AZIENDA OSPEDALIERA DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE

MODELLO AE / 2 N. 158 del 04.09.2020 CIG: Z0B2E2B1F9

in applicazione delle disposizioni di cui all'art. 36 comma 2 lettera a) del D.Lgs n. 50/2016 e s.m.i.

FORNITURA PRINCIPIO ATTIVO CLOFAZIMINA COMPRESSE DA 50 MG

Premesso che:

- Con nota del 03.09.2020, acquisita al protocollo n. 4489 del 04.09.2020 del Settore Provveditorato, il Direttore dell'UOC di Malattie Infettive del P.O. Garibaldi di Nesima ha richiesto l'acquisto di n. 6 confezioni del principio attivo CLOFAZIMINA CPR da 50 MG <<necessario per il trattamento di tre pazienti affetti da grave forma di MICOBATTERIOSI NON TUBERCOLARE>>, ai sensi del D.M. 11/02/1997;
- la nota risulta trasmessa dall'UOC di Farmacia che richiede l'approvvigionamento del farmaco precisando, altresì, di aver provveduto , attesa l'urgenza , ad inoltrare richiesta di preventivo offerta agli Operatori Economici:
  - Farmaceutica Internazionale Italiana;
  - Profarmaitalia Srl;
  - Ottopharma;
  - Unipharma Sa;
- il termine assegnato per la presentazione dell'offerta è indicato per il giorno 07.09.2020;

RITENUTO CHE il valore presunto della fornitura, Iva esclusa, rientra nei limiti di importo di € 40.000,00 Iva esclusa previsto dall'art. 1 del Decreto del Presidente del Consiglio dei Ministri del 11.07.2018;

PRESO ATTO che prima del termine previsto per la scadenza della presentazione delle offerte tutti gli Operatori Economici hanno riscontrato la richiesta di questa Azienda:

- **PROFARMA ITALIA: Dichiara la mancanza di disponibilità del prodotto;**
- **OTTOPHARMA prot. Settore Provveditorato n. 4493 del 04.09.2020;**
- **FARMACEUTICA INTERNAZIONALE ITALIANA , prot. Settore Provveditorato n. 4494 del 04.09.2020;**
- **UNIPHARMA, prot. Settore Provveditorato n. 4495 del 04.09.2020;**

PRESO ATTO delle offerte economiche degli Operatori Economici concorrenti formulate per il principio attivo CLOFAZIMINA compresse da 50 mg

DITTA	PRINCIPIO ATTIVO	PREZZO UNITARIO	PREZZO A CONFEZIONE
OTTOPHARMA	CLOFAZIMINA / LAMPREME 50 MG 100 CPR	1,32	132,00

DITTA	PRINCIPIO ATTIVO	PREZZO UNITARIO	PREZZO A CONFEZIONE
FARMACEUTICA INTERNAZIONALE ITALIANA	CLOFAZIMINA / LAMPREME 50 MG 100 CPR	1,0250	102,50 MINIMO D'ORDINE 10 CONFEZIONI SPESE DI SPEDIZIONE GRATUITE
FARMACEUTICA INTERNAZIONALE	CLOFAZIMINA / LAMPREME 50 MG 100 CPR	1,0250	102,50 MINIMO D'ORDINE 6

ITALIANA			CONFEZIONI – SPESE DI SPEDIZIONE 70,00

DITTA	PRINCIPIO ATTIVO	PREZZO UNITARIO a cpr	PREZZO A CONFEZIONE
UNIPHARMA SA	CLOFAZIMINA / LAMPREME 50 MG 100 CPR	0,98	98,00
	Spese di trasporto	30,00	

Sulla base di quanto premesso IL RUP propone l'acquisto presso la seguente ditta dei prodotti richiesti
UNIPHARMA SA
Principio attivo: **CLOFAZIMINA**
Nome Commerciale : LAMPRENE 50 MG 100 CAPS
Prezzo unitario offerto Iva esclusa: €. 0,98
Prezzo a confezione da 100 capsule €. 98,00
Quantità richiesta n. 6 confezioni
Prezzo complessivo della fornitura : €.588,00 Iva esclusa
Spese di trasporto €. 30,00

IMPORTO COMPLESSIVO €. 646,80 IVA INCLUSA escluso spese di trasporto

Autorizzazione di spesa n. 103 sub 1 anno 2020 conto economico 20001000008 –Prodotti farmaceutici senza AIC

IL RESPONSABILE DEL PROCEDIMENTO Dott.ssa Olga Marletta

- **TENUTO CONTO DELLA FASE ISTRUTTORIA: propedeutica alla presente autorizzazione svolta dal Responsabile dell'Istruttoria;**
- **VISTA: la possibilità di disporre dei necessari fondi sulla procedura AREAS;**
- **VISTO l'esito della contrattazione;**
- **VISTA la proposta di aggiudicazione**

SI AUTORIZZA IL RESPONSABILE DELL'ISTRUTTORIA ALLA FORMALIZZAZIONE DELLA PROCEDURA DI ACQUISTO DEI BENI/SERVIZI INDICATI IN EPIGRAFE .

