg twice daily			
Bacterial Vaginosis	or				
	1	2000mg as a single dose			
	5-7	400mg twice daily			
	or				
	1	2000mg 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	200 mg three times daily

(b) Intestinal disease in less susceptible subjects and chronic amoebic hepatitis	5-10	400 mg three times daily	200 mg three times daily	100 mg four times daily	100 mg three times daily
(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	100 mg three times daily
(d) Symptomless cyst passers	5-10	400-800 mg three times daily	200-400 mg three times daily	100-200 mg four times daily	100-200 mg three times daily
	Alternatively, doses may be expressed by body weight 35 to 50mg/kg daily in 3 divided doses for 5 to 10 days, not to exceed 2400mg/day				
Giardiasis	3 or	2000mg once daily	1000mg once daily	600-800mg once daily	500mg once daily
	5 or	400mg three times daily			
	7 - 10	500mg twice daily			
			Alternatively, as expressed in mg per kg of body weight: 15 – 40mg/kg/day divided in 2 – 3 doses.		
Acute Ulcerative Gingivitis	3	200mg three times daily	100mg three times daily	100mg twice daily	50mg three times
Acute Dental Infections	3-7	200mg three times daily			
Leg Ulcers and Pressure Sores	7	400mg three times daily			

Dosage is given in terms of metronidazole or metronidazole equivalent.

* Children and babies weighing less than 10Kg should receive proportionally smaller doses.

** Metronidazole is well tolerated by the elderly, but a pharmacokinetic study suggests cautious use of high dosage regimen in this age group.

Eradication of *Helicobacter pylori* in paediatric patients:

As a part of combination therapy, 20mg/kg/day not to exceed 500mg twice daily for 7– 14 days. Official guidelines should be consulted before initiating therapy.

Method of administration

For oral administration only.

Shake the bottle well before use.

If a dose of under 5ml is required, the suspension should be administered using an oral dosing device.

4.3 Contraindications

Known hypersensitivity to metronidazole, nitroimidazoles and/or hydroxybenzoates or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use

Regular clinical and laboratory monitoring (especially leucocyte count) are advised if administration of Metronidazole for more than 10 days is considered to be necessary and patients should be monitored for adverse reactions such as peripheral or central neuropathy (such as paraesthesia, ataxia, dizziness, convulsive seizures).

There is the possibility that after *Trichomonas vaginalis* has been eliminated a gonococcal infection might persist.

The elimination half-life of metronidazole remains unchanged in the presence of renal failure. The dosage of metronidazole therefore needs no reduction. Such patients however, retain the metabolites of metronidazole. The clinical significance of this is not known at present.

In patients undergoing haemodialysis, metronidazole and metabolites are efficiently removed during an eight-hour period of dialysis. Metronidazole should therefore, be re-administered immediately after haemodialysis.

No routine adjustment in the dosage of Metronidazole need be made in patients with renal failure undergoing intermittent peritoneal dialysis (IPD) or continuous ambulatory peritoneal dialysis (CAPD).

Metronidazole is mainly metabolised by hepatic oxidation. Substantial impairment of metronidazole clearance may occur in the presence of advanced hepatic insufficiency.

Significant cumulation may occur in patients with hepatic encephalopathy and the resulting high plasma concentrations of metronidazole may contribute to the symptoms of encephalopathy.

Metronidazole should be administered with caution to patients with hepatic encephalopathy. The daily dosage may be reduced to one third and may be administered once daily.

Metronidazole should be used with caution in patients with active or chronic severe peripheral and central nervous system disease due to the risk of neurological aggravation.

Patients should be warned that metronidazole may darken urine.

Due to inadequate evidence on the mutagenicity risk in humans (see section 5.3), the use of Metronidazole for longer treatment than usually required should be carefully considered.

Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome with very rapid onset after treatment initiation in patients with Cockayne syndrome have been reported with products containing metronidazole for systemic use. In this population, metronidazole should therefore be used after careful benefit- risk assessment and only if no alternative treatment is available. Liver function tests must be performed just prior to the start of therapy, throughout and after end of treatment until liver function is within normal ranges, or until the baseline values are reached. If the liver function tests become markedly elevated during treatment, the drug should be discontinued.

Patients with Cockayne syndrome should be advised to immediately report any symptoms of potential liver injury to their physician and stop taking metronidazole.

