**Summary of Product Characteristics**

## 1. Name of the medicinal Product

DYGYL-200

## 2. Qualitative and Quantitative Composition

### 2.2 Qualitative declaration

Metronidazole BP 200 mg

**Quantitative declaration**

For full list of Excipients, see section 6.1.

## 3. Pharmaceutical Form

Oral Dosage Form, Tablets

White coloured, round shaped, biconvex, break line on one side and plain on other side of film coated tablets.

Distribution Category: POM

The Score Line is not intended for division of the tablet should be swallowed whole.

## 4. Clinical Particulars

### 4.1 Therapeutic Indications

It is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria identified or are suspected to be the cause. It is active against a wide range of pathogenic micro-organisms notably spec ies of Bacteroides, Fusobacteria, Clostridia, Eubacteria, anaerobic cocci and Gardnerella vaginal is. It is also active against Trichomonas, Entamoeba histolytica, Giardia lambliaand Balantidium coli.

Metronidazole tablets is indicated in adults and children for the following indications:

Prevention of post-operative infections due to anaerobic bacteria, particularly species of bacteroids and anaerobic streptococci.

Septicaemia, bactcraemia, peritonitis, brain abscess, nccrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellu litis and post-operative wound infections from which pathogenic anaerobes isolated.

Urogenital trichomoniasis in the female (Trichomonal vaginalis), and in man.

Bacterial vaginosis (non-specific vaginitis, anaerobic vaginosis or Gardnerel lavaginitis).

All forms of amoebiasis (intestinal, extra- intestinal and asymptomatic cyst passers)

Giardiasis

Acute ulcerative gingivitis

Anaerobically- infected leg ulcers and pressure sores

Acute dental infections (eg. acute pericoronit is and acute apical infections)

### 4.2 Posology and Method of Administration

**Summary of Product Characteristics**

**Route of administration:** *Oral,* It is recommended that the tablets be taken during or after a meal. Should be swallowed with water (not chewed).

*Prophylaxis againsl anaerobic infection*: Chiefly in the context of abdominal (especially colorcctal) and gynaecological surgery.

Treatment of established anaerobic infection:

**Adults:** 800 mg followed by 400 mg 8 hourly.

**Children:**

**Children > 8 weeks to 12 years of age:** 20-30mg/kg/day as a single dose or divided into 7.5mglkg every 8 hours. The daily dose may be increased to 40mg/kg, depending on the severity of the infection. Durat ion 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 newborns with a gestation age < 40 weeks, accumulation of metron idazole can occur during the first week of life, therefore the concentrations of metronidazole in serum should preferable be monitored after a few days therapy.

**Protozoal and other infections:** Dosage is given in terms of metronidazole or metronidazole equivalent.

| **Infections** | **Dosage Schedule** | | | |
|---|---|---|---|---|
| | Adults and children over 10 years | Children | | |
| | | 7 - 10 years: | 3 - 7 years | 1 - 3 years |
| ***Urogenital Trichomoniasis*** | 10 tablets daily as a single dose for one day; or 1 tablet three times daily for seven days. Or 400 mg twice daily for 5- 7 days. | 40 mg/kg orally as a single dose or 15-30 mg/kg/day divided in 2-3 doses; not to exceed 2000 mg/dose. | | |
| **Bacterial vaginosis: Adults and children over 10 years**: 400 mg twice daily for 5- 7 days or 1 day 2000 mg as a single dose. | | | | |
| ***Amoebiasis*** Invasive intestinal Susceptible Patients | 800 mg three times daily for five days. | 400 mg three times daily | 200 mg four times daily | 200 mg three times daily |
| Intestinal disease in less susceptible subjects and chronic amoebic hepatitis | 400 mg three times daily for 5-10 days | 200 mg three times daily | 100 mg four times daily | 100 mg three times daily |
| Amoebic liver abscess also other forms of extra-intestinal amoebiasis | 400 mg three times daily for 5 days | 200 mg three times daily | 100 mg four times daily | 100 mg three times daily |

| | | | | |
|---|---|---|---|---|
| Symptomless cyst passers | 400-800 mg three times daily for 5-10 days | 200-400 mg three times daily | 100-200 mg four times daily | 100-200 mg three times daily |
| Giardiasis | 2000 mg once Daily for 3 days or 400 mg three times daily for 5 days or 500mg twice daily 7-10 days | 1000 mg once daily | 600-800 mg once daily | 500 mg once daily |
| | Alternatively, as expressed in mg per kg of body weight: 15-40 mg/kg/day divided in 2-3 doses. | | | |
| Dosage is given in terms of metronidazole or metronidazole equivalent | | | | |
| Acute ulcerative gingivitis | 200 mg three times daily for 3 days | 100 mg three times daily | 100 mg twice daily | 50 mg three times daily |
| Acute dental infections | 200 mg three times daily 3-7 days | - | | |
| Leg ulcers and pressure sores | 400 mg three times daily for 7 days | - | | |

Children and infants weighing less than 10 kg should receive proportionally smaller dosages.

