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Via G. Tartini, 2 - 20158 - MILANO
Tel. 02.375787 • e-mail: crominfoto@tiscali.it
AZIENDA CERTIFICATA UNI EN ISO 9001:2008
89034260 (int. version 3)
29 GEN 2019
TYPE OF MATERIAL: LEAFLET FOLDED | DESCRIPTION: PRIFTIN 150 MG 3X8 | COUNTRY: SOUTH AFRICA | LOGO VERSION: // | MIN. FONT SIZE: 6.8 pt.
CODE: 89034260 744214 | VERSION: 2 b | OLD CODE: 00000000 000000 | DIE CUT: I027 | DIMENSIONS mm: 420 x 296 (210 x 148) | COLOURS N°: 1 | COLOUR 1: BLACK

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:
PRIFTIN® (Film-coated tablet)

COMPOSITION:
Active ingredient: rifapentine.
Each film-coated tablet contains 150 mg rifapentine.

Excipients:
Calcium stearate, microcrystalline cellulose, pregelatinised starch, sodium ascorbate, sodium lauryl sulphate and sodium starch glycolate.
Tablet film-coat: disodium edetate, hydroxypropyl cellulose, hypromellose, indigo carmine (FD&C blue No. 2 aluminium lake), polyethylene glycol, propylene glycol, red iron oxide, sodium ascorbate and titanium dioxide.
Sugar free.

CATEGORY AND CLASS:
A 20.2.3 Tuberculostatics

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties
Rifapentine belongs to the rifamycin class of antibiotics which exert their antibacterial action by selectively inhibiting the DNA-dependent RNA polymerase of susceptible bacteria.
It forms a stable complex with bacterial DNA-dependent RNA polymerase, leading to repression of RNA synthesis and cell death.
Rifapentine and its 25-desacetyl metabolite accumulate in human monocyte-derived macrophages and are bactericidal to both intracellular and extracellular *Mycobacterium tuberculosis* organisms at concentrations achievable by the recommended oral dosing regimens. 25-Desacetyl rifapentine, the active metabolite, is almost as active as rifapentine.

Susceptible microorganisms:
Mycobacterium tuberculosis
Rifapentine shows cross-resistance with rifampicin.

Resistance:
Most organisms resistant to other rifamycins are likely to be resistant to rifapentine.
Resistance to rifamycin antibiotics has been determined to occur as a single step mutation of the gene that encodes for the beta subunit of the DNA-dependent RNA polymerase.
However, other mechanisms of rifamycin resistance cannot be ruled out.
Appropriate susceptibility tests should be performed in the event of persistently positive cultures.

Pharmacokinetic properties
When 600 mg oral doses of rifapentine were administered once daily or once every 72 hours to healthy volunteers for 10 days (4 doses), mean C_{trough} were below the limit of quantification suggesting no accumulation; moreover single dose AUC (0-∞) of rifapentine was similar to its AUC_{ss} (0-72 h) values after 4 repeated doses, suggesting no significant auto-induction effect.
Based on the data observed after a single oral dose of 900 mg in healthy subjects, no plasma accumulation of rifapentine and 25-desacetyl rifapentine (active metabolite) is expected after once weekly administration of PRIFTIN.
The pharmacokinetic parameters of rifapentine and 25-desacetyl rifapentine on day 10 following oral administration of 600 mg PRIFTIN every 72 hours to healthy volunteers are described in **Table 1**.

Table 1 – Pharmacokinetics of Rifapentine and 25-Desacetyl Rifapentine in Healthy Volunteers

Parameter	Rifapentine	25-Desacetyl Rifapentine
	Mean ± SD	
Cmax (µg/ml)	15,05 ± 4,62	6,26 ± 2,06
AUC (0-72 h) (µg*h/ml)	319,54 ± 91,52	215,88 ± 85,96
T½ (h)	13,19 ± 1,38	13,35 ± 2,67
Tmax (h)	4,83 ± 1,80	11,25 ± 2,73
Cl/F (l/h)	2,03 ± 0,60	--

The pharmacokinetic parameters of rifapentine and 25-desacetyl rifapentine following single-dose oral administration of 900 mg PRIFTIN in combination with 900 mg isoniazid in fed conditions are described in **Table 2**.

Table 2 – Mean ± SD Pharmacokinetic Parameters of Rifapentine and 25-Desacetyl Rifapentine in Healthy Volunteers when PRIFTIN is Co-administered with Isoniazid Under Fed Conditions (N = 16)

Parameter	Rifapentine	25-Desacetyl Rifapentine
Cmax (µg/ml)	25,8 ± 5,83	13,3 ± 4,83
AUC (µg*h/ml)	817 ± 128	601 ± 187
T½ (h)	16,6 ± 5,02	17,5 ± 7,42
Tmax (h) *	8 (3 – 10)	24 (10 – 36)
Cl/F (l/h)	1,13 ± 0,174	NA**

* Median (Min – Max)
** Not applicable

Absorption:
The absolute bioavailability of rifapentine has not been determined. Based on mass balance study, absorption was estimated as almost complete.
Rifapentine bioavailability is affected by food.
When the tablet is administered with food the bioavailability of rifapentine and its active metabolite increases by 40 % to 50 %. This increase in bioavailability is not affected by the meal composition including the amount of lipids.
Rifapentine should be taken with food in order to maximise rifapentine and 25-desacetyl rifapentine exposures and reduce inter-subject variability.

In contrast, the ingestion of the meal decreases isoniazid exposures (C_{max} and AUC by 46 % and of 23 %, respectively with the low fat, high carbohydrate breakfast).

Distribution:
In healthy volunteers, rifapentine and 25-desacetyl rifapentine were highly 97,7 % and 93,2 % bound to plasma proteins, respectively. Similar extent of protein binding was observed in healthy volunteers, asymptomatic HIV-infected subjects and hepatically impaired subjects.
Following oral dosing of rifapentine in fed condition, the apparent volume of distribution is 32 l.
The intrapulmonary distribution was studied in healthy subjects who received a single oral dose of rifapentine (600 mg). The peak concentrations in plasma, in epithelial lining fluid, and in alveolar cells were 26,2; 3,7 and 5,3 µg/ml, respectively. Although the intrapulmonary rifapentine (RPT) concentrations were less than the plasma RPT concentrations at all time periods, they remained above the RPT and 25-desacetyl rifapentine (25-DRPT) Minimum Inhibitor Concentration (MIC) for the 48-h observation period.

Metabolism:
Rifapentine was hydrolysed by an esterase enzyme to form a single microbiologically active metabolite 25-desacetyl rifapentine.
This metabolite represents 60 to 70 % of rifapentine AUC.

Elimination:
After administration of 14C-rifapentine, the majority of the dose is excreted in faeces (70 %), while urine is a minor pathway for excretion (17 %). Plasma clearance after oral administration of rifapentine, is low with values in the range of 1,5 to 2 l/h. The apparent elimination of rifapentine and 25-desacetyl rifapentine are monophasic with a terminal half-life ranging from 13 to 17 h.
The main elimination pathways are metabolism for rifapentine and biliary excretion in faeces for both rifapentine and its metabolite 25-desacetyl rifapentine. Renal clearance is a minor pathway of excretion for rifapentine and its metabolite.