Cases of severe bullous skin reactions such as Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) or acute generalised exanthematous pustulosis (AGEP) have been reported with metronidazole. If symptoms or signs of SJS, TEN or AGEP are present, treatment with metronidazole must be immediately discontinued.

Excipient Warnings

This medicine contains 100 mg sorbitol in each ml.

- The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.
- Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

This medicine contains 300 mg of sucrose in each ml. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase- isomaltase insufficiency should not take this medicine.

This medicine contains 100 mg of Liquid Glucose in each ml.

This medicine contains 20 mg propylene glycol in each ml.

- Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce adverse effects in children less than 5 years old.
- While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis.
- Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

This medicine contains Methyl Hydroxybenzoate which may cause allergic reactions (possibly delayed).

This medicine contains less than 1 mmol sodium (23 mg) per 5ml, that is to say essentially 'sodium-free'.

Unsuitable for phenylketonurics.

4.5 Interaction with other medicinal products and other forms of interactions

Patients should be advised not to take alcohol during metronidazole therapy and for at least 48 hours afterwards because of the possibility of a disulfiram-like (antabuse effect) reaction.

Psychotic reactions have been reported in patients who were using metronidazole and disulfiram concurrently.

Some potentiation of anticoagulant therapy has been reported when metronidazole has been used with the warfarin type oral anti-coagulants. Dosage of the anticoagulant may require reducing. Prothrombin time should be monitored. No interactions have been reported of the heparin type.

Lithium retention accompanied by evidence of possible renal damage has been reported in patients treated simultaneously with lithium and metronidazole. Lithium treatment should be tapered or withdrawn before administering metronidazole. Plasma concentration of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

Patients receiving phenobarbital or phenytoin metabolise metronidazole at a much greater rate than normally, reducing the half life to approximately three hours.

Increased serum carbamazepine levels and toxicity have been seen in patients given concomitant metronidazole.

Aspartate amino transferase assays may give spuriously low values in patients taking metronidazole, depending on the method used.

Clinicians who contemplate continuous therapy for the relief of chronic conditions, for periods no longer than those recommended, are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Metronidazole reduces the clearance of 5-fluorouracil and can therefore result in increased toxicity of 5-fluorouracil.

Patients receiving ciclosporin or tacrolimus with metronidazole are at risk of elevated ciclosporin / tacrolimus serum levels. Serum ciclosporin / tacrolimus and serum creatinine should be closely monitored when coadministration is necessary.

Plasma levels of busulfan may be increased by metronidazole which may lead to severe busulfan toxicity.

4.6 Fertility, pregnancy and lactation

There is inadequate evidence of the safety of metronidazole in pregnancy. Metronidazole should not therefore be given during pregnancy or during lactation unless the physician considers it essential, in these circumstances short, high dosage regimes are not recommended.

A significant amount of metronidazole is found in breast milk and breast feeding should be avoided after a large dose. This could give a bitter taste to the milk.

4.7 Effects on ability to drive and use machines

Patients should be warned about the potential for drowsiness, dizziness, confusion, hallucinations, convulsions or transient visual disorders, and advised not to drive or operate machinery if these symptoms occur.

4.8 Undesirable effects

The frequency of adverse events listed below is defined using the following convention:

very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

Frequency, type and severity of adverse reactions in children are the same as in adults.

Serious adverse reactions occur very rarely with standard recommended regimens. However, clinicians who contemplate continuous therapy for the relief of chronic conditions, for periods longer than those recommended are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Blood and lymphatic system disorders:

Very rare: agranulocytosis, neutropenia, thrombocytopenia and pancytopenia, often reversible on drug withdrawal, although fatalities have occurred.

Not known: A moderate leucopenia has been reported in some patients but the white cell count has always returned to normal before or after treatment has been completed.

Immune system disorders:

Rare: Anaphylaxis.

Not known: urticaria, angioedema and fever.

Metabolism and nutrition disorders:

Not known: anorexia.

Psychiatric disorders:

Very rare: psychotic disorders, including confusion and hallucinations. Not known: depressed mood.

Nervous system disorders:

Very rare:

- Encephalopathy (eg. confusion, fever, headache, hallucinations, paralysis, light sensitivity, disturbances in sight and movement, stiff neck) and subacute cerebellar syndrome (eg. ataxia, dysarthria, gait impairment, nystagmus and tremor) have been reported very rarely which may resolve on discontinuation of the drug
- Drowsiness, dizziness, convulsions, headache, ataxia, inco-ordination of movement.