IL DIRIGENTE RESPONSABILE AD INTERIM
SETTORE PROVVEDITORATO
(Ing. Salvatore Vitale)

ARNAS GARIBALDI
AZIENDA OSPEDALIERA DI RILIEVO NAZIONALE E DI ALTA SPECIALIZZAZIONE
P.O. «GARIBALDI - NESIMA
Via Palermo n. 636 Catania

04.09.2020

Università di Catania
ISTITUTO DI MALATTIE INFETTIVE
Direttore: Prof. Stefano Cosentino
Tel. 095/759 86 47/50 - Fax 095/759 86 66

Alla cortese attenzione del
Direttore della Farmacia
P.O. Garibaldi Nesima.

Si richiede l'acquisto di n° 6 confezioni di CLOFAZIMINA (nome commerciale Lamprene) cpr 50 mg, necessarie per il trattamento di tre pazienti affette da grave forma di MICOBATTERIOSI NON TUBERCOLARE.

Catania, 03/09/2020

Il DIRETTORE

C.A. Dottssa MARCHETTA
Si richiede l'acquisto.
Ho provveduto ad inviare mail a ditte estere per richiesta offerta

Olga Marletta <omarletta@arnasgaribaldi.it>

Dott.ssa Marletta

Fwd: Sales offer 20003803

1 messaggio

04.09.2020

barbara.busa@libero.it <barbara.busa@libero.it> 3 settembre 2020 15:20
Rispondi a: barbara.busa@libero.it
A: omarletta <omarletta@arnasgaribaldi.it>

Ciao Olga io credo che tra le tre questa è la ditta che offre meglio
Non aspettiamo più nessun altro preventivo puoi procedere
Barbara

Inviato da Libero Mail per iOS

—— Messaggio inoltrato ——
Da: Maria Ilenia Saporito <saporito@unipharma.ch>
A: barbara.busa@libero.it <barbara.busa@libero.it>
Data: giovedì 3 settembre 2020, 15:11 +0200
Oggetto: Sales offer 20003803

Sales offer n° 20003803 by Unipharma SA - Lugano.

Your ref.

Offered products:
077808 Lamprene 50 mg 100 caps

Thank you for your request
SAPORITO Ilenia

3 allegati

UPH_OFC_20003803.pdf
196K

STS_SPC_077808_Lamprene.pdf
464K

ModImport_077808_Lamprene.docx
22K

Unipharma SA
Via Figino, 6
6917 – Barbengo Lugano – Switzerland
Tel. +41 91 985 62 11
Fax. +41 91 985 62 22
E-mail: sales@unipharma.ch

Cert. N°23997

Offerta cliente

M-COM 05

DESTINATARIO	6016	**OFFERTA N°**	2020-20003803
Azienda:	Nuovo Ospedale Garibaldi	**Città:**	Catania
Persona di riferimento:	Barbara BUSÀ	**Reparto:**	Farmacia interna
Fax:	barbara.busa@libero.it	**Telefono:**	
MITTENTE			
Autore messaggio:	SAPORITO Ilenia	**Telefono:**	0041 91 985 62 11

Cambio mese corrente EUR 0.94 (pari a CHF 1.00) **Lugano,** 03.09.2020

Oggetto:

Egregi signori,
con riferimento alla vostra richiesta in oggetto abbiamo il piacere di allegare: listino prezzi, costi di spedizione e condizioni di vendita.

Per ulteriori informazioni potete contattare i numeri seguenti:

Ufficio vendite e pronta disponibilità
Direttore: Maurizio Nanni
Collaboratori: Monica Colombo, Federico Wessel, Ilenia Saporito, Mariangela Li Greci

Orari d'ufficio da lunedì a venerdì 08^{00}–12^{00}/13^{00}–17^{30}
E-mail: sales@unipharma.ch
Reperibilità nelle 24 ore al di fuori dell'orario d'ufficio telefonando semplicemente al numero abituale: 0041 91 985 62 11
Disponiamo del sito www.unipharma.ch al quale potete accedere per cercare i prodotti di cui necessitate.

Centro di documentazione scientifica e servizio informazione sui farmaci svizzeri ed esteri
Direttore tecnico: Antonella Calvelli, *farmacista*

Banche dati: Compendium, Rote Liste, Vidal, Pharmavista, Tropimed, Phyto, Martindale, Medical letter, Internet e vasta documentazione tratta da riviste, pubblicazioni, biblioteche, ecc.