Medicine interactions:
Potential of rifapentine to affect other medicines
- Cytochrome P450 substrates

In vitro, rifapentine and its metabolite (25-desacetyl-rifapentine) are potent inducers of CYP3A4. *In vivo* in humans, rifapentine has also been shown to be a potent CYP3A4 inducer: rifapentine daily (from 5 mg/kg) decreased midazolam exposure by 90 %; rifapentine 600 mg twice weekly dosing reduced indinavir (protease inhibitor substrate of CYP3A4) exposure by 70 %. There is no clinical data evaluating the interaction between CYP3A substrate and rifapentine at dosing regimen recommended for latent tuberculosis infection (LTBI) (900 mg weekly dosing). However, rifapentine is also predicted a potent inducer at this dosing regimen.

In vitro, rifapentine is an inducer of CYP2C8 and CYP2C9 and its metabolite (25-desacetyl-rifapentine) is a potential inhibitor of CYP2C8. No clinical interaction study was performed to assess *in vivo* potential of rifapentine to interact with medicines metabolised by CYP2C8/C9 but the risk of interaction is likely. The *in vivo* net effect, resulting from induction and inhibition of CYP2C8 was not evaluated but a higher impact of induction can be predicted.

In vitro studies showed that rifapentine and its metabolite (25-desacetyl-rifapentine) are inducers of CYP2B6 and that rifapentine is an inhibitor of CYP2B6. Interactions with CYP2B6 substrate was evaluated in one clinical study with efavirenz which is known as a very sensitive CYP2B6 substrate. After a single and repeated weekly administration of rifapentine 900 mg, no or minor modification (≤ 15 %) of steady-state exposure of efavirenz was observed.

In vitro, rifapentine and its metabolite are not inducers of CYP1A2. Based on *in vitro* data, it is predicted that rifapentine and its metabolite have no potential to inhibit CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4 and CYP2E1, *in vivo* in humans.
- Transporter substrates

In vitro, rifapentine has been shown to inhibit several transporters (P-gp, BCRP and OATP1B1/B3, OCT1). However, the risk of clinically significant interaction resulting from inhibition of BCRP, OATP1B1/B3, evaluated using a mechanistic static approach, was considered as minimal. Moreover, rifamycins are known to induce some of these transporters (such as P-gp, OATP1B1/OATP1B3) via activation of PXR and could balance the inhibition effect. For P-gp, interactions have been evaluated in humans with 2 substrates of P-gp, raltegravir and tenofovir suggesting a limited effect.
However, because of narrow therapeutic index of digoxin (P-gp substrate), appropriate monitoring and dose adjustment of digoxin may be necessary in case of co-administration with rifapentine (see INTERACTIONS).

Potential of other medicines to affect rifapentine
Rifapentine is metabolised by esterases and its main metabolite, 25-desacetyl-rifapentine, is not metabolised. There is lack of risk of interaction with CYP450 inducer and as well as inhibitor medicines (such as triazole antifungal agents frequently co-administered in HIV-infected patients). Similarly, taking into account the high passive diffusion component in the hepatocyte uptake or the good intestinal permeability, potential interaction with transporters inhibitor/inducer medicines are not expected.

Special populations:
Elderly patients
In elderly (≥ 65 years), following single oral administration of 600 mg, mean rifapentine and 25-desacetyl-rifapentine exposures were increased (41 % for rifapentine AUC, 58 % for 25-desacetyl-rifapentine) compared to healthy young subjects (historical comparison). However, no dose adjustments were recommended for elderly subjects based on safety results in elderly healthy subjects and elderly patients with LTBI.

Paediatric patients
In healthy adolescents, rifapentine and 25-desacetyl-rifapentine PK were not different from those observed in healthy adults.
In paediatrics (younger than 12-years old), a significant correlation was observed between clearance and age: clearance adjusted to body weight increased with decreasing age.
Based on these findings, a weight band dosing (**Table 3**) was selected for rifapentine in children with LTBI and validated with PK and safety data in this population.
In children (2 – 12 years of age) receiving doses based on weight, while the mean rifapentine dosages in mg/kg were 2-fold higher than in adults (23 versus 11 mg/kg), exposures were 31 % and 41 % higher than adults for rifapentine and 25-desacetyl-rifapentine respectively, exposures that in adults have been associated with successful treatment of LTBI. Among children, exposure was about 25 % lower in those who could not swallow the whole tablets and received crushed tablets but still higher than in adults.
Despite the generally increased exposure observed in children, higher mg/kg PRIFTIN doses were well tolerated.

Hepatic impairment
Following oral administration of a single 600 mg dose of PRIFTIN to mild to severe hepatic impaired patients, the pharmacokinetics of rifapentine and 25-desacetyl metabolite were similar in patients with various degrees of hepatic impairment. In comparison to healthy subjects, rifapentine and 25-desacetyl-rifapentine exposure (AUC) were increased in subjects with hepatic impairment by 19 % to 25 % and 77 % to 99 %, respectively.

Renal impairment
The pharmacokinetics of rifapentine have not been evaluated in renal impaired patients. However, the risk of an impact of impaired renal function on PK is considered as minimal; only about 17 % of an administered dose is excreted via the kidneys. The clinical significance of impaired renal function on the disposition of rifapentine and its 25-desacetyl metabolite is not known.

Asymptomatic HIV-infected volunteers
In asymptomatic HIV-infected subjects, rifapentine and 25-desacetyl metabolite PK profiles were not significantly different from those observed in healthy subjects. The safety and PK results indicated that no dose adjustment for PRIFTIN is necessary for asymptomatic HIV-infected patients.

INDICATIONS:
PRIFTIN in combination with isoniazid (INH) is indicated for the treatment of latent tuberculosis infection (LTBI) caused by *Mycobacterium tuberculosis* in adults and children 2 years and older who are at high risk of progression to tuberculosis disease (including those in close contact with active tuberculosis patients, recent conversion to a positive tuberculin skin test, HIV-infected patients, or those with pulmonary fibrosis on radiograph).
Active tuberculosis disease should be ruled out before initiating treatment for latent tuberculosis infection.

PRIFTIN must always be used in combination with isoniazid as a 12-week once-weekly regimen for the treatment of latent tuberculosis infection.

CONTRAINDICATIONS:
PRIFTIN is contraindicated in patients with hypersensitivity to rifapentine or any of the other rifamycins (e.g. rifampicin and rifabutin), or to any of the tablet excipients.
PRIFTIN is contraindicated in patients with porphyria. Based on experience with rifampicin, it may be assumed that rifapentine can also induce delta-aminolevulinic acid synthetase and therefore cause an acute attack of porphyria.
Acute or chronic liver disease.

WARNINGS AND SPECIAL PRECAUTIONS:
Warnings
- ***Hepatotoxicity***

PRIFTIN may cause serious hepatic disease/injury.
Patients with abnormal liver tests and/or liver disease should only be given PRIFTIN if no safer alternative is available, and then with caution and under strict medical supervision (see CONTRAINDICATIONS).
In such patients, careful monitoring of liver parameters (especially serum transaminases and bilirubin) should be carried out prior to therapy and then every 2 to 4 weeks during therapy. If there are indications of a liver reaction or of the hepatic condition worsening, PRIFTIN should be discontinued.
Hepatotoxicity of other antituberculosis medicines (e.g. isoniazid, pyrazinamide) used in combination with rifapentine should also be taken into account.