Not known:

- During intensive and/or prolonged metronidazole therapy a few instances of peripheral neuropathy or transient epileptiform seizures have been reported. In most cases neuropathy disappeared after treatment was stopped or when dosage was reduced.
- Aseptic meningitis has been reported.

Eye disorders:

Very rare: transient visual disorders such as diplopia and myopia have been reported.

Not known: Optic neuropathy/neuritis has been reported.

Ear and labyrinth disorders:

Not known: hearing impaired/hearing loss (including sensorineural), tinnitus.

Gastrointestinal disorders:

Not known: Unpleasant taste in the mouth, oral mucositis, furred tongue, nausea, vomiting, gastro-intestinal disturbances such as epigastric pain and diarrhoea.

Hepatobiliary disorders:

Very rare:

- Abnormal liver function tests, increase in liver enzymes (AST, ALT, alkaline phosphatase), cholestatic or mixed hepatitis, and hepatocellular liver injury, jaundice and pancreatitis, reversible on drug withdrawal have been reported.
- Cases of liver failure requiring liver transplant have been reported in patients treated with metronidazole in combination with other antibiotic drugs.

Skin and subcutaneous tissue disorders:

Very rare: skin rashes, pustular eruptions, acute generalised exanthematous pustulosis, pruritus, flushing.

Not known: Erythema multiforme may occur, which may be reversed on drug withdrawal. Stevens-Johnson syndrome or toxic epidermal necrolysis, fixed drug eruption.

Musculoskeletal, connective tissue and bone disorders:

Very rare: myalgia, arthralgia.

Renal and urinary disorders:

Very rare: darkening of the urine (due to metronidazole metabolite).

Amodis Suspension contains glycerol, which can cause headache, gastro-intestinal disturbance and diarrhoea.

The hydroxybenzoates used in Amodis Suspension may cause immediate or delayed hypersensitivity reactions.

4.9 Overdose

Single oral doses of metronidazole, up to 12 g have been reported in suicide attempts and accidental overdoses. Symptoms were limited to vomiting, ataxia and slight disorientation. There is no specific antidote for metronidazole overdose. In cases of suspected massive overdose, symptomatic and supportive treatment should be instituted.

5 PHARMACEUTICAL PROPERTIES

5.1 Pharmacodynamics properties

The selective action of this compound against anaerobes and anoxic and hypoxic cells is due to the mode of action. The nitro group of metronidazole acts as electron acceptor and is thus reduced to a chemically reactive drug form. This produces biochemical lesions in the cells, thus causing death. The major site of action is believed to be DNA, where it causes loss of the helical structure and inhibits synthesis.

5.2 Pharmacokinetic properties

It is readily absorbed from the gastro-intestinal tract and widely distributed in body tissues. Half life in plasma is about 8-10 hours. About 10% is bound to plasma proteins.

It penetrates well into body tissues and fluids, including vaginal secretions, seminal fluid, saliva and breast milk. Therapeutic concentrations are also achieved in cerebrospinal fluid.

Unchanged metronidazole and several metabolites are excreted in the urine, the liver is the main site of metabolism and the major metabolites are as a result of side chain oxidation, forming glucuronides.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Liquid Glucose
Dispersible Cellulose
Liquid Sorbitol (Non-crystallizing)
Propylene Glycol
Glycerol
Polysorbate 80
Methyl Hydroxybenzoate
Propyl Hydroxybenzoate
Aspartame
Orange Liquid (Sweet) Essence No.1 NA
Anhydrous Disodium Hydrogen Phosphate
Sodium Dihydrogen Phosphate Dihydrate
Purified Water q.s. to

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Please refer to expiry date on label/outer carton.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.
Use within 28 days after opening at temperature below 30°C.

6.5 Nature and contents of container

60 mL amber PET bottles with "SQUARE" printed white HDPE cap.

6.6 Special precautions for disposal

Shake the bottle well before use.

If a dose of under 5ml is required, the suspension should be administered using an oral dosing device.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MANUFACTURER

SQUARE PHARMACEUTICALS PLC.
Square Road, Salgaria, Pabna 6600,
Bangladesh

8 DATE OF REVISION OF THE TEXT

13 November 2025