				History # - Date
Part Number - Version #:	Region(Market):	Reference Version:	Cutting Dimensions:	
Macao-03-001	Macao	CA-1628-01	585 x 260 mm (Folded: 147 x 30 mm)	
Component description:				
Leaflet Ruxolitinib All strength Tube 585x260mm				
Colors to be printed:		Technical Colors (Non-printing):		
Process Black		cut	technical dimensions	
			comments	
NB: Color separation to make printing tools is printer´s responsibility in order to achieve approved design.				

FRONT SIDE

147 mm

731.912 mm

30 mm

260 mm

Lumirix®
Ruxolitinib Cream 15mg/g

1. NAME OF THE MEDICINAL PRODUCT
Lumirix® Cream 15 mg/g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
One gram of cream contains 15 mg of ruxolitinib (as phosphate).
Excipients with known effect
Propylene glycol (E1520), 150 mg/g of cream, Cetyl alcohol, 30 mg/g of cream
Stearyl alcohol, 17.5 mg/g of cream Methyl parahydroxybenzoate (E218), 1 mg/g of cream Propyl parahydroxybenzoate, 0.5 mg/g of cream, Butylated hydroxytoluene (as an antioxidant in paraffin, white soft) (E321) For the full list of excipients, see section 6.1.

PHARMACEUTICAL FORM
Cream, White to off-white cream.

CLINICAL PARTICULARS
4.1 Therapeutic indications
Lumirix® is indicated for the treatment of non-segmental vitiligo with facial involvement in adults and adolescents from 12 years of age.

4.2 Posology and method of administration
Lumirix® should be initiated and supervised by physicians with experience in the diagnosis and treatment of non-segmental vitiligo.

Posology
Adults
The recommended dose is a thin layer of cream applied twice daily to the depigmented skin areas up to a maximum of 10% of body surface area (BSA), with a minimum of 8 hours between two applications of ruxolitinib cream. 10% BSA represents an area as large as 10 times the palm of one hand with the 5 fingers. Ruxolitinib cream should be used at the smallest skin area necessary.
No more than two tubes of 100 grams a month should be used.
Satisfactory repigmentation may require treatment beyond 24 weeks. If there is less than 25% repigmentation in treated areas at week 52, treatment discontinuation should be considered.
Once satisfactory repigmentation is achieved, treatment in those areas can be stopped. If depigmentation recurs after treatment discontinuation, therapy can be reinitiated on the affected areas.
Special populations
Hepatic impairment
No studies with ruxolitinib cream have been performed in patients with hepatic impairment. However, due to limited systemic exposure, dose adjustment is not necessary in patients with hepatic impairment.
Renal impairment
No studies with ruxolitinib cream have been performed in patients with renal impairment. However, due to limited systemic exposure, dose adjustment is not necessary in patients with renal impairment. As a precautionary measure, ruxolitinib cream should not be used by patients with end stage renal disease, due to lack of data regarding the safety.
Elderly
A limited number of patients aged 65 years and above have been enrolled in the clinical studies with Lumirix® in vitiligo to determine whether they respond differently from younger subjects (see section 5.1). No dose adjustment is required in patients aged 65 years and above.
Paediatric population
For adolescents (12-17 years) the posology is the same as for adults.
The safety and efficacy of ruxolitinib cream in children below 12 years of age have not been established. No data are available.
Method of administration
The cream is for cutaneous use only. Avoid washing treated skin for at least 2 hours after application of ruxolitinib cream.
The cream should not be applied to the lips to avoid its ingestion.
Patients should be instructed to wash their hands after applying the cream, unless it is their hands that are being treated. If someone else applies the cream to the patient, they should wash their hands after application.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Pregnancy and breastfeeding (see section 4.6).