- ***Hypersensitivity and related reactions***

Hypersensitivity reactions may occur in patients receiving PRIFTIN. Signs and symptoms of these reactions may include hypotension, urticaria, angioedema, acute bronchospasm, conjunctivitis, thrombocytopenia, neutropenia or flu-like syndrome (weakness, fatigue, muscle pain, nausea, vomiting, headache, fever, chills, aches, rash, itching, sweats, dizziness, shortness of breath, chest pain, cough, syncope, palpitations) (see SIDE EFFECTS).
Monitor patients receiving PRIFTIN therapy for signs and/or symptoms of hypersensitivity reactions. If these symptoms occur, administer supportive measures and discontinue PRIFTIN.

- ***Medicine interactions***

PRIFTIN is an inducer of CYP3A4 and CYP2C8/9. Concomitant use of rifapentine with other medicines metabolised by these enzymes, such as protease inhibitors, certain reverse transcriptase inhibitors, and hormonal contraception may cause a significant decrease in plasma concentrations and loss of therapeutic effect of these medicines (see INTERACTIONS and Pharmacokinetic properties – Medicine Interactions).
PRIFTIN has also been shown to inhibit and to induce P-gp which could modify plasma exposure of digoxin (a P-gp substrate with narrow therapeutic index). Appropriate monitoring and dose adjustment of digoxin may be necessary in case of co-administration with rifapentine (see INTERACTIONS and Pharmacokinetic properties – Medicine Interactions).

Precautions
Clostridium difficile-Associated Diarrhoea
Pseudomembranous colitis has been reported to occur with rifamycins such as PRIFTIN. Diarrhoea, particularly if severe and/or persistent, occurring during treatment or in the initial weeks following treatment may be symptomatic of *Clostridium difficile*-associated disease, the most severe form of which is pseudomembranous colitis. If pseudomembranous colitis is suspected, PRIFTIN should be stopped immediately and the patient treated appropriately without delay. Medications inhibiting the peristalsis are contraindicated in this clinical situation.

Discolouration of body fluids
PRIFTIN may produce a predominantly red-orange discolouration of body tissues and/or fluids (e.g. skin, teeth, tongue, urine, faeces, saliva, sputum, tears, sweat and cerebrospinal fluid).
Contact lenses or dentures may become permanently stained.

Effects on ability to drive and use machinery:
Do not drive or operate machines if you experience any side effects of PRIFTIN which could adversely affect your ability to drive or use machines.

INTERACTIONS:
Effect of PRIFTIN on other medicines
- ***Effect on medicines metabolised by CYP3A4 and CYP2C8/9***

PRIFTIN is an inducer of CYP3A4 and CYP2C8/9.
Therefore, PRIFTIN may increase the metabolism of other co-administered medicines that are metabolised by these enzymes.
Appropriate monitoring and dosage adjustment may be necessary if medicines metabolised by CYP3A4 or CYP2C8/9 are co-administered with PRIFTIN.
Induction of enzyme activities by PRIFTIN occurred after the first dose of PRIFTIN. Enzyme activities returned to baseline levels in general 14 days after discontinuing PRIFTIN.

Examples of such substances include:
- Antiretroviral medicines:
  - Protease Inhibitors: indinavir, darunavir, lopinavir, saquinavir, ritonavir
  - Non-Nucleoside Reverse Transcriptase Inhibitors: rilpirivine
  - Nucleoside Reverse Transcriptase Inhibitors: zidovudine
- Antifungals: itraconazole, ketoconazole, voriconazole
- Narcotic analgesics: methadone, alfentanil, buprenorphine
- Hypoglycaemic agents: repaglinide
- Calcium channel blockers: felodipine, diltiazem, verapamil, nifedipine
- Alpha/Beta Adrenergic Antagonists: alfuzosin, propranolol
- Ergot alkaloid derivates: ergotamine
- Oral anti-vitamin K anticoagulant: warfarin
- Hormonal contraceptives: oral, transdermal and implant
- Immunosuppressants: ciclosporin, tacrolimus, sirolimus
- Benzodiazepines: midazolam.

- ***Effect of PRIFTIN on transporter substrates***

In vitro, PRIFTIN has been shown to inhibit and to induce P-gp which could modify plasma exposure of digoxin (P-gp substrate) (see Pharmacokinetic properties – Medicine Interactions).
Because of narrow therapeutic index of digoxin, appropriate monitoring and dose adjustment of digoxin may be necessary in case of co-administration with PRIFTIN.

- ***Effect of PRIFTIN on Antiretroviral medicines***

\- *Protease Inhibitors and certain Reverse Transcriptase Inhibitors*
Concomitant use of rifapentine with Protease Inhibitors and certain Reverse Transcriptase Inhibitors, metabolised by CYP3A4 or CYP2C8/9, may cause a significant decrease in plasma concentrations and loss of therapeutic effect of these medicines.
\- *Fixed dose combination of Efavirenz, Emtricitabine and Tenofovir*
Once-weekly co-administration of 900 mg PRIFTIN with the antiretroviral fixed dose combination of efavirenz 600 mg, emtricitabine 200 mg and tenofovir disoproxyl fumarate 300 mg in HIV-infected patients did not result in any substantial change in steady state exposures of efavirenz, emtricitabine and tenofovir. No clinically significant change in CD4 cell counts or viral loads were noted.
No need for dose adjustment of fixed dose combination of efavirenz, emtricitabine and tenofovir, if co-administered with PRIFTIN 900 mg once-weekly.
\- *Raltegravir*
Once-weekly co-administration of 900 mg PRIFTIN with raltegravir resulted in a 71 % mean increase in raltegravir AUC_{0-12}, and an 89 % increase in C_{max}. No need for dose adjustment of raltegravir, if co-administered with PRIFTIN 900 mg once-weekly.

- ***Hormonal contraceptives***

PRIFTIN may reduce the effectiveness of hormonal contraceptives.
Women taking oral contraception, transdermal patch, or other systemic hormonal contraceptives who need PRIFTIN therapy should discuss with their doctor regarding the use of an additional non-hormonal means of contraception or the change of their contraceptive pill.

Effect of other medicines on PRIFTIN
Potential interaction with CYP450 inducer/inhibitor medicines, as well as with transporters inhibitor/inducer medicines are not expected (see Pharmacokinetic properties – Medicine Interactions).
Since PRIFTIN is highly bound to albumin, drug displacement interactions with non-steroidal anti-inflammatory drugs (NSAIDs), sulfonylureas and oral anticoagulants may also occur.

Interferences with laboratory and diagnostic tests
Therapeutic concentrations of rifampin have been shown to inhibit standard microbiological assays for serum folate and vitamin B_{12}. Similar interferences should be considered for PRIFTIN. Therefore, alternative assay methods should be considered.

HUMAN REPRODUCTION:
Pregnancy
Safety in pregnancy and lactation has not been established .
Women who are pregnant should not be treated with PRIFTIN.
Human data:
Rifampicin is known to cause postnatal haemorrhages in the mother and infant when taken during the last few weeks of pregnancy. Since PRIFTIN might have a similar effect, appropriate coagulation testing should be performed when pregnant women are inadvertently exposed to PRIFTIN during late pregnancy. Treatment with vitamin K may be indicated.

Lactation
Mothers on treatment with PRIFTIN should not breastfeed their babies.
It is not known whether PRIFTIN is excreted in human milk.
PRIFTIN may produce a red-orange discolouration of body fluids, including breast milk.

DOSAGE AND DIRECTIONS FOR USE:
Dosage
PRIFTIN should be administered once-weekly in combination with isoniazid for 12 weeks as directly observed therapy (DOT).