Ufficio di Sanità Aeroportuale	Ciampino	Tel/Fax 06 7949 4220
Corriere TNT		Numero verde 199 803 868

Ci auguriamo che la nostra offerta sia di vostro interesse e, assicurandovi fin da ora un servizio rapido ed accurato, distintamente vi salutiamo.

UNIPHARMA SA

SAPORITO Ilenia

Unipharma SA
Via Figino, 6
6917 – Barbengo Lugano – Switzerland
Tel. +41 91 985 62 11
Fax. +41 91 985 62 22
E-mail: sales@unipharma.ch

Cert. N°23997

Offerta cliente

M-COM 05

OFFERTA N°2020-20003803
VALIDA DAL 03.09.2020 AL 03.10.2020

Nr Art	Descrizione	Produttore	Titolare AIC	Origine	Conservazione	gg consegna	Prezzo EUR	Prezzo unitario EUR
77808	Lamprene 50 mg 100 caps	Catalent Germany Eberbach GmbH	Novartis Pharma AG	Switzerland	temperatura ambiente	10	98.00	0.98000

Composizione:

Nr Art	Prodotto	DenominazionePrincipale	Dose
77808	Lamprene 50 mg 100 caps	Clofaziminum	50 mg

Costi di spedizione, imballo e sdoganamento:

Corriere	Da Kg	Fino a Kg	Porto EUR
Fisso € 30	0.00	10'000.00	30.00

Unipharma SA
Via Figino, 6
6917 – Barbengo Lugano – Switzerland
Tel. +41 91 985 62 11
Fax. +41 91 985 62 22
E-mail: sales@unipharma.ch

Cert. N°23997

Offerta cliente

M-COM 05

CONDIZIONI DI VENDITA UNIPHARMA SA

Prezzi

Tutti i prezzi comunicati per scritto si intendono in franchi svizzeri (CHF) o EURO, IVA esclusa e non includono il costo dell'imballaggio, del trasporto e dello sdoganamento.
In linea di massima vengono applicati i prezzi riportati nei listini in vigore e nelle offerte salvo variazioni di listino da parte del fornitore principale.

Accettazione degli ordini

Nessun valore minimo economico è richiesto.
Gli ordini vengono accettati con l'indicazione del prezzo in CHF o EURO al cambio concordato.

Fatturazione

Le fatture vengono emesse in CHF/EURO al cambio sopra menzionato.

Termine di consegna

Se un ordine al momento del suo arrivo si riferisce del tutto o in parte a merce non disponibile sarà nostra cura informare di ciò il cliente, avvisandolo dell'avvenuta ordinazione vincolante da parte nostra della merce che verrà riservata a suo nome.
Le spedizioni avvengono

- in giornata per le specialità registrate in Svizzera presso Swissmedic
- entro 20 giorni per le specialità da ordinare all'estero, conformemente alla disponibilità del fornitore principale.

La consegna al vostro domicilio è garantita entro e non oltre 48 ore dalla spedizione.

Trasporto

Le spese di trasporto, se non concordato diversamente, sono a carico del cliente.
I trasporti vengono effettuati secondo le indicazioni delle Aziende produttrici rispettando la catena del freddo, se necessario.

Formalità doganali

Ufficio di entrata della merce: Ciampino o Ponte Chiasso (CO)
La dichiarazione di Nulla osta è da intestare all'Ufficio doganale di sanità aerea di Ciampino.

Consegna della merce

La merce viene consegnata all'indirizzo indicato dal cliente con gli obblighi di dogana ed anticipo IVA e spese di trasporto già assolti.
Per l'IVA a carico del cliente, da noi anticipata e fatturata, sarà rimessa in originale la bolla doganale da allegare ai documenti contabili.

Pagamento

Le fatture devono essere saldate entro 90 giorni dalla data della fattura, versando l'importo sul nostro conto 247-959.570.62J – IBAN CH88 0024 7247 9595 7062J – Swift UBSWCHZH80A presso UBS SA – 6900 Lugano

Garanzia

Per i danni riscontrati all'arrivo dev'essere fatta riserva al vettore. Altri danni (difetti del materiale, consegna errata o quantità mancanti) devono esserci comunicati entro 8 giorni dal ricevimento della merce. I reclami avanzati oltre tale termine non potranno più essere presi in considerazione. La nostra responsabilità cessa alla consegna del prodotto.
Escludiamo ogni responsabilità per danni causati alle persone, alle cose o ai beni dall'utilizzo della merce oggetto della fornitura. Sono escluse le richieste di risarcimento di clienti o terzi destinate a riparare eventuali danni causati dall'utilizzo della merce oggetto dei fornitura, quindi di null'altro – in particolare secondo i principi di responsabilità del prodotto – salvo diversamente prescritto per legge.