**Elderly:** Metronidazole is well tolerated elderly, cautious should be taken for use of high dosage regimens in this age group.

Eradication of Helicobacter pylori in paediatric patients: a combination therapy, 20 mg/kg/ day not to exceed 500 mg twice daily for 7- 14 days. Official guidelines should be referred before initiating therapy.

### 4.3 Contraindications

Contraindicated in patients with known hypcrsensitivity to nitroimidazoles, metronidazole or any of the excipients.

### 4.4 Special Warnings and Special Precautions for Use:

**Significant guidance should be given on the appropriate use of Antibacterial agents.**

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.

Plasma concentrations of lithium, creat inine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole. Prothrombin times should be monitored.

Patients should be monitored for adverse reactions such as peripheral or central neuropathy (such as paraesthesia, ataxia, dizziness, and convulsive seizures). 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 suffer from severe hepatotoxicity/acute hepatic failure, an incurable outcome with very rapid onset after treatment initiation with cockayne syndrome may occur for systemic use. Patients should be advised to immediately report if any symptoms of cockayne syndrome and potentialliver injury to their physician and stop the therapy.

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 va lues are reached. If the liver function tests become markedly elevated, the therapy should be avoid.
There may chances of severe bullous skin reactions such as Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) or acute generalised exanthematous pustulosis (AGEP) may occur. If symptoms or signs severe bullous skin reactions are present, therapy must be immediately stopped. There may chances of while treat of trichomonas vaginal is eliminated a gonococcal infection can 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.

Metronidazole should be re-administered immediately after haemodialysis. In patients undergoing haemodialysis metronidazole and metabolites are efficiently removed during an eight hour period of dialysis. No routine adjustment in the dosage of metronidazole need be made in patien ts with renal failure undergoing intermittent peritoneal dialysis (IDP) or continuous ambulatory peritoneal dialysis (CAPD).

Metronidazole should be administered with caution to patients with hepatic encephalopathy since it is mainly metabolized by hepatic oxidation and substantial impainnent of metronidazole clearance. The daily dosage should be reduced to one third and may be administered once daily.

Patients should be monitor and warned that metron idazole may darken urine.
The longer treatment required should be carefully use of metronidazole to avoid mutagenicity.

**4.5 Interaction with other medicinal products and other forms of interaction**

Metronidazole potentiation interaction with of oral anticoagulant (warfarin). Metronidazole should be advised not to take with alcohol to avoid disulfiram-like (antabuse effect) reaction, by using metronidazole and disulfiram concurrently it may produce psychotic reactions. Lithium treatment should be tapered or withdrawn before administering metronidazole to avoid renal damage. Phenobarbital or phenytoin metabolise metronidazole at a much greater rate than normally. Metronidazole reduces the clearance of 5 fluorouracil and can therefore result in increased toxicity of 5 nuorouracil. Ciclosporine

are at risk of elevated ciclosporin serum levels. Serum ciclosporine and serum creatinine should be closely monitored when coadministration is necessary. Metronidazole increase plasma levels of busulfan which may lead to severe busulfan toxicity.

### 4.6 Pregnancy and Lactation

Metronidazole should not be given during pregnancy or during lactation unless the physician considers it essential; in these circumstances the short, high-dosage regimens are not recommended.

### 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

In general, metronidazole is well tolerated, but mild symptoms may occur. The Use of recommendation high dose for longer than periods may risk of peripheral neuropathy. **Blood and lymphatic system disorders:** agranulocytosis, neutropenia, thrombocytopenia, pancytopenia: Not known: leucopenia.

**Immune system disorders:** Rare: anaphylaxis not known: angiodema, urticaria, 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 (i.e. confusion, fever, headache, hallucinations, paralysis, and light sensitivity, disturbances in sight and movement, stiff neck) and subacute cerebellar syndrome (eg. ataxta, dysathria, gait impairment, nystagmus and tremor) which may resolve on discontinuation of the therapy. drowsiness, dizziness, and convulsions, headaches not known: prolonged metronidazole therapy, or transient epilepticform seizures have been reported, aseptic meningitis

**Eye disorders:** Very rare: vision disorders such as diplopia and myopia, which, in most cases, is transient, not known: optic neuropathy/neuritis.