Adults and children 12 years and older:
The recommended dose of PRIFTIN should be determined based on weight of the patient up to a maximum of 900 mg once-weekly (see **Table 3**). The recommended dose of isoniazid is 15 mg/kg (rounded to the nearest 50 mg or 100 mg) up to a maximum of 900 mg once-weekly for 12 weeks.

Children 2 - 11 years:
The recommended dose of PRIFTIN should be determined based on weight of the patient up to a maximum of 900 mg once-weekly (see **Table 3**). The recommended dose of isoniazid is 25 mg/kg (rounded to the nearest 50 mg or 100 mg) up to a maximum of 900 mg once-weekly for 12 weeks.

Table 3 – Weight based dose of PRIFTIN in the treatment of latent tuberculosis infection

Weight range	PRIFTIN dose	Number of PRIFTIN tablets
10 – 14 kg	300 mg	2
14,1 – 25 kg	450 mg	3
25,1 – 32 kg	600 mg	4
32,1 – 50 kg	750 mg	5
> 50 kg	900 mg	6

Special populations
Paediatric patients:
The youngest patient included in the clinical efficacy trial was 2 years. No data are available for patients below 2 years old.

Elderly patients:
No dose adjustment required.

Hepatic impairment:
No dose adjustment required (see CONTRAINDICATIONS and WARNINGS AND SPECIAL PRECAUTIONS).

Renal impairment:
No dose adjustment required.

Administration
Patients should be informed that adherence to the treatment regimen for PRIFTIN and other substances is essential for effective treatment, and the importance of not missing any doses must be stressed.
PRIFTIN, in combination with isoniazid, should be given with food.
For patients who cannot swallow tablets, the tablets may be crushed and added to a small amount of semi-solid food, all of which should be consumed immediately (see Pharmacokinetic properties).
Interactions with antacids have not been studied. However, in the clinical efficacy study, patients were advised to take PRIFTIN at least 1 hour before or 2 hours after the ingestion of antacids.

SIDE EFFECTS:
The following CIOMS frequency rating is used, when applicable: Very common ≥ 10 %; Common ≥ 1 and < 10 %; Uncommon ≥ 0,1 % and < 1 %; Rare ≥ 0,01 and < 0,1 %; Very rare < 0,01 %; Not known (cannot be estimated from available data).

Clinical trials experience:
The safety profile of PRIFTIN in combination with isoniazid given once-weekly is based on the study TBTC-S26. In this study, PRIFTIN in combination with isoniazid given once-weekly for 3 months (3RPT/INH) was compared to a comparator given once daily for 9 months in an open-label, randomised trial in patients with a positive tuberculin skin test, and at high risk for progression from latent tuberculosis infection to active tuberculosis disease.
A total of 4 040 patients received at least one dose of the 3RPT/INH regimen, including 348 children 2 – 17 years of age and 105 HIV-infected individuals. A total of 3 759 received at least one dose of the comparator regimen, including 342 children 2 years to 17 years of age and 95 HIV-infected individuals. Patients were followed for 33 months from the time of enrolment.

Table 4 – Adverse drug reactions (i.e. considered by the investigator to be possibly, probably, or definitely related to the medicine) reported in at least 3 patients treated with 3RPT/INH*

System Organ Class	Frequency	*3RPT/INH patients (%)*	*Comparator patients (%)*
Infections and infestations			
Influenza	Uncommon	8 (0,2)	1 (0,03)
Immune system disorders			
Hypersensitivity	Common	160 (3,96)	18 (0,48)
Nervous system disorders			
Headache	Uncommon	14 (0,35)	10 (0,27)
Gastrointestinal disorders			
Nausea	Uncommon	11 (0,3)	6 (0,2)
Upper abdominal pain	Uncommon	3 (0,07)	2 (0,05)
Hepatobiliary disorders			
Hepatitis	Uncommon	18 (0,45)	103 (2,74)
Skin and subcutaneous tissue disorders			
Skin reaction	Uncommon	31 (0,77)	21 (0,56)
Muscular and connective tissue disorders			
Myalgia	Uncommon	4 (0,1)	0
General disorders and administration site conditions			
Influenza-like illness	Uncommon	8 (0,2)	0
Fatigue	Uncommon	4 (0,1)	6 (0,16)
Chills	Uncommon	4 (0,1)	0
Pyrexia	Uncommon	4 (0,1)	1 (0,03)
Asthenia	Rare	3 (0,07)	0

* Includes events reported through 60 days after last dose of study medicine

The following adverse drug reactions were reported in less than 3 patients (frequency: rare):
pancreatitis, oesophageal irritation, pneumonia.

Paediatric population:
Six-hundred and ninety children 2 years – 17 years of age received at least one dose of study medicines in the main study. An additional 342 children 2 years – 17 years of age received at least one dose in the paediatric extension study (total 1 032 children; 539 received 3RPT/INH and 493 received the comparator).
No children in either treatment arm developed hepatotoxicity.
Children in the 3RPT/INH group experienced less rifamycin hypersensitivity reaction (7 (1,3 %)) than adults.
Adverse reactions in children 2 years – 11 years of age and 12 years – 17 years of age were similar.

HIV population:
Two-hundred HIV-infected patients with latent tuberculosis infection received at least one dose of study medicines in the main study and an additional 193 patients received at least one dose in the extension study (total of 393; 207 received 3 RPT/INH and 186 received comparator). Compared to the HIV-negative patients enrolled in the main study, a higher proportion of HIV-infected patients in each treatment arm experienced a treatment emergent adverse reaction, including a higher incidence of hepatotoxicity. Hepatotoxicity occurred less frequently in patients in the 3RPT/INH arm (3/207 (1,5 %)) than in the comparator arm (14/186 (7,5 %)).
Rifamycin hypersensitivity occurred in only one HIV-infected patient in 3RPT/INH arm.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
An overdose may precipitate side effects and increase the severity thereof.
Treatment should be symptomatic and supportive.

IDENTIFICATION:
PRIFTIN is supplied as round, dark-pink, normal convex, engraved film-coated tablets.

PRESENTATION:
24 tablets packed in grey aluminium formable foil blister strips (3 blisters x 8 tablets) in cardboard cartons.

STORAGE INSTRUCTIONS:
Store at or below 30 °C.
Protect from excessive heat and humidity.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:
51/20.2.3/1081

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
sanofi-aventis south africa (pty) ltd.
2 Bond Street
Midrand 1685
South Africa

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:
Date of registration: 26 October 2018

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:
PRIFTIN® (Film-coated tablet)
Rifapentine 150 mg

Read all of this leaflet carefully before you start taking PRIFTIN:
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- PRIFTIN has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

WHAT PRIFTIN CONTAINS:
The active substance of PRIFTIN is rifapentine. Each film-coated tablet contains 150 mg rifapentine.

The other ingredients are:
Calcium stearate, microcrystalline cellulose, pregelatinised starch, sodium ascorbate, sodium lauryl sulphate and sodium starch glycolate.
Tablet film-coat: disodium edetate, hydroxypropyl cellulose, hypromellose, indigo carmine (FD&C blue No. 2 aluminium lake), polyethylene glycol, propylene glycol, red iron oxide, sodium ascorbate and titanium dioxide.
Sugar free.