Ritorni

Ritorni di merce sono accettati solo se preventivamente concordati.

Richiamo del prodotto

In caso di ritiro di specialità o di un lotto per ragioni di sicurezza da parte del fabbricante, il cliente viene immediatamente informato. Il cliente dovrà comunicare ad Unipharma il numero di pezzi giacenti presso i propri magazzini e procedere al reso entro 7 giorni dal ricevimento dell'avviso di richiamo. A ricevimento della merce verrà emessa nota di credito.

Foro competente

Per qualsiasi controversia, se non diversamente concordato, viene applicato il Diritto Svizzero: il foro competente è quello di Lugano.

NOVARTIS

Regulatory Affairs

LAMPRENE® (clofazimine)

50 or 100 mg capsules, soft

International Package Leaflet (IPL)

NOTICE

The Novartis Core Data Sheet (CDS) displays the company's current position on important characteristics of the product, including the Core Safety Information according to ICH E2C.

The Novartis CDS contains all relevant information relating to indications, dosage regimen, pharmacology and Core Safety Information which Novartis requires to be listed for the product in all countries where the product is registered.

IPL Creator:	Kiran Kumar Chilipi
CDS Author(s):	Raghuram Akinapelli
Effective date:	30-Nov-2017
Safety Label Change (SLC) Tracking number:	2017-PSB/GLC-0897-s
Document status:	Final

LAMPRENE®

Drugs for the treatment of lepra.

DESCRIPTION AND COMPOSITION

Pharmaceutical form

Capsules, soft

Active substance

Each capsule contains 50 or 100 mg of micronized clofazimine suspended in an oil-wax base.

Excipients

Capsules:
Butylated hydroxytoluene; Citric acid, anhydrous; Propylene glycol; Rapeseed oil, refined; Lecithin (E322); Beeswax, yellow; Soybean oil, hydrogenated; Soya-bean oils, partially hydrogenated

Capsule shells:
Ethyl parahydroxybenzoate sodium; Propyl parahydroxybenzoate sodium; Ethylvanillin; Gelatin; Glycerol 85%; Black iron oxide (E172); Red iron oxide (E172); p-Methoxy acetophenone

Pharmaceutical formulations may vary between countries.

INDICATIONS

Leprosy:

Lamprene, used only in combination with rifampicin and dapsone, is indicated as treatment for multibacillary (MB) forms of leprosy:

- for all types of leprosy with positive skin smear
- for all cases clinically diagnosed as MB leprosy with more than 5 skin lesions
- for all cases of relapse of previously treated MB leprosy
- for erythema nodosum leprosum (ENL)

Multidrug therapy (MDT) is necessary in order to prevent the emergence of resistant strains of *Mycobacterium leprae*.

Drug resistant Tuberculosis (DR-TB):

Lamprene is indicated, as part of the World Health Organization (WHO) shorter or WHO conventional treatment regimens, for the treatment of pulmonary drug-resistant tuberculosis (DR-TB) including:

- Multidrug-resistant tuberculosis (MDR-TB)
- Rifampicin resistant tuberculosis (RR-TB)
- Extensively drug-resistant TB (XDR-TB)

DOSAGE REGIMEN AND ADMINISTRATION

Multibacillary leprosy:

Lamprene is administered only as part of a multidrug therapy, in combination with dapsone and rifampicin for the treatment of multibacillary leprosy. Multidrug therapy (MDT) is necessary in order to prevent the emergence of resistant strains of *Mycobacterium leprae*.

For the treatment of leprosy, the WHO recommends the following regimens:

Table-1 MDT dosage

	Dapsone	Rifampicin	Lamprene (clofazimine)
Adults and adolescents (15 years and above)	Days 1-28 100 mg once daily as self-medication	Day 1 only of each cycle* 600 mg under supervision	Day 1 only of each cycle* 300 mg under supervision and Days 2-28 50 mg once daily as self-medication
Children (10 to 14 years)	Days 1-28 50 mg once daily as self-medication	Day 1 only of each cycle* 450 mg under supervision	Day 1 only of each cycle* 150 mg under supervision and Days 2-28 50 mg on alternate days (i.e. day 3, 5, 7, ...) as self-medication

This triple combination should be given for 12 months (i.e. *12 consecutive 28-day treatment cycles). An additional 12 months of this triple combination may be necessary for MB patients showing evidence of relapse.

Children below 10 years: The dose should be adjusted according to body weight: 1 to 2 mg/kg clofazimine + 10 to 20 mg/kg rifampicin + 1 to 2 mg/kg dapsone. As an example, Lamprene (clofazