XIFAXAN® (RIFAXIMIN) 200 MG FILM COATED TABLETS

1 NAME OF THE MEDICINE

Rifaximin

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

XIFAXAN 200 mg tablets are pink, circular, biconvex film-coated tablets.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

XIFAXAN® 200 mg is a pink, circular, biconvex film-coated tablet. The tablets are packaged in PVC/PE/PVDC/Aluminium blisters in cartons containing 9 tablets.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

XIFAXAN is indicated for the treatment of patients (≥ 12 years of age) with travellers' diarrhoea caused by non-invasive strains of *Escherichia coli* (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE, and Section 5.1 PHARMACODYNAMIC PROPERTIES - Clinical trials)

Travellers' diarrhoea describes a clinical picture predominantly observed in subjects travelling from developed to developing countries. It is most frequently caused by enterotoxigenic *Escherichia coli* (ETEC), enteroaggregative *E. coli* (EAEC) and other non-invasive pathogens.

4.2 DOSE AND METHOD OF ADMINISTRATION

The recommended dose of XIFAXAN is one 200 mg tablet taken orally three times a day for 3 days (total 9 doses). It can be taken with or without food. XIFAXAN should not be used for more than 3 days even if symptoms continue. A second course of treatment must not be taken.

4.3 CONTRAINDICATIONS

XIFAXAN is contraindicated in patients with a hypersensitivity to rifaximin, any of the rifamycin antimicrobial agents, or to any of the excipients. Hypersensitivity reactions have included exfoliative dermatitis, angioneurotic oedema, and anaphylaxis.

Cases of intestinal obstruction.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Identified precautions

Xifaxan should not be used in patients with diarrhoea complicated by fever or blood in the stool or diarrhoea due to pathogens other than *Escherichia coli*.

Xifaxan should therefore only be considered as an option in travel to areas where there is a low incidence of *Campylobacter* and, specifically, not involving travel in SE Asia.

Travellers' diarrhoea not caused by Escherichia Coli

Clinical data have shown that rifaximin is not effective in the treatment of travellers' diarrhoea caused by invasive enteric pathogens such as *Campylobacter* spp, *Salmonella* spp and *Shigella* spp, which typically produce dysentery-like diarrhoea characterised by fever, blood in the stool and high stool frequency.

If symptoms worsen, treatment with XIFAXAN should be interrupted. If symptoms have not resolved after 3 days of treatment, or recur shortly afterwards, a second course of XIFAXAN should not be administered.

Clostridium difficile-Associated Diarrhoea

Clostridium difficile-associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including XIFAXAN, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon which may lead to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Use with P-glycoprotein inhibitors

Caution should be exercised when concomitant use of rifaximin and a P-glycoprotein inhibitor such as ciclosporin is needed (see Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

Use with warfarin

Both decreases and increases in international normalized ratio (in some cases with bleeding events) have been reported in patients maintained on warfarin and prescribed rifaximin. If co-administration is necessary, the international normalized ratio should be carefully monitored with the addition or withdrawal of rifaximin. Adjustments in the dose of oral anticoagulants may be necessary (see Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

Use in hepatic impairment

Because of the limited systemic absorption of rifaximin, no specific dosing adjustment is recommended for patients with hepatic insufficiency.

Use in renal impairment

No clinical data are available on the use of rifaximin in patients with impaired renal function.

Use in the elderly

Clinical studies with rifaximin 200 mg for travellers' diarrhoea did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger subjects.

Paediatric use

The safety and effectiveness of XIFAXAN for the treatment of travellers' diarrhoea have not been established in patients under 12 years of age and therefore it is not recommended in this age group.

Effects on laboratory tests

Both decreases and increases in international normalized ratio (in some cases with bleeding events) have been reported in patients maintained on warfarin and prescribed rifaximin.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

In vitro studies have shown that rifaximin did not inhibit cytochrome P450 isozymes 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1 and CYP3A4 at concentrations up to 200 ng/mL (at least 10 times the clinical Cmax). Rifaximin is not expected to inhibit these enzymes in clinical use.

In healthy subjects, clinical drug interaction studies demonstrated that rifaximin did not significantly affect the pharmacokinetics of CYP3A4 substrates, however, in hepatic impaired patients it cannot be excluded that rifaximin may decrease the exposure of concomitant CYP3A4 substrates administered (e.g. warfarin, antiepileptics, antiarrhythmics, and oral contraceptives), due to the higher systemic exposure with respect to healthy subjects.

An in vitro study suggested that rifaximin is a moderate substrate of P-glycoprotein (P-gp) and metabolised by CYP3A4. It is unknown whether concomitant drugs which inhibit CYP3A4 can increase the systemic exposure of rifaximin.

In healthy subjects, co-administration of a single dose of ciclosporin (600 mg), a potent P-glycoprotein inhibitor, with a single dose of rifaximin (550 mg) resulted in 83-fold and 124-fold increases in rifaximin mean Cmax and AUC. Ciclosporin is also an inhibitor of OATP, breast cancer resistance protein (BCRP) and a weak inhibitor of CYP3A4; the relative contribution of inhibition of each transporter by ciclosporin to the increase in rifaximin exposure is unknown. The clinical significance of this increase in systemic exposure is unknown.

The potential for drug-drug interactions to occur at the level of transporter systems has been evaluated in vitro and these studies suggest that a clinical interaction between rifaximin and other compounds that undergo efflux via P-gp and other transport proteins is unlikely (MRP2, MRP4, BCRP and BSEP).

Both decreases and increases in international normalized ratio have been reported in patients maintained on warfarin and prescribed rifaximin. If co-administration is necessary, the international normalized ratio should be carefully monitored with the addition or withdrawal of rifaximin. Adjustments in the dose of oral anticoagulants may be necessary.
There is no experience regarding administration of rifaximin to subjects who are taking another rifamycin antibacterial agent to treat a systemic bacterial infection.

No drug interaction studies investigating the concomitant intake of rifaximin and other drugs that might be used during an episode of traveller’s diarrhoea (e.g. loperamide,

charcoal) are available. However, in an efficacy study the safety (incidence and type of adverse events) of loperamide and rifaximin administered concomitantly was comparable to those of loperamide alone and rifaximin alone.

Patients should take rifaximin at least 2 hours after the administration of charcoal.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

There were no effects on fertility in rats treated with rifaximin at oral doses up to 300 mg/kg/day (about 4.5 times the clinical dose (600 mg/day)based on body surface area).

Use in pregnancy – Pregnancy Category B1

Nonclinical studies of placental transfer of rifaximin/metabolites have not been conducted. There was no evidence of teratogenicity in pregnant rats or rabbits treated with rifaximin during the period of organogenesis at respective oral doses up to 300 and 1000 mg/kg/day. The dose in rats was about 4.5 times the clinical dose (600 mg/day) based on body surface area. Compared with clinical exposure (plasma AUC) at the, the exposure in rabbits was less than that in healthy volunteers at 600 mg/day.

Use in lactation

It is unknown whether rifaximin/metabolites are excreted in human milk.
A risk to the child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue rifaximin therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Oral administration of rifaximin to rats from early gestation to weaning at doses up to 300 mg/kg/day (about 4.5 times the clinical dose (600 mg/day) based on body surface area) did not elicit any adverse effects on gestation or parturition, or on offspring viability, development and reproductive performance.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The safety of XIFAXAN 200 mg taken three times a day was evaluated in patients with travellers' diarrhoea consisting of 320 patients in two placebo-controlled clinical trials with 95% of patients receiving three or four days of treatment with XIFAXAN. The

population studied had a mean age of 31.3 (18-79) years of which approximately 3% were ≥ 65 years old, 53% were male and 84% were White, 11% were Hispanic.

Discontinuations due to adverse reactions occurred in 0.4% of patients. The adverse reactions leading to discontinuation were taste loss, dysentery, weight decrease, anorexia, nausea and nasal passage irritation.