WHAT PRIFTIN IS USED FOR:
PRIFTIN contains rifapentine which belongs to the rifamycin class of antibiotics. It is used with other anti-tuberculosis (TB) medicines to treat inactive (latent) tuberculosis infection and to prevent it's progression to active tuberculosis disease in people aged 2 years and older who are at risk. PRIFTIN should not be used in people with active TB.
For the treatment of latent tuberculosis infection PRIFTIN must always be used in combination with the anti-tuberculosis medicine isoniazid.

BEFORE YOU TAKE PRIFTIN:
Do not take PRIFTIN if:
- you are hypersensitive (allergic) to rifapentine or to a group of medicines called rifamycins (e.g. rifampicin and rifabutin), or to any of the ingredients of PRIFTIN.
- you have a condition called porphyria (a group of disorders that can cause nerve or skin (blisters and itching) problems due to a problem with the production of haem (blood pigment) and red blood cells within the body).
- you have acute or chronic liver disease.

Take special care with PRIFTIN:
Tell your doctor or healthcare professional before you are given PRIFTIN tablets if you:
- have liver problems. Your doctor may do a blood test to check your liver function before and while you take PRIFTIN (see: Do not take PRIFTIN if:).
- have active TB disease.
- know that you have TB that is resistant to treatment with some medicines.
- are pregnant or breastfeeding or if you are planning to become pregnant or to breastfeed (see: Pregnancy and Breastfeeding).
- take medicines to treat HIV infection or take oral contraceptives. Using these medicines with PRIFTIN may make them less effective (see: Taking other medicines with PRIFTIN).
- use a medicine called digoxin (used to make the heart beat stronger and with a more regular rhythm). Your doctor will monitor your dose of digoxin as it could change due to PRIFTIN. Even small changes need to be monitored to prevent serious side effects from occurring (also see: Taking other medicines with PRIFTIN).
- **wear contact lenses or dentures. PRIFTIN may change the normal colour of your skin, mouth and body fluids and cause your skin, teeth, tongue, urine, stools, saliva, sputum, tears, sweat, and breast milk to turn a red-orange colour. Contact lenses or dentures may become permanently stained.**

If you experience any of the following after or while you are taking PRIFTIN, tell your doctor or healthcare provider immediately:
- If you experience symptoms of a hypersensitivity (allergic) reaction after taking PRIFTIN, e.g. low blood pressure, hives, swelling of the face, lips, tongue or throat, difficulty breathing, red eyes or flu-like syndrome (weakness, extreme tiredness, muscle pain, nausea and vomiting, headache, fever, chills, aches, rash, itching, sweats, dizziness, shortness of breath, chest pain, cough, fainting, fast heartbeat). These may be symptoms of a serious allergic reaction and you must immediately stop taking PRIFTIN and go to the casualty department at your nearest hospital. Also see: Possible side effects.
- PRIFTIN may cause serious liver problems. Stop taking PRIFTIN and call your doctor right away if you have any of the following signs and symptoms of liver problems: nausea, vomiting, stomach pain, loss of appetite, tiredness, yellowing skin or whites of your eyes, dark urine. See: Possible side effects.
- PRIFTIN may cause a type of diarrhoea called *Clostridium difficile*-associated diarrhoea (CDAD) which may occur during or after taking PRIFTIN. The severity of CDAD can range from mild diarrhoea to severe diarrhoea that may cause death (fatal colitis). Tell your doctor immediately if you have diarrhoea while you are taking or after you have stopped taking PRIFTIN. See: Possible side effects.

Taking PRIFTIN with food and drink:
Take PRIFTIN and isoniazid tablets with food.

Pregnancy and Breastfeeding:
Safety of PRIFTIN during pregnancy and breastfeeding has not been established. You should not be treated with PRIFTIN if you are pregnant.
If you are pregnant or breastfeeding or planning to become pregnant or to breastfeed your baby, please consult your doctor, pharmacist or other healthcare professional for advice, before taking this medicine.
You should not breastfeed your baby if you are on treatment with PRIFTIN.
It is not known if PRIFTIN passes into your breast milk. PRIFTIN may potentially cause discolouration of breast milk, since PRIFTIN causes a red-orange discolouration of body fluids.

Driving and using machinery:
Do not drive or operate machines if you experience any side effects of PRIFTIN which could adversely affect your ability to drive or use machines.

Important information about some of the ingredients of PRIFTIN:
PRIFTIN is sugar free.

Taking other medicines with PRIFTIN:
Always tell your healthcare professional if you are taking any other medicine (including complementary or traditional medicine).
Using PRIFTIN with other medicines may affect each other causing serious side effects or causing one of the medicines to be ineffective.
Before you take PRIFTIN, tell your doctor or healthcare professional if you are taking or have recently taken any of the medicines mentioned below.
PRIFTIN may make the following medicines work less well:
- medicines used to treat HIV infection: indinavir, darunavir, lopinavir, saquinavir, ritonavir, rilpirivine, zidovudine
- antifungal medicine (to treat fungal infections): itraconazole, ketoconazole, voriconazole
- pain killers (narcotic analgesics): methadone, alfentanil, buprenorphine
- medicines used for diabetes to lower blood sugar: repaglinide
- medicines to lower blood pressure, called calcium channel blockers: felodipine, diltiazem, verapamil, nifedipine
- medicines to lower blood pressure called alpha/beta adrenergic antagonists: alfuzosin, propranolol
- medicines to treat migraine, sometimes referred to as ergot alkaloid derivates: ergotamine
- medicines used to prevent the blood from clotting (anticoagulants): warfarin
- hormonal contraceptives for women. If you are using any form of contraception, such as contraceptive tablets, transdermal patches (patches used on the skin) or an implant while taking PRIFTIN tablets, you should discuss the need to use an additional non-hormonal means of contraception or to change your contraceptive pill with your doctor or healthcare professional to make sure that your method of contraception is still effective
- medicines used to lower your immune system: ciclosporin, tacrolimus, sirolimus
- medicines used as sedatives or to treat anxiety: midazolam.

Other medicines which could be affected by PRIFTIN:
- digoxin (used to make the heart beat stronger and with a more regular rhythm). Your doctor will monitor your dose of digoxin as it could change due to PRIFTIN. Even small changes need to be monitored to prevent serious side effects from occurring. Also see: Take special care with PRIFTIN
- medicines used for inflammation (e.g. ibuprofen, diclofenac)
- medicines used to lower blood sugar in diabetes: glipizide.

PRIFTIN may also interact with the laboratory tests to determine folate and vitamin B_{12} in your blood. Make sure that you inform your doctor or healthcare professional that you are using PRIFTIN before such tests are performed.

HOW TO TAKE PRIFTIN:
Do not share medicines prescribed for you with any other person.
Always take PRIFTIN exactly as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are unsure.
- PRIFTIN should be taken once-weekly in combination with another anti-TB medicine, isoniazid, for 12 weeks as directly observed therapy (DOT). DOT is a way of helping people during their treatment, e.g. your treatment will be monitored weekly by visiting your local clinic, hospital or nurse and they will make sure you take your treatment correctly.
- Your doctor will calculate the number of tablets you should take weekly based on your weight. This dose will therefore be calculated for you personally.
- It is important to take all of your PRIFTIN and your other TB medicine (isoniazid). Do not skip doses. Skipping doses may cause PRIFTIN to not work as well and may increase the chance that your TB will not be treatable by PRIFTIN or other medicines.
- Take PRIFTIN and isoniazid with food. This may help prevent nausea, vomiting or stomach upsets due to the medication.
- It is preferable to take antacids at least 1 hour before or 2 hours after your dose of PRIFTIN tablets.
- If you cannot swallow PRIFTIN tablets whole, they can be crushed and mixed with a small amount of semisolid food. Be sure to take all of the semisolid food with PRIFTIN in it right away.