**Ear and labyrinth disorders:** Not known: heanng impaired/hearing loss (including sensorineural), tinnitus.

**Gastrointestinal disorders:** Not known: Metallic taste disorders, oral mucositis, furred tongue, nausea, vomiting, gastro- intestinal disturbances such as epigastric pain and diarrhoea.

**Hepatobiliary disorders:** Very rare: increase in liver enzymes (AST, ALT, alkaline phosphatase), cholestatic or mixed hepatitis and hepatocellular liver injury, jaundice and pancreatitis which is reversible on drug withdrawal. 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 generalized exathematous pustulosis, pntritis, flushing, erythema multifonne, 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 urine (due to metronidazole metabolite).

### 4.9 Overdose

Symptoms: Single oral doses of metronidazole, approx. up to 12 g have reported in accidentally. Symptoms may occur vomiting, ataxia and slight disorientation.

Treatment: There is no specific treatment for gross overdosage, but early emesis or gastric lavage is recommended of value within few hours of ingestion. Further treatment is symptomatic and supportive.

## 5. Pharmacological Properties

### 5.1 Pharmacodynamics Properties

Metronidazole is a 5-nitroimidazole derivative and it has antiprotozoal and antibacterial actions and is effective against Trichomonas vaginalis and other protozoa including entamoeba histolytica and giardia lamblia and against anaerobic bacteria.

### 5.2 Pharmacokinetic Properties

Metronidazole is rapidly and almost completely absorbed after oral administration peak plasma concentrations occur after 20 min to 3 hours. The half-life of metronidazole is 8.5 ± 2.9 hours. Metronidazole it is rapidly removed from the plasma by dialysis. Metronidazole is excreted in milk.

### 5.3 Preclinical Safety Data

Metronidazole has been shown to be carcinogenic in the mouse and in the rat following chronic oral administration however similar studies in the hamster have given negative results. Epidemiological studies have provided no clear evidence of an increased carcinogenic risk in humans. Metronidazole has been shown to be mutagenic in bacteria in vitro. In studies conducted in mammalian cells in vitro as well as in rodent or humans in vivo, there was inadequate evidence of a mutagenic effect of metronidazole, with some studies reporting mutagenic effects, while others studies were negative.

## 6. Pharmaceutical Particulars

**Summary of Product Characteristics**

## 6.1 List of Excipients

Microcrystalline Cellulose (Plain)

Maize Starch

Gelatin

Microcrystal line Cellulose (PH 102)

Magnesium stearate

Purified Water

Isopropyl Alcohol (IPA)

Dichloromethane (Methylene Dichloride)

Colour White SC-SP-3180 (Spraycel)

**Composition of Colour White SC-SP-3180 (Spraycel):**

Hypromellose (Methocel-E-15)

Polyethylene Glycol-4000

Purified Talc

Titanium Dioxide

## 6.2 Incompatibilities

Not applicable

## 6.3 Shelf Life

36 Months

## 6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light.

## 6.5 Nature and Contents of Container

10 Tablets are packed in Alu-PVC Blister pack. Such 10 Blisters are packed in a printed carton with packing insert.

## 6.6 Special precaution for disposal and other handling

No special requirements for disposal.

# 7. Marketing Authorization Holder And Manufacturing Site Addresses

## 7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited

Trimul Estate, Khatraj, Taluka: Kalol,

District: Gandhinagar Gujarat, India.

Telephone no.: +91-79-41078096

Fax: +91-79-41078062

Email: hiren@lincolnpharma.com

Website: www.lincolnpharma.com

**7.2 Name and Address of manufacturing site(s)**

Lincoln Pharmaceuticals Limited

Trimul Estate, Khatraj, Taluka: Kalol,

District: Gandhinagar Gujarat, India.

Telephone no.: +91-79-41078096

Fax: +91-79-41078062

Email: hiren@lincolnpharma.com

Website: www.lincolnpharma.com

**8. Marketing Authorization Number**

TAN 22 HM 0368

**9. Date of First <Registration> / Renewal of The <Registration>**

It will be applicable after registration of this product.

10. **Date of Revision of the Text**

06/2022

**11. Dosimetry (If Applicable)**

Not Applicable

**12. Instructions for preparation of radiopharmaceuticals (if Applicable)**

Not Applicable