All adverse reactions for XIFAXAN 200 mg three times daily that occurred at a frequency ≥ 2% in the two placebo-controlled trials combined are provided in Table 1. (These include adverse reactions that may be attributable to the underlying disease).

Table 1. All adverse reactions with an incidence ≥2% among patients receiving Rifaximin tablets, 200 mg three times daily, in placebo-controlled studies.

MedDRA Preferred term	Number (%) of Patients	
	XIFAXAN Tablets, 600 mg/day N = 320	placebo N = 228
Flatulence	36 (11%)	45 (20%)
Headache	31 (10%)	21 (9%)
Abdominal pain NOS	23 (7%)	23 (10%)
Rectal tenesmus	23 (7%)	20 (9%)
Defecation urgency	19 (6%)	21 (9%)
Nausea	17 (5%)	19 (8%)
Constipation	12 (4%)	8 (4%)
Pyrexia	10 (3%)	10 (4%)
Vomiting NOS*	7 (2%)	4 (2%)

*NOS: Not otherwise specified

The following adverse reactions, presented by body system, have also been reported in <2% of patients taking XIFAXAN in the two placebo-controlled clinical trials where the 200 mg tablet was taken three times a day for travellers' diarrhoea. The following includes adverse reactions regardless of causal relationship to drug exposure.

Blood and Lymphatic System Disorders: Lymphocytosis, monocytosis, neutropenia

Ear and Labyrinth Disorders: Ear pain, motion sickness, tinnitus

*Gastrointestinal Disorders: A*bdominal distension, diarrhoea NOS (not otherwise specified) , dry throat, faecal abnormality NOS, gingival disorder NOS, inguinal hernia NOS, dry lips, stomach discomfort

General Disorders and Administration Site Conditions: Chest pain, fatigue, malaise, pain NOS, weakness

Infections and Infestations: Dysentery NOS, respiratory tract infection NOS, upper respiratory tract infection NOS

Injury and Poisoning: Sunburn

Investigations: Aspartate aminotransferase increased, blood in stool, blood in urine, weight decreased

Metabolic and Nutritional Disorders: Anorexia, dehydration

Musculoskeletal, Connective Tissue, and Bone Disorders: Arthralgia, muscle spasms, myalgia, neck pain

Nervous System Disorders: Abnormal dreams, dizziness, migraine NOS, syncope, loss of taste

Psychiatric Disorders: Insomnia

Renal and Urinary Disorders: Choluria, dysuria, hematuria, polyuria, proteinuria, urinary frequency

Respiratory, Thoracic, and Mediastinal Disorders: Dyspnea NOS, nasal passage irritation, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, rhinitis NOS, rhinorrhea

Skin and Subcutaneous Tissue Disorders: Clamminess, rash NOS, sweating increased

Vascular Disorders: Hot flashes NOS

Post-marketing Experience

The following adverse reactions have been identified during the post-marketing phase of rifaximin. The frequency of these reactions is not known (cannot be estimated from the available data).

Table 2. Post-marketing experience

MedDRA System Organ Class	**Frequency unknown**
Infections and infestations	Clostridial infections
Blood and lymphatic system disorder	Thrombocytopenia
Immune system disorders	Anaphylactic reactions,

	Angioedema, Hypersensitivity
Vascular disorders	Presyncope
Hepatobiliary disorders	Liver function test abnormalities
Skin and subcutaneous tissue disorders	Dermatitis, Eczema, Erythemas, Pruritis NEC, Urticaria
Investigations	International normalised ratio abnormalities

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

No specific information is available on the treatment of overdosage with XIFAXAN.

In clinical trials with patients suffering from travellers' diarrhoea, doses of up to 1,800 mg/day have been tolerated without any severe clinical signs. Even in patients/subjects with normal bacterial flora, rifaximin in dosages of up to 2,400 mg/day for 7 days did not result in any relevant clinical symptoms related to the high dosage.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Rifaximin is a non-aminoglycoside semi-synthetic, non-systemic antibiotic derived from rifamycin SV.

Rifaximin acts by binding to the beta-subunit of bacterial DNA-dependent RNA polymerase resulting in inhibition of bacterial RNA synthesis.

Rifaximin has a broad antimicrobial spectrum against most of the Gram-positive and Gram-negative, aerobic and anaerobic bacteria responsible for intestinal infections.

Due to the very low absorption from the gastro-intestinal tract, rifaximin is locally acting in the intestinal lumen and clinically not effective against invasive pathogens, even though these bacteria are susceptible *in vitro*.

Clinical trials

The safety and efficacy of rifaximin given as 200 mg tablets taken three times a day was evaluated in 2 randomized, multi-centre, double-blind, placebo-controlled studies in adult subjects with travellers' diarrhoea. One study was conducted at clinical sites in Mexico, Guatemala, and Kenya (Study 1). The other study was conducted in Mexico, Guatemala, Peru, and India (Study 2). Stool specimens were collected before treatment and 1 to 3 days following the end of treatment to identify enteric pathogens. The predominant pathogen in both studies was *Escherichia coli*.

The clinical efficacy of rifaximin was assessed by the time to return to normal, formed stools and resolution of symptoms. The primary efficacy endpoint was time to last unformed stool (TLUS) which was defined as the time to the last unformed stool passed, after which clinical cure was declared.

Study 1

Table 3 displays the median TLUS and the number of patients who achieved clinical cure for the intent to treat (ITT) population of Study 1. The duration of diarrhoea was significantly shorter in patients treated with rifaximin than in the placebo group. More patients treated with rifaximin were classified as clinical cures than were those in the placebo group.

Table 3: Clinical Response in Study 1 (ITT population)

	rifaximin 200 mg tds (n=125)	placebo (n=129)	Estimate (97.5% CI)	P-value
Median TLUS (hours)	32.5	58.6	1.78[a] (1.26, 2.50)	0.0002
Clinical cure, n (%)	99 (79.2)	78 (60.5)	18.7[b] (5.3, 32.1)	0.001

[a] Hazard ratio

[b] Difference in rates

Microbiological eradication (defined as the absence of a baseline pathogen in culture of stool after 72 hours of therapy) rates for Study 1 are presented in Table 42 for patients with any pathogen at baseline *Escherichia coli* was the only pathogen with sufficient numbers to allow comparisons between treatment groups.

Even though rifaximin had microbiologic activity similar to placebo, it demonstrated a clinically significant reduction in duration of diarrhoea and a higher clinical cure rate than placebo. Therefore, patients should be managed based on clinical response to therapy rather than microbiological response.

Table 4: Microbiological Eradication Rates in Study 1: Subjects with an identified Baseline Pathogen

(Study Locations: Mexico, Guatemala, Kenya)

	rifaximin	placebo
Overall (all pathogens)	48/70 (69%)	41/61 (67%)
E. coli	38/53 (72%)	40/54 (74%)
Invasive bacterial pathogens (*salmonella, shigella, campylobacter* spp)	5/8 (63%)	4/5 (80%)
Protozoa (cryptosporidium, giardia, entamoeba spp)	17/25 (68%)	11/16 (69%)
Other	1/1 (100%)	4/4 (100%)

Study 2

The results of Study 2 supported the results presented for Study 1. In addition, this study provided evidence that subjects treated with rifaximin with fever and/or blood in the stool at baseline had prolonged TLUS. These subjects had lower clinical cure rates than those without fever or blood in the stool at baseline. Many of the patients with fever and/or blood in the stool (dysentery-like diarrhoeal syndromes) had invasive pathogens, primarily *Campylobacter jejuni*, isolated in the baseline stool.

Also in this study, the majority of the subjects treated with rifaximin who had *Campylobacter jejuni* isolated as a sole pathogen at baseline failed treatment and the resulting clinical cure rate for these patients was 23.5% (4/17). In addition to not being different from placebo, the microbiologic eradication rates for subjects with *Campylobacter jejuni* isolated at baseline were much lower than the eradication rates seen for *Escherichia coli*.