If you take more PRIFTIN than you should:
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take PRIFTIN:
Since your weekly dose of PRIFTIN will be given to you via directly observed therapy (DOT) which includes a visit to, for example, your local clinic or hospital, it is unlikely that you will forget to take a dose. However, if you have missed the visit to your local clinic or hospital, visit them as soon as possible and do not skip the whole week until the next appointment.

POSSIBLE SIDE EFFECTS:
PRIFTIN can have side effects. Not all side effects reported for PRIFTIN are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking PRIFTIN, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop taking PRIFTIN and tell your doctor immediately or go to the casualty department at your nearest hospital:
Frequent:
- hypersensitivity (allergic) reaction: this may present as a sudden life-threatening allergic reaction and the signs may include low blood pressure, hives, swelling of the face, lips, tongue or throat, difficulty breathing, red eyes or flu-like syndrome (see below).

Less frequent:
- flu-like syndrome (weakness, extreme tiredness, muscle pain, nausea and vomiting, headache, fever, chills, aches, rash, itching, sweats, dizziness, shortness of breath, chest pain, cough, fainting, fast heartbeat). See: Take special care with PRIFTIN.
- hepatitis (inflammation of the liver) and liver problems (symptoms may include: nausea, vomiting, stomach pain, loss of appetite, tiredness, yellowing of the skin or whites of your eyes, dark urine). See: Take special care with PRIFTIN.
- diarrhoea called *Clostridium difficile*-associated diarrhoea (CDAD) which may occur during or after taking PRIFTIN. The severity of CDAD can range from mild diarrhoea to severe diarrhoea that may cause death (fatal colitis). See: Take special care with PRIFTIN.
- pancreatitis (inflammation of the pancreas) (symptoms may include upper abdominal pain that radiates into the back; swollen and tender abdomen; nausea and vomiting, fever and increased heart rate)
- pneumonia (infection of the lungs; symptoms may include fever and chills, cough, difficulty breathing, shortness of breath when you climb stairs).

These are all very serious side effects. If you have them, you may have had a serious reaction to PRIFTIN. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
Less frequent:
- influenza (flu)
- upper abdominal pain
- skin reaction
- pain in one or more muscles (myalgia)
- chills
- fever
- abnormal physical weakness or lack of energy (asthenia).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Less Frequent:
- headache
- fatigue or extreme tiredness
- irritation of the oesophagus (the tube that sends food from your throat down to your stomach).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

STORING AND DISPOSING OF PRIFTIN:
Store at or below 30 °C.
Protect from excessive heat and humidity.
Do not expose the tablets to direct sunlight and do not remove the tablets from the blisters until ready for use in order to protect them from excessive heat and moisture.
Store all medicine out of reach of children.
Do not use this medicine after the expiry date shown on the label.
Return all unused medicine to your pharmacist.

PRESENTATION OF PRIFTIN:
24 tablets packed in grey aluminium formable foil blister strips (3 blisters x 8 tablets) in cardboard cartons.

IDENTIFICATION OF PRIFTIN:
PRIFTIN is supplied as round, dark-pink, normal convex, engraved film-coated tablets.

REGISTRATION NUMBER:
51/20.2.3/1081

NAME AND ADDRESS OF REGISTRATION HOLDER:
sanofi-aventis south africa (pty) ltd.
2 Bond Street
Midrand 1685
South Africa
011 256 3700

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PASIËNTINLIGTINGSBROSJURE

SKEDULERINGSTATUS:

S4

EIENDOMSNAAM, STERKTE EN FARMASEUTIESE VORM:
PRIFTIN® (Filmbedekte tablet)
Rifapentien 150 mg

Lees hierdie hele brosjure versigtig voordat jy begin om PRIFTIN te neem:
- Hou hierdie brosjure. Jy mag dit weer moet lees.
- Indien jy verdere vrae het, vra asseblief jou dokter of jou apteker daaroor.
- PRIFTIN is vir jou persoonlik voorgeskryf en jy behoort nie jou medisyne met ander persone te deel nie. Dit kan hulle skade aandoen, al is hulle simptome dieselfde as joune.

WAT PRIFTIN BEVAT:
Die aktiewe stof in PRIFTIN is rifapentien. Elke filmbedekte tablet bevat 150 mg rifapentien.

Die ander bestanddele is:
Kalsiumstearaat, mikrokristallyne sellulose, vooraf-gegelatiniseerde stysel, natriumaskorbaat, natriumlaurielsulfaat, en natrium-stysel-glikolaat.
Filmbedekking van tablet: dinatriumedetaat, hidroksipropielsellulose, hipromellose, indigo-karmyn (FD&C blou Nr. 2 aluminiumlak), poliëtileenglikol, propileenglikol, rooi ysteroksied, natriumaskorbaat en titaandioksied.
Suikervry.

WAARVOOR PRIFTIN GEBRUIK WORD:
PRIFTIN bevat rifapentien, wat aan die rifamisien-klas van antibiotika behoort. Dit word saam met ander anti-tuberkulose (TB) medisyne gebruik om onaktiewe (latente) tuberkulose infeksie te behandel en om die progressie daarvan na aktiewe tuberkulose in persone van 2 jaar en ouer wat aan risiko blootgestel is, te voorkom.
PRIFTIN moet nie deur persone met aktiewe TB gebruik word nie.
Vir die behandeling van latente tuberkulose infeksie, moet PRIFTIN altyd in kombinasie met die anti-tuberkulose medisyne, isoniasied, gebruik word.

VOORDAT JY PRIFTIN NEEM:
Moenie PRIFTIN neem nie, indien:
- jy hipersensitief (allergies) is vir rifapentien of 'n groep medisyne wat rifamisiene (bv. rifampisien en rifabutien) genoem word, of enige van die ander bestanddele van PRIFTIN.
- jy 'n toestand het wat porfirie genoem word ('n groep siektes wat senuwee- of velprobleme (blase en jeuk) kan veroorsaak as gevolg van 'n probleem met die produksie van heem (bloed kleurstof) en rooibloedselle binne in die liggaam).
- jy akute of chroniese lewer siekte het.

Neem spesiale sorg met PRIFTIN:
Vertel jou dokter of gesondheidsorgdeskundige voordat jy PRIFTIN tablette gegee word, indien jy:
- lewerprobleme het. Jou dokter mag 'n bloedtoets doen om jou lewerfunksie na te gaan voordat, en terwyl jy PRIFTIN neem (sien: Moenie PRIFTIN neem nie, indien:).
- aktiewe TB-siekte het.
- jy bewus is dat jy TB het wat weerstandig is teen behandeling met sekere medisyne.
- jy swanger is of borsvoed of as jy beplan om swanger te word of te borsvoed (sien: Swangerskap en Borsvoeding).
- medisyne om MIV-infeksie te behandel of orale kontraseptiewe middels neem. Die gebruik van hierdie medisyne saam met PRIFTIN mag hulle minder effektief maak (sien: Neem van ander medisyne saam met PRIFTIN).
- 'n medisyne neem wat digoksien genoem word (dit word gebruik om die hart sterker en met 'n meer egalige ritme te laat klop). Jou dokter sal jou dosis digoksien moniteer omdat dit moontlik as gevolg van PRIFTIN mag verander. Selfs klein veranderings moet gemoniteer word om te verhoed dat ernstige newe-effekte voorkom (sien ook: Neem van ander medisyne saam met PRIFTIN).
- **kontaklense of kunstande dra. PRIFTIN mag die normale kleur van jou vel, mond en liggaamsvloeistowwe verander en veroorsaak dat jou vel, tande, tong, urien, stoelgang, speeksel, sputum, trane, sweet en borsmelk 'n rooi-oranje kleur ontwikkel. Kontaklense en kunstande kan moontlik permanent verkleur word.**