4.4 Special warnings and precautions for use
The cream is not for ophthalmic, oral, or intravaginal use (see section 4.2). In cases of accidental exposure in the eyes or mucous membranes, the cream should be thoroughly wiped off and/or rinsed with water.
Malignancy and Lymphoproliferative Disorders
Malignancies, including lymphomas, were observed in clinical trials of oral JAK inhibitors used to treat inflammatory conditions. Patients who are current or past smokers are at additional increased risk.
Malignancies, including lymphomas, have occurred in patients receiving JAK inhibitors used to treat inflammatory conditions. In a large, randomized, postmarketing safety study of an oral JAK inhibitor in RA patients, a higher rate of malignancies (excluding non-melanoma skin cancer) was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lymphomas was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lung cancers was observed in current or past smokers treated with the JAK inhibitor compared to those treated with TNF blockers. In this study, current or past smokers had an additional increased risk of overall malignancies.
Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Lumirix, particularly in patients with a known malignancy (other than successfully treated non-melanoma skin cancers), patients who develop a malignancy when on treatment, and patients who are current or past smokers.
Non-melanoma skin cancer
Non-melanoma skin cancers including basal cell and squamous cell carcinoma have occurred in patients treated with Lumirix. Perform periodic skin examinations during Lumirix treatment and following treatment as appropriate. Exposure to sunlight and UV light should be limited by wearing protective clothing and using broad-spectrum sunscreen.
Major Adverse Cardiovascular Events (MACE)
In a large, randomized, postmarketing safety study of an oral JAK inhibitor in RA patients
50 years of age and older with at least one cardiovascular risk factor, a higher rate of major
adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial
infarction (MI), and non-fatal stroke was observed with the JAK inhibitor compared to those treated with TNF blockers. Patients who are current or past smokers are at additional increased risk.
Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Lumirix, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors.
Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. Discontinue Lumirix if patients that have experienced a myocardial infarction or stroke.
Thrombosis
Thromboembolic events were observed in clinical trials with Lumirix.
Thrombosis, including deep vein thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis have been reported in patients receiving JAK inhibitors used to treat inflammatory conditions. Many of these adverse reactions were serious and some resulted in death.
In a large, randomized, postmarketing safety study of an oral JAK inhibitor in RA patients 50 years of age and older with at least one cardiovascular risk factor, higher rates of overall thrombosis, DVT, and PE were observed compared to those treated with TNF blockers.
Avoid Lumirix in patients who may be at increased risk of thrombosis. If symptoms of thrombosis occur, discontinue Lumirix and evaluate and treat patients appropriately.
Excipients with known effect
Propylene glycol
This medicinal product contains 150 mg propylene glycol (E1520) in each gram of cream which may cause skin irritation.
Cetyl alcohol and stearyl alcohol
This medicinal product contains cetyl alcohol and stearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).
Parahydroxybenzoates
This medicinal product contains methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).
Butylated hydroxytoluene
This medicinal product contains butylated hydroxytoluene (E321) which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

4.5 Interaction with other medicinal products and other forms of interaction
No interaction studies have been performed with topically administered ruxolitinib.
The potential for interactions with ruxolitinib is considered to be low because of the limited systemic exposure following topical administration.
Based on in vitro data, ruxolitinib is predominantly cleared by cytochrome P450 3A4 (CYP3A4) metabolism. Interaction potential was evaluated for oral ruxolitinib in dedicated clinical pharmacology studies that included co-administration of strong or moderate CYP3A4 inhibitors or a strong inducer. The plasma AUC is approximately doubled with co-administration of a potent inhibitor of CYP3A4 while only a modest increase was seen with co-administration of a moderate CYP3A4 inhibitor.
The use of ruxolitinib cream in combination with other topical medicinal products used to treat vitiligo has not been evaluated and co-application on the same skin areas is not recommended.
Other topical medicinal products used to treat other conditions on the same skin areas should be applied with a minimum of 2 hours after the application of ruxolitinib cream. This is also applicable to the use of sunscreen or emollients.

4.6 Fertility, pregnancy and lactation
Contraception in women of childbearing potential
Women of childbearing potential have to use effective contraception during treatment and for 4 weeks after discontinuation of treatment.
Pregnancy
There are no or limited amount of data from the use of ruxolitinib in pregnant women. Data on systemic absorption of topical ruxolitinib during pregnancy are lacking. There could also be individual factors (e.g. damaged skin barrier, excessive use) that contribute to an increased systemic exposure.
Animal studies have shown that ruxolitinib is embryotoxic and foetotoxic following oral administration. Teratogenicity was not observed in rats or rabbits (see section 5.3). Lumirix® is contraindicated during pregnancy (see section 4.3).
Breast-feeding
No data are available regarding the presence of ruxolitinib in human milk, the effects on the breastfed child, or the effects on milk production after topical application of Lumirix®. Following oral administration of ruxolitinib to lactating rats, ruxolitinib and/or its metabolites were present in the milk with a concentration 13-fold higher than the maternal plasma concentration. In juvenile rat studies, oral administration of ruxolitinib resulted in effects on growth and bone measures (see section 5.3). Lumirix® is contraindicated during breast-feeding (see section 4.3) and treatment must be discontinued approximately 4 weeks before the beginning of breastfeeding.
Fertility
There are no human data on the effect of ruxolitinib on fertility. In animal studies, no effect of oral ruxolitinib on fertility was observed.