Table 5: Clinical and biological outcome by Baseline Pathogen Category: MITT population (Study Locations: Mexico, Guatemala, Peru, India)

Pathogen	rifaximin (N=128)	placebo (N=62)	ciprofloxacin (N=58)
Median TLUS (hours)			
Any pathogen	40.3 [N=128]	48.3 [N=62]	28.3 [N=58]
Diarrhoeagenic *E. coli*	24.0 [N=73]	38.0 [N=38]	23.4 [N=40]
Inflammatory/invasive pathogens Campylobacter jejuni Salmonella Shigella	NC [N=45]	67.5 [N=18]	65.0 [N=13]
Other pathogens	65.3 [N=10]	NC [N=6]	NC [N=5]
No pathogens (ITT population)	23.5 [N=69]	71.6 [N=39]	29.7 [N=43]
Clinical Wellness			
Any pathogen	94/128 (73.4%)	40/62 (64.5%)	43/58 (74.1%)
Diarrhoeagenic *E. coli*	65/73 (89.0%)	28/38 (73.7%)	33/40 (82.5%)
Inflammatory/invasive pathogens Campylobacter jejuni Salmonella Shigella	22/45 (48.9%)	9/18 (50.0%)	8/13 (61.5%)
Other pathogens	7/10 (70.0%)	3/6 (50.0%)	2/5 (40.0%)
No pathogens (ITT population)	57/69 (86.2%)	22/39 (56.4%)	36/43 (83.7%)
Microbiological Eradication			
Any pathogen	77/128 (60.2%)	31/62 (50.0%)	46/58 (79.3%)
Diarrhoeagenic *E. coli*	56/73 (76.7%)	24/38 (63.2%)	37/40 (92.5%)
Inflammatory/invasive pathogens Campylobacter jejuni Salmonella Shigella	25/45 (55.6%)	10/18 (55.6%)	10/13 (79.3%)
Other pathogens	4/10 (40.0%)	0/6 (0.0%)	2/5 (40.0%)

MIIT = Modified intent-to-treat. NC= not calculable; median TLUS could not be calculated of more than one-half of the subjects in the group failed to achieve wellness.

In an unrelated open-label, pharmacokinetic study of oral rifaximin 200 mg taken every 8 hours for 3 days, 15 adult subjects were challenged with Shigella flexneri 2a, of

whom 13 developed diarrhoea or dysentery and were treated with rifaximin. Although this open-label challenge trial was not adequate to assess the effectiveness of rifaximin in the treatment of shigellosis, the following observations were noted: eight subjects received rescue treatment with ciprofloxacin either because of lack of response to rifaximin treatment within 24 hours (2), or because they developed severe dysentery (5), or because of recurrence of Shigella flexneri in the stool (1); five of the 13 subjects received ciprofloxacin although they did not have evidence of severe disease or relapse.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Pharmacokinetic studies in rats, dogs and humans demonstrated that after oral administration, rifaximin in the polymorph α form is virtually not absorbed (less than 1% absorbed). After a single dose and multiple doses of rifaximin in healthy subjects, the mean time to reach peak plasma concentrations was about an hour. The pharmacokinetic (PK) parameters were highly variable and the accumulation ratio based on AUC was 1.37.

After repeated administration of therapeutic doses of rifaximin in healthy volunteers and patients with damaged intestinal mucosa (Inflammatory Bowel Disease), plasma levels are negligible (less than 10 ng/mL). An increase of rifaximin systemic absorption was observed when administered within 30 minutes of a high-fat breakfast. This was not clinically relevant.

Distribution

Rifaximin is moderately bound to human plasma proteins. *In vivo*, the mean protein binding ratio was 67.5% in healthy subjects when rifaximin was administered.

Metabolism

A mass balance study carried out in healthy volunteers (see Section 5.2 PHARMACOKINETIC PROPERTIES - Excretion) suggests that absorbed rifaximin undergoes metabolism with minimal renal excretion of the unchanged drug. The enzymes responsible for metabolizing rifaximin are unknown.

Excretion

Rifaximin is almost exclusively excreted in faeces.

In a mass balance study, after administration of 400 mg ^{14}C-rifaximin orally to healthy volunteers, of the 96.94% total recovery, 96.62% of the administered radioactivity was recovered in faeces almost exclusively as the unchanged drug and 0.32% was recovered

in urine mostly as metabolites with 0.03% as the unchanged drug. Rifaximin accounted for 18% of radioactivity in plasma.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Rifaximin was not genotoxic in the bacterial reverse mutation assay, chromosomal aberration assay, rat bone marrow micronucleus assay, rat hepatocyte unscheduled DNA synthesis assay, or the CHO/HGPRT mutation assay.

Carcinogenicity

The carcinogenic potential of rifaximin was examined in a 2 year study with CD rats. Oral administration at doses up to 250 mg/kg/day (about 4 times the clinical dose (600 mg/day) based on body surface area) produced no evidence of a carcinogenic effect except for an increased trend in malignant schwannomas in the heart in males but not females, at an incidence (5%) exceeding the maximum historical control incidence (1.7%). Despite lack of statistical significance of pairwise testing and absence of this finding in females, a possible relationship to treatment cannot be dismissed.

There was no increase in tumours in Tg.rasH2 mice treated orally with rifaximin for 26 weeks at doses up to 2000 mg/kg/day (mean plasma concentrations 8 times the clinical C_{max} in healthy volunteers based on Cmax values.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Excipients present in the tablets are; microcrystalline cellulose, glyceryl diisostearate, sodium starch glycolate type A, colloidal anhydrous silica, purified talc. The film coating contains hypromellose, titanium dioxide, disodium edetate, propylene glycol, and iron oxide red.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

The tablets are packaged in PVC/PE/PVDC/Aluminium blisters in cartons containing 9 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

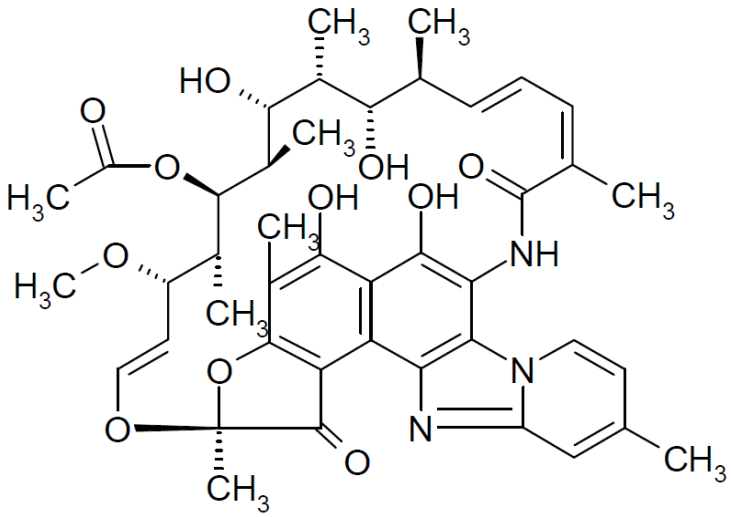
In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Rifaximin is a red orange crystalline powder and is soluble in methanol, chloroform, acetone and ethyl acetate. It is practically insoluble in water. It has a pKa of 6.77. The partition co-efficient (*n*-octanol – water) is 2.76 (Log P_{ow}).

Rifaximin has the chemical formula $C_{43}H_{51}N_3O_{11}$ and a molecular weight of 785.9

Chemical structure



(2S,16Z,18E,20S,21S,22R,23R,24R,25S,26R,27S,28E)5,6,21,23-Tetrahydroxy-27-methoxy-2,4, 11, 16,20,22,24,26-octamethyl-1, 15-dioxo-1 ,2-dihydro-2, 7-(epoxypentadeca[1,11, 13]trienoimino)[1]benzofuro[4,5-e]pyrido[l ,2-a]benzimidazol-25-yl acetate.

CAS number
80621-81-4

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 - Prescription Only Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

26 May 2015

10 DATE OF REVISION

16 April 2020

10.1 SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Reformat to new PI form
8	Update sponsor address