Indien jy enige van die volgende ondervind na inname van PRIFTIN of terwyl jy PRIFTIN neem, moet jy dadelik jou dokter of gesondheidsorgdeskundige daarvan vertel:
- Indien jy simptome van 'n hipersensitiwiteitsreaksie (allergiese reaksie) ondervind nadat jy PRIFTIN geneem het, bv. lae bloeddruk, galbulte, swelling van die gesig, lippe, tong of keel, asemhalingsprobleme, rooi oë of griepagtige sindroom (swakheid, uitermatige moegheid, spierpyn, naarheid en braking, hoofpyn, koors, kouekoors, pyne, veluitslag, jeuk, sweet, duiseligheid, kortasem, borspyn, hoes, floutes, vinnige hartklop). Dit mag simptome van 'n ernstige allergiese reaksie wees en jy moet dadelik die inname van PRIFTIN staak en na die noodafdeling van jou naaste hospitaal gaan. Sien ook: Moontlike newe-effekte.
- PRIFTIN mag ernstige lewerprobleme veroorsaak. Staak die inname van PRIFTIN en skakel jou dokter dadelik indien jy enige van die volgende tekens en simptome van lewerprobleme ontwikkel: naarheid, braking, maagpyn, verlies aan aptyt, moegheid, vergeling van die vel of die wit gedeelte van jou oë, donker urien. Sien: Moontlike newe-effekte.
- PRIFTIN mag 'n soort diarree veroorsaak wat *Clostridium difficile*-geassosieerde diarree (CDAD) genoem word wat terwyl, of na inname van PRIFTIN, mag voorkom. Die erns van CDAD kan wissel van ligte diarree tot ernstige diarree wat sterftes kan veroorsaak (noodlottige kolitis). Vertel jou dokter dadelik as jy diarree het terwyl jy PRIFTIN neem of nadat jy PRIFTIN inname gestaak het. Sien: Moontlike newe-effekte.

Inname van PRIFTIN saam met kos en drank:
Neem PRIFTIN en isoniasied tablette saam met kos.

Swangerskap en Borsvoeding:
Veiligheid van PRIFTIN tydens swangerskap en borsvoeding is nie vasgestel nie. Jy behoort nie PRIFTIN te ontvang indien jy swanger is nie.
Indien jy swanger is of borsvoed, of beplan om swanger te word of om jou baba te borsvoed, moet jy asseblief jou dokter, apteker of ander gesondheidsorgdeskundige raadpleeg vir advies voordat jy hierdie medisyne neem.
Jy behoort nie jou baba te borsvoed indien jy PRIFTIN behandeling ontvang nie.
Alhoewel dit nie bekend is of PRIFTIN in jou borsmelk uitgeskei word nie, mag PRIFTIN potensieel verkleuring van borsmelk veroorsaak, omdat PRIFTIN 'n rooi-oranje verkleuring van liggaamsvloeistowwe veroorsaak.

Bestuur en gebruik van masjinerie:
Moenie bestuur of masjiene hanteer nie, indien jy enige newe-effekte van PRIFTIN ondervind wat jou vermoë om te bestuur en masjiene te gebruik, moontlik nadelig kan beïnvloed.

Belangrike inligting oor sommige van die bestanddele van PRIFTIN:
PRIFTIN is suikervry.

Neem van ander medisyne saam met PRIFTIN:
Jy moet altyd jou gesondheidsorgdeskundige daarvan vertel indien jy enige ander medisyne (insluitend komplementêre of tradisionele medisyne) neem.
Indien PRIFTIN saam met ander medisyne gebruik word, kan hulle mekaar affekteer wat ernstige newe-effekte kan veroorsaak of veroorsaak dat een van die medisyne nie effektief is nie.
Voordat jy PRIFTIN neem, moet jy jou dokter of gesondheidsorgdeskundige vertel indien jy tans enige van die medisyne wat hierna gelys word, neem of onlangs geneem het.
PRIFTIN mag veroorsaak dat die volgende medisyne minder effektief werk:
- medisyne wat gebruik word om MIV-infeksie te behandel: indinavir, darunavir, lopinavir, sakinavir, ritonavir, rilpirivien, sidovudien
- swamwerende medisyne (om swaminfeksies te behandel): itrakonasool, ketokonasool, vorikonasool
- pynstillers (narkotiese analgetika): metadoon, alfentaniel, buprenorfien
- medisyne wat gebruik word vir diabetes om bloedsuiker te verlaag: repaglinied
- medisyne wat gebruik word om bloeddruk te verlaag, wat kalsiumkanaalblokkeerders genoem word: felodipien, diltiasem, verapamiel, nifedipien
- medisyne wat gebruik word om bloeddruk te verlaag, wat alfa-/beta-adrenergiese antagoniste genoem word: alfusosien, propranolol
- medisyne om migraine te behandel, waarna soms verwys word as ergot alkaloïed- derivate: ergotamien
- medisyne wat gebruik word om te verhoed dat bloed stol (antikoagulante): warfarien
- hormonale kontraseptiewe vir vroue. Indien jy enige soort van kontrasepsie gebruik, soos kontraseptiewe tablette, transdermale plakkers (plakkers wat op die vel gebruik word), of 'n inplantaat terwyl jy PRIFTIN neem, behoort jy die behoefte om 'n addisionele nie-hormonale voorbehoedmiddel te gebruik of om jou kontraseptiewe pil te verander, te bespreek met jou dokter of gesondheidsorgverskaffer om seker te maak dat jou metode van kontrasepsie steeds effektief is
- medisyne wat gebruik word om jou immuunsisteem te verlaag: siklosporien, takrolimus, sirolimus
- medisyne wat as kalmeermiddels of vir die behandeling van angstigheid gebruik word: midazolam.

Ander medisyne wat deur PRIFTIN geaffekteer kan word:
- digoksien (gebruik om die hart sterker en met 'n meer gereelde ritme te laat klop). Jou dokter sal jou dosis digoksien moniteer omdat dit moontlik kan verander weens PRIFTIN. Selfs klein veranderings moet gemoniteer word om ernstige newe-effekte te verhoed. Sien ook: Neem spesiale sorg met PRIFTIN
- medisyne wat gebruik word vir inflammasie (bv. ibuprofen, diklofenak)
- medisyne wat gebruik word om bloedsuiker te verlaag in diabetes: glipisied.

PRIFTIN mag ook inmeng met die laboratoriumtoetse wat gebruik word om folaat en vitamien B_{12} in jou bloed te bepaal. Maak seker dat jy 'n dokter of gesondheidsorgdeskundige vertel dat jy PRIFTIN neem voordat sulke toetse gedoen word.