4.7 Effects on ability to drive and use machines
Ruxolitinib cream has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
Summary of the safety profile
Safety was primarily evaluated in the pivotal studies, for up to one year. In the long-term extension study (see section 5.1), safety up to 2 years was consistent with the profile reported in the pivotal studies. The most common adverse reaction is application site acne (5.8%).
Tabulated list of adverse reactions
Adverse reactions are ranked under headings of frequency, with the most frequent first, using the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).
Table 1: Adverse reactions:

System Organ Class	Frequency	Adverse Reaction
General disorders and administration site conditions	Common	Application site acne

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose
Overdose following cutaneous administration is unlikely. If too much of the cream has been applied, the excess can be wiped off.
In cases of accidental ophthalmic, oral mucosa, or intravaginal exposure, the cream should be thoroughly wiped off and/or rinsed with water (see sections 4.2 and 4.4).

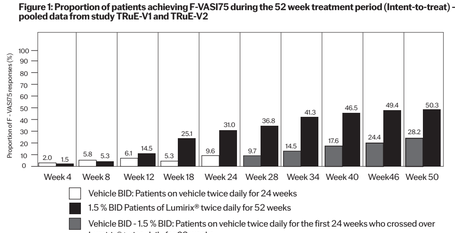
PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Other dermatological preparations, agents for dermatitis, excluding corticosteroids, ATC code: D11AH09
Mechanism of action
Ruxolitinib is a Janus Kinase (JAK) inhibitor with selectivity for the JAK1 and JAK2 isoforms. Intracellular JAK signalling involves recruitment of STATs (signal transducers and activators of transcription) to cytokine receptors, and subsequent modulation of gene expression. Autoimmune IFNγ producing cytotoxic T lymphocytes are thought to be directly responsible for melanocyte destruction in human vitiligo. Recruitment of cytotoxic lymphocytes to lesional skin is mediated via IFNγ dependent chemokines, such as CXCL10. Downstream signalling of IFNγ is JAK1/2 dependent and treatment with ruxolitinib reduces CXCL10 levels in vitiligo patients.
Clinical efficacy and safety
Two double-blind, randomised, vehicle-controlled studies of identical design (TRuE-V1 and TRuE-V2) enrolled a total of 674 patients who have vitiligo on the face and total body vitiligo area (facial and nonfacial) not exceeding 10% BSA, with disease extent at initiation ranging from 3.2% to 10.1% of BSA, aged 12 years and older (10.7% of patients were 12 to 17 years of age and 6.7% were 65 years or older). Females constituted 53.1% of patients, 81.9% of patients were White, 4.7% were Black, and 4.2% were Asian. The majority of patients had Fitzpatrick skin types III, IV, V, or VI (67.5%).
In both studies, patients were randomised 2:1 to treatment with ruxolitinib cream or vehicle twice daily for 24 weeks with affected BSA not exceeding 10%, followed by an additional 28 weeks of treatment with ruxolitinib cream BID for all patients. The primary efficacy endpoint was the proportion of patients achieving a 75% repigmentation in the facial Vitiligo Area Scoring Index (F-VASI75) at week 24. Key secondary endpoints included the proportions of patients achieving a 90% repigmentation in F-VASI (F-VASI90), 50% improvement in total body Vitiligo Area Scoring Index (T-VASI50), and a Vitiligo Noticeability Scale (VNS) score of 4 or 5 (vitiligo "a lot less noticeable" or "no longer noticeable").
Repigmentation of treated vitiligo lesions and superiority of ruxolitinib cream over vehicle cream were observed for both studies, as demonstrated by statistically significant differences in response rates for F-VASI75/90, T-VASI50, and VNS score of 4 or 5 at week 24 (Table 2).
Similar treatment responses at week 52 are seen for those who crossed over from vehicle to ruxolitinib (Figure 1).

Table 2: Percent of patients with vitiligo achieving the primary and key secondary endpoints at week 24 (intent-to-treat)[a]

	TRuE-V1		TRuE-V2	
	Ruxolitinib 1.5% cream	**Vehicle**	**Ruxolitinib 1.5% cream**	**Vehicle**
	(N = 221)	(N = 109)	(N = 222)	(N = 109)
F-VASI75 (%)	29.8	7.4	30.9	11.4
Response rate difference (95% CI)	22.3[b] (14.214, 30.471)	-	19.5[c] (10.537, 28.420)	-
F-VASI90 (%)	15.3	2.2	16.3	1.3
Response rate difference (95% CI)	13.2[d] (7.497, 18.839)	-	15.0[e] (9.250, 20.702)	-
T-VASI50 (%)	20.6	5.1	23.9	6.8
Response rate difference (95% CI)	15.5[d] (8.339, 22.592)	-	17.1[e] (9.538, 24.721)	-
VNS 4 or 5 (%)	24.5	3.3	20.5	4.9
Response rate difference (95% CI)	21.2[c] (14.271, 28.143)	-	15.5[d] (8.515, 22.561)	-

[a] Primary and key secondary outcomes were corrected using multiple imputation method.
b p-value < 0.0001
c p-value < 0.001
d p-value < 0.005
e p-value < 0.01

Figure 1: Proportion of patients achieving F-VASI75 during the 52 week treatment period (Intent-to-treat) – pooled data from study TRuE-V1 and TRuE-V2



At week 52, the observed response rate for F-VASI90, T-VASI50 and VNS was 30.3%, 51.1%, and 36.3%respectively for the ITT pooled population.

Durability of response

A Phase 3, double-blind, vehicle-controlled, randomised, withdrawal and treatment-extension study of ruxolitinib cream twice daily enrolled 458 eligible patients with vitiligo who had completed either of the parent studies using ruxolitinib (TRuE-V1 and TRuE-V2; week 52); patients were assigned to either cohort A or B with a follow-up up to 104 weeks.

Cohort A comprised 116 patients who reached ≥ F-VASI90 at week 52 of the parent study. These patients were re-randomised to either ruxolitinib or vehicle (i.e. withdrawal) to study relapse
(< F-VASI75). A relapse occurred in 15% of patients in the ruxolitinib group, and in 29% of patients in the vehicle group. In the latter group, the majority of relapses (9/16) occurred during the first 4 months after stopping ruxolitinib cream. Among the 16 patients in the vehicle group who relapsed and were retreated, re-treatment resulted in a regained F-VASI75 in 12 (75%) patients in a median of 12 weeks and F-VASI90 was regained by 11 (69%) patients in a median of 15 weeks.
Cohort B comprised 342 patients who reached < F-VASI90 at week 52 of the parent study. These patients continued with open-label ruxolitinib treatment; at week 104, among patients originally randomised to ruxolitinib cream twice daily, 66% reached F-VASI75, and 34% reached F-VASI90.

Paediatric population
A total of 72 adolescents (12 to < 18 years; n = 55 ruxolitinib cream, n = 17 vehicle) were included in the pivotal studies. Adolescents showed equal response rates in primary and key secondary endpoints at 24 weeks when treated with ruxolitinib, as compared to adults from 18-65 years of age.
The European Medicines Agency has deferred the obligation to submit the results of studies with Lumirix® in one or more subsets of the paediatric population for the treatment of vitiligo (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption
The pharmacokinetics of ruxolitinib cream were investigated in 429 subjects with vitiligo aged 12 years and older (12.6% were 12-17 years of age) with a mean ± STD BSA involvement of 7.31 ± 2.02% (range 3.2% to 10.0%). Subjects applied approximately 1.58 mg/cm2 of ruxolitinib cream (dose range was approximately 0.18 grams to 8.4 grams of ruxolitinib cream per application) to the same skin areas twice daily for 24 weeks.

The mean ± STD steady-state trough plasma concentrations was 56.9 ± 62.6 nM with a projected AUC0-12h at 683 ± 751 h*nM, which is approximately 25% of the observed mean AUC0-12h at steady state (2716 h*nM) following 15 mg twice daily oral administration in healthy participants. The mean (geometric mean) topical bioavailability for ruxolitinib cream in vitiligo participants in the pooled data of the two Phase 3 studies was 9.72% (5.78%).

Distribution
Based on an in vitro study, ruxolitinib is 97% bound to human plasma proteins, mostly to albumin.

Biotransformation
Ruxolitinib is metabolised by CYP3A4 and to a lesser extent by CYP2C9.

Elimination
The mean elimination half-life of orally administered ruxolitinib is approximately 3 hours. The mean apparent terminal half-life of ruxolitinib following topical application of Lumirix® was estimated in 9 adult and adolescent patients with ≥ 25% BSA involvement with atopic dermatitis and is approximately 116 hours, reflecting the slow drug absorption rate rather than the drug elimination rate.

Special populations
Renal impairment
The estimated AUC which is adjusted for the pharmacological activity of ruxolitinib plus the metabolites increases approximately two-fold in case of end stage renal disease (ESRD). As a precautionary measure, Lumirix® should not be used by patients with ESRD, due to lack of data regarding the safety.

Hepatic impairment
Although the AUC was increased following oral administration of ruxolitinib to patients with hepatic impairment, there was no clear relationship between the severity of hepatic impairment and the increase in AUC. A dosing advice for patients with hepatic impairment is not necessary.

5.3 Preclinical safety data
Ruxolitinib has been evaluated in safety pharmacology, repeated dose toxicity, genotoxicity and reproductive toxicity, and carcinogenicity studies following oral administration. Additional studies were conducted following dermal administration in minipigs and mice. Target organs associated with the pharmacological action of ruxolitinib in repeated dose oral studies include bone marrow, peripheral blood and lymphoid tissues. Infections generally associated with immunosuppression were noted in dogs. Margins (based on unbound AUC) at non-adverse levels in chronic toxicity studies were approximately 6- and 200-fold in male and female rats, and 10-fold in dogs, relative to systemic exposure observed in patients with vitiligo that applied 1.5% ruxolitinib cream twice daily. Adverse decreases in blood pressure along with increases in heart rate were noted in a dog telemetry study, and an adverse decrease in minute volume was noted in a respiratory study in rats. The margins (based on unbound Cmax) at the non-adverse level in the dog and rat studies were approximately 300-fold and 100-fold greater, respectively, than systemic exposure observed in patients with vitiligo that applied 1.5% ruxolitinib cream twice daily. No adverse effects were noted in an evaluation of the neuropharmacological effects of ruxolitinib in rats.

A 3-month dermal repeat dose study revealed decreased lymphocyte counts in mice. Margins (based on unbound AUC) at non-adverse levels were approximately 10-fold in male and 24-fold in female mice relative to systemic exposure observed in patients with vitiligo that applied 1.5% ruxolitinib cream twice daily. Non-adverse decreased peripheral lymphocyte counts were also noted in minipigs in a 9-month dermal toxicity study. Margins (based on

[redacted]	History # - Date

Part Number - Version #:	Region(Market):	Reference Version:	Cutting Dimensions:
Macao-03-001	Macao	CA-1628-01	585 x 260 mm (Folded: 147 x 30 mm)

Component description:

Leaflet Ruxolitinib All strength Tube 585x260mm

Colors to be printed:	Technical Colors (Non-printing):
Process Black	cut technical dimensions comments

NB: Color separation to make printing tools is printer's responsibility in order to achieve approved design.

BACK SIDE

147 mm

731.912 mm

260 mm

unbound AUC) at non-adverse levels in minipigs were approximately 3-fold relative to systemic exposure observed in patients with vitiligo that applied 1.5% ruxolitinib cream twice daily. This effect was not observed in a 3-month dermal toxicity study in minipigs. No evidence of systemic toxicity was observed in Gottingen minipigs following topical administration of 1.5% ruxolitinib cream formulation twice daily for up to 9 months.

In juvenile rat studies, oral administration of ruxolitinib resulted in effects on growth and bone measures. Reduced bone growth was observed at doses ≥ 5 mg/kg/day when treatment started on postnatal day 7 (comparable to human newborn) and at ≥ 15 mg/kg/day when treatment started on postnatal days 14 or 21 (comparable to human infant, 1–3 years). Fractures and early termination of rats were observed at doses ≥ 30 mg/kg/day when treatment was started on postnatal day 7. Based on unbound AUC, the exposure at the NOAEL (no observed adverse effect level) in juvenile rats treated as early as postnatal day 7 was approximately 20-fold that of adult patients with vitiligo, while reduced bone growth and fractures occurred at exposures that were 22- and 150-fold that of adult patients with vitiligo, respectively. The effects were generally more severe in males and when administration was initiated earlier in the postnatal period. Other than bone development, the effects of ruxolitinib in juvenile rats were similar to those in adult rats. Juvenile rats are more sensitive than adult rats to ruxolitinib toxicity.

In embryofetal development studies, oral administration of ruxolitinib to rats and rabbits during gestation resulted in decreased foetal weight and increased post-implantation loss at doses associated with maternal toxicity. There was no evidence of a teratogenic effect in rats and rabbits. Margins (based on unbound AUC) at non-adverse levels for developmental toxicity in rats were approximately 25-fold the systemic exposure observed in patients with vitiligo that applied 1.5% ruxolitinib cream twice daily. No effects of oral ruxolitinib were noted on fertility in male or female rats. In a pre- and postnatal development study, a slightly prolonged gestation period, reduced number of implantation sites, and reduced number of pups delivered were observed. In the pups, decreased mean initial body weights and short period of decreased mean body weight gain were observed. In lactating rats, ruxolitinib and/or its metabolites were excreted into the milk with a concentration that was 13-fold higher than the maternal plasma concentration. Ruxolitinib was not mutagenic or clastogenic.
Ruxolinitib showed no carcinogenic potential following topical administration in mice or following oral administration in Sprague-Dawley rats and Tg.rasH2 mice.

PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Butylated hydroxytoluene (as an antioxidant in paraffin, white soft) (E321)
Cetyl alcohol
Dimeticone (E900)
Disodium edetate (E385)
Self -emulsifying Glyceryl stearate
Macrogol
Medium chain triglycerides
Methyl parahydroxybenzoate (E218)
Paraffin (E905), Liquid light
Paraffin (E905), White soft Phenoxyethanol
Polysorbate 20 (E432)
Propylene glycol (E1520)
Propyl parahydroxybenzoate Purified water
Stearyl alcohol Xanthan gum (E415)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
21 months After first opening: 6 months.

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Laminate tube with an inner lining of low-density and high-density polyethylene with a polypropylene cap, or aluminium tube with internal lacquer coating with a polypropylene puncture cap.

Tube of 100 g. One tube per carton.

6.6 Special precautions for disposal
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

MANUFACTURER

Tiofarma B.V.
Oud- Beijerland, 3261 ME,
Netherlands

DATE OF REVISION OF THE TEXT
Date of first authorization: 29 August 2024

Lumirix®
Ruxolitinib Cream 15mg/g

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1.What Lumirix® is and what it is used for

Lumirix® contains the active substance ruxolitinib. It belongs to a group of medicines called Janus kinase inhibitors.

Lumirix® is used on the skin to treat vitiligo with facial involvement in adults and adolescents from 12 years. Vitiligo is an autoimmune disease, where the body's immune system attacks the cells that produce the skin pigment melanin. This causes a loss of melanin, leading to patches of pale pink or white skin. In vitiligo, ruxolitinib reduces the immune system's activity against the melanin-producing cells, allowing the skin to produce pigment and regain its normal colour.

2. What you need to know before you use

- if you are allergic to ruxolitinib or any of the other ingredients of this medicine (listed in section 6).
- if you are pregnant or breastfeeding.

Warnings and precautions
Talk to your doctor or pharmacist before using Lumirix®.
Lumirix® is not for use on the lips, in the eyes, mouth or vagina. If cream accidentally gets into these areas, thoroughly wipe off and/or rinse off the cream with water.

Children under 12 years
Do not give Lumirix® to children younger than 12 years because it has not been studied in this age group.

Other medicines and Lumirix®
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.
Using Lumirix® at the same time as other medicines on the affected skin is not recommended, as it has not been studied.
After applying Lumirix®, wait at least 2 hours before applying other medicines, sunscreen or body creams/oils to the same skin area.

Pregnancy and breast-feeding
Lumirix® should not be used by pregnant or breast-feeding women as this has not been investigated. If you are a woman of childbearing age, you should use an effective contraception during treatment and during 4 weeks after applying Lumirix® for the last time.
It is not known if ruxolitinib passes into breast milk after applying it to the skin. The effects of this medicine in breastfed infants are unknown; therefore, Lumirix® should not be used if you are breast-feeding or planning to breastfeed. You may start breast-feeding approximately four weeks after applying Lumirix® for the last time.

Driving and using machines
Lumirix® is unlikely to have an effect on your ability to drive and use machines.

Lumirix® contains propylene glycol, cetyl alcohol, stearyl alcohol, methyl parahydroxybenzoate, propyl parahydroxybenzoate and butylated hydroxytoluene

- This medicine contains 150 mg propylene glycol (E1520) in each gram of cream, which may cause skin irritation.
- Cetyl alcohol and stearyl alcohol may cause local skin reactions (e.g. contact dermatitis).
- Methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate may cause allergic reactions (possibly delayed).
- Butylated hydroxytoluene (E321) may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

3. How to use Lumirix®
Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose

- Apply a thin layer of cream twice daily to affected areas of your skin. Wait at least 8 hours between applications.
- The cream should not be used on more than 10% (one tenth) of your body. This surface area represents the equivalent to ten times the palm of one hand with the five fingers.

Method of administration

- This medicine is for use on the skin only.
- Do not apply to skin surfaces other than the ones instructed by your doctor. The medicine should be used at the smallest skin area necessary.
- Wash your hands after applying this medicine, unless you are treating your hands. If someone applies this medicine to you, they should wash their hands after application.
- Avoid washing treated skin for at least 2 hours after application of Lumirix®.

Duration of use
Your doctor will decide how long you should use the cream for.
A minimum duration of 6 months is recommended but satisfactory treatment may require over 12 months. If you achieve satisfactory repigmentation of treated areas, consult your doctor to discuss if treatment of those areas could be stopped. Consult your doctor if you experience loss of repigmentation after stopping treatment.
Do not use more than two 100 gram tubes a month.

If you use more Lumirix® than you should
Wipe off the excess cream if this occurs.

If you forget to use Lumirix®
If you forget to apply the cream at the scheduled time, do it as soon as you remember, then continue your normal dosing schedule. However, if the next scheduled dose is due within 8 hours, skip the missed dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.
The following side effects have been reported with Lumirix®:

Common (may affect up to 1 in 10 people)

- acne at application site

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Lumirix®
Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the tube and carton after EXP. The expiry date refers to the last day of that month.
Do not store above 30°C.
Once the tube has been opened, use the cream within 6 months but not after the expiry date.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

What Lumirix® contains

- The active substance is ruxolitinib. One gram of cream contains 15 mg of ruxolitinib.
- The other ingredients are butylated hydroxytoluene (E321), cetyl alcohol, dimeticone (E900), disodium edetate (E385), glyceryl stearate, paraffin (E905), macrogol, medium chain triglycerides, methyl parahydroxybenzoate (E218), phenoxyethanol, polysorbate 20 (E432), propylene glycol (E1520), propyl parahydroxybenzoate, purified water, stearyl alcohol, xanthan gum (E415).

See section 2 "Lumirix® contains propylene glycol, cetyl alcohol, stearyl alcohol, methyl parahydroxybenzoate, propyl parahydroxybenzoate and butylated hydroxytoluene".

What Lumirix® looks like and contents of the pack
Lumirix® cream is coloured white to off-white, supplied in a tube containing 100 g cream. There is one tube per carton.

Manufactured By:

Tiofarma B.V.
Hermanus Boerhaavestraat 1
Oud-Beijerland, 3261 ME, Netherlands

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Lumirix®
Ruxolitinib Cream 15mg/g

因本說明書包含重要訊息，使用本藥前請仔細閱讀該說明書
- 請保管好本說明書，以便再次閱讀。
- 如果您有任何其他問題，請諮詢您的醫生或藥劑師。
- 此為您的處方藥，請勿給他人使用，這可能會傷害他們，即使他們的疾病症狀與您的相同。
- 如果您使用本藥發生任何副作用，請諮詢您的醫生或藥劑師。這包括本說明書中未提及的任何可能的副作用。請參閱第4節。

本說明書包含的內容

1.Lumirix® 是什麼及其用途
Lumirix® 含有活性成份蘆可替尼, 屬於JAK抑制劑藥物.

Lumirix® 用於治療12歲及以上青少年及成人伴隨臉部受影響的白癜風. 白癜風是一種自體免疫疾病, 身體的免疫系統攻擊產生皮膚色素的黑色素細胞, 導致黑色素流失, 最後引起皮膚出現淡粉紅色或白色斑塊。在白癜風中, 蘆可替尼可降低免疫系統對黑色素生成細胞的活躍程度, 使皮膚產生色素並恢復正常顏色.

2. 使用Lumirix®前的注意事項
以下情況請勿使用**Lumirix®**

- 對蘆可替尼或本藥物的任何其他成份過敏 (列於第6節).
- 妊娠或哺乳.

警告和注意事項

使用 Lumirix®前, 請諮詢您的醫生或藥劑師.

Lumirix® 不得用於、眼睛、口腔或陰道. 如果乳膏意外接觸這些區域, 請徹底抹走和/或用水沖洗.

歲以下兒童12
請勿將 Lumirix® 用於12歲以下的兒童, 因尚未在該年齡組別進行研究.

其他藥物和 Lumirix®
如果您正在使用, 最近已使用或可能使用任何其他藥物, 請告知您的醫師或藥劑師.
和其他藥物, 因為此用法尚未有研究支持Lumirix® 和其他藥物, 因為此用法尚未有研究支持.

使用 Lumirix® 後, 至少等待2小時, 然後才可在相同的皮膚區域使用其他藥物、防曬霜或身體乳膏/油.

妊娠和哺乳
孕婦或哺乳期婦女不應使用 Lumirix® 因尚未對此組別患者進行研究. 如果您是育齡女性, 您應在治療期間以及最後一次使用 Lumirix 後4週內使用有效的避孕措施.

蘆可替尼在皮膚上塗抹後會否遷入母乳仍存不確定性. 此藥對母乳餵哺嬰兒的影響尚不清楚; 因此, 如果您正在母乳餵哺或計劃母乳餵哺, 則不應使用 Lumirix® 您可以在最後一次使用 Lumirix® 約4週後開始母乳餵哺.

駕駛和使用機器
Lumirix® 不太可能影響您駕駛和使用機器的能力.

Lumirix® 含有丙二醇、十六醇、十八醇、羥苯甲酯、羥苯丙酯和二丁基羥基甲苯

- **本藥每克含150 mg丙二醇，可能引起皮膚刺激.**
- **十六醇和十八醇可能引起局部皮膚反應（例如接觸性皮炎）.**
- **羥苯甲酯和羥苯丙酯可能導致過敏反應（可能延遲出現）.**
- **二丁基羥基甲苯可能引起局部皮膚反應（例如接觸性皮炎），或眼睛和黏膜刺激.**

3. 如何使用**Lumirix®**
請務必嚴格按照您的醫生或藥劑師的指示使用本藥. 如果您不確定, 請諮詢您的醫生或藥劑師

建議劑量
- 每日兩次在受影響的皮膚部位塗抹薄薄的一層乳膏, 兩次用藥之間至少相隔8小時.
- 乳膏的用量不得超過您身體表面積的10% (10分1). 此表面積相當於一隻手掌連同5根手指的10倍.

用藥方法
- 本藥僅用於皮膚.
- 請勿塗抹於醫生指示以外的皮膚表面. 該藥物應在必要的最小皮膚面積上使用.
- 使用此藥後請洗手, 除非您正在治療手部. 如果其他人幫您塗抹此藥, 他們應在使用後洗手.
- 使用Lumirix® 後, 至少2小時內應避免清洗治療過的皮膚.

使用時間
您的醫生將決定您應使用乳膏的治療時間.
建議至少持續6個月, 而達到滿意的效果可能需要治療超過12個月. 如果你對治療部位的復色效果滿意, 請諮詢你的醫生, 討論這些部位是否可以停止治療. 如果您在停止治療後出現複色消失, 請諮詢您的醫生.

每月不應使用超過兩支, 100 g的乳膏.

如果您使用的Lumirix® 超過您應該使用的量
如果出現這種情況, 請聯絡多餘的乳膏 .

如果您忘記使用Lumirix®
如果您忘記在預定時間塗抹乳膏, 請在想起來的時候儘快塗抹, 然後繼續按正常用藥時間使用. 但是, 如果距下一次計劃給藥在8小時內, 則跳過錯過的該次用藥. 如果您對本藥的使用有任何疑問, 請諮詢您的醫生或藥劑師.

4. 可能的副作用
與所有藥物一樣, 這種藥物也會引起副作用, 但不是每個人都會發生。

以下是 Lumirix® 會出現副作用的報告:
常見 (最多可影響**10**分1人)
- 外用藥部位痤瘡

報告副作用
如果您出現任何副作用, 請諮詢您的醫生或藥劑師。這包括本說明書中未提及的任何可能的副作用.

5. 如何儲存 **Lumirix®**
請將此藥放在兒童看不到或接觸不到的地方。
在藥管和紙盒上標明的有效期後請勿使用本藥。有效期指當月最後一天.

請勿儲存在 30°C 以上。
打開藥管後, 應在6個月內使用完, 但不得晚於有效日期。
請勿通過污水或家居垃圾丟棄任何藥物。諮詢您的藥劑師如何丟棄不再使用的藥物。這些措施將有助於保護環境.

6. 包裝及其他資訊 **Lumirix®** 含有

- 活性成份為蘆可替尼。每克乳膏含15 mg蘆可替尼.
- 其他成分為丙二醇、羥苯甲酯、羥苯丙酯、黃原膠、輕質液狀石蠟、甘油硬脂酸酯SE, 聚山梨酯20, 白凡士林、十六醇、十八醇、二甲矽油350, 中鏈甘油三酸酯、純化水、依地酸二鈉、聚乙二醇200, 苯氧乙醇、二丁基羥基甲苯.

見第2節 "Lumirix® 含有丙二醇、十六醇、十八醇、羥苯甲酯、羥苯丙酯和二丁基羥基甲苯".

Lumirix®的外觀和包裝內容
Lumirix® 為白色至類白色乳膏, 每支含100 g, 每盒一支.

生產廠:

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