HOE OM PRIFTIN TE NEEM:
Moenie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie.
Jy moet PRIFTIN altyd presies volgens jou dokter of apteker se instruksies neem. Jy moet jou dokter of apteker vra indien jy nie seker is nie.
- PRIFTIN behoort een keer weekliks in kombinasie met 'n ander anti-TB-medisyne, isoniasied, geneem te word vir 12 weke as direk waargenome terapie (DOT). DOT is 'n manier om mense gedurende hul behandeling te help, bv. jou behandeling sal weekliks gemoniteer word deur besoek aan jou plaaslike kliniek, hospitaal of verpleegster, en hulle sal seker maak dat jy jou behandeling korrek neem.
- Jou dokter sal die getal tablette wat jy weekliks behoort te gebruik, bereken gegrond op jou gewig. Die dosis sal dus persoonlik vir jou bereken word.
- Dit is belangrik om al jou PRIFTIN en jou ander TB-medisyne (isoniasied) te neem. Moenie dosisse oorslaan nie. Oorslaan van dosisse mag veroorsaak dat PRIFTIN nie so goed werk nie en mag die kans verhoog dat jou TB nie met PRIFTIN of ander medisyne behandel sal kan word nie.
- Neem PRIFTIN en isoniasied saam met kos. Dit sal moontlik help om naarheid, braking of maagongesteldhede weens die medikasie voorkom.
- Dit is verkieslik om teensuurmiddels ten minste 1 uur voor of 2 uur na jou dosis PRIFTIN tablette te neem.
- Indien jy PRIFTIN tablette nie heel kan insluk nie, kan dit vergruis en met 'n klein hoeveelheid half-soliede kos gemeng word. Maak seker dat jy al die half-soliede kos saam met die PRIFTIN onmiddellik neem.

Indien jy meer PRIFTIN neem as wat jy behoort te neem:
In geval van 'n oordosis, moet jy jou dokter of apteker raadpleeg. Indien albei nie beskikbaar is nie, moet jy die naaste hospitaal of gifbeheersentrum kontak.

Indien jy vergeet om PRIFTIN te neem:
Aangesien jou weeklikse dosis PRIFTIN direk vir jou gegee sal word deur die waargenome terapie (DOT) wat 'n besoek aan jou plaaslike kliniek of hospitaal sal insluit, is dit onwaarskynlik dat jy sal vergeet om 'n dosis te neem. Indien jy egter 'n besoek aan jou plaaslike kliniek of hospitaal verpas het, moet jy dit so gou as moontlik besoek en nie die hele week oorslaan tot die volgende afspraak nie.

MOONTLIKE NEWE-EFFEKTE:
PRIFTIN kan newe-effekte veroorsaak. Nie alle newe-effekte wat vir PRIFTIN aangemeld is, word in hierdie brosjure ingesluit nie. Indien jou algemene gesondheid sou vererger of as jy enige nadelige effekte sou ondervind terwyl jy PRIFTIN neem, moet jy asseblief jou dokter, apteker of ander gesondheidsorgdeskundige vir advies raadpleeg.

Indien enige van die volgende sou voorkom, moet jy die inname van PRIFTIN staak en dadelik jou dokter daarvan vertel of na die noodafdeling by jou naaste hospitaal gaan:
Frekwent:
- hipersensitiwiteitsreaksie (allergiese reaksie): dit mag presenteer as 'n skielike lewensbedreigende allergiese reaksie en die tekens mag lae bloeddruk, galbulte, swelling van die gesig, lippe, tong of keel, asemhalingsprobleme, rooi oë of griepagtige sindroom insluit (sien hierna).

Minder frekwent:
- griepagtige sindroom (swakheid, uitermatige moegheid, spierpyn, naarheid en braking, hoofpyn, koors, kouekoors, pyne, veluitslag, jeuk, sweet, duiseligheid, kortasem, borspyn, hoes, floutes, vinnige hartklop). Sien: Neem spesiale sorg met PRIFTIN.
- hepatitis (inflammasie van die lewer) en lewerprobleme (simptome mag insluit: naarheid, braking, maagpyn, verlies aan aptyt, moegheid, vergeling van die vel of die wit dele van jou oë, donker urien). Sien: Neem spesiale sorg met PRIFTIN.
- diarree wat *Clostridium difficile*-geassosieerde diarree (CDAD) genoem word wat terwyl, of na inname van PRIFTIN, mag voorkom. Die erns van CDAD kan wissel van ligte diarree tot ernstige diarree wat sterftes kan veroorsaak (noodlottige kolitis). Sien: Neem spesiale sorg met PRIFTIN.
- pankreatitis (inflammasie van die pankreas) (simptome mag insluit: pyn in die boonste buik wat uitsprei na die rug; geswolle en teer buik; naarheid en braking, koors en verhoogde harttempo)
- pneumonie (infeksie van die longe; simptome mag koors en kouekoors, hoes, asemhalingsprobleme, en kortasem as jy trappe klim, insluit).

Dit is almal baie ernstige newe-effekte. Indien jy dit ontwikkel, het jy moontlik 'n ernstige reaksie teen PRIFTIN gehad. Jy het moontlik dringende mediese aandag of hospitalisasie nodig.

Vertel jou dokter dadelik of gaan na die ongevalleafdeling van jou naaste hospitaal indien jy van enige van die volgende bewus word:
Minder frekwent:
- influensa (griep)
- boonste abdominale pyn
- velreaksie
- pyn in een of meer spiere (mialgie)
- kouekoors
- koors
- abnormale swakheid of gebrek aan energie (astenie).

Dit is almal ernstige newe-effekte. Jy het moontlik dringende mediese aandag nodig.

Vertel jou dokter indien jy van enige van die volgende bewus word:
Minder frekwent:
- hoofpyn
- moegheid of uitermatige moegheid
- irritasie van die esofagus (die buis wat kos van jou keel tot in jou maag afstuur).

Indien jy bewus word van enige newe-effekte wat nie in hierdie brosjure genoem word nie, moet jy asseblief jou dokter of apteker daarvan vertel.

OPBERGING EN WEGDOENING VAN PRIFTIN:
Bêre by of onder 30 °C.
Beskerm teen buitensporige hitte en humiditeit.
Moenie die tablette aan direkte sonlig blootstel en moenie die tablette uit die stulpverpakkings verwyder nie totdat dit gereed is vir gebruik om die tablette teen buitensporige hitte en vog te beskerm.
Bewaar alle medisyne buite bereik van kinders.
Moenie hierdie medisyne na die vervaldatum wat op die etiket aangedui word, gebruik nie.
Gee alle ongebruikte medisyne terug aan jou apteker.

AANBIEDING VAN PRIFTIN:
24 tablette verpak in grys gevormde aluminiumfoelie stulpverpakkingstroke (3 stulpverpakkings x 8 tablette) in kartonhouer.

IDENTIFIKASIE VAN PRIFTIN:
PRIFTIN word verskaf as ronde, donker-pienk, normaal konvekse, gegraveerde filmbedekte tablette.

REGISTRASIENOMMER:
51/20.2.3/1081

NAAM EN ADRES VAN DIE REGISTRASIEHOUER:
sanofi-aventis south africa (edms) bpk.
Bondstraat 2
Midrand 1685
Suid-Afrika
011 256 3700

DATUM VAN PUBLIKASIE VAN DIE PASIËNTINLIGTINGSBROSJURE:
Datum van registrasie: 26 Oktober 2018

89034260
744214

CROM...FOTO
29 GEN 2019
89034260 (int. version 3)
LEAFLET FOLDED PRIFTIN 150 MG 3X8
SOUTH AFRICA
420 x 296 (210 x 148)
BLACK
6.8 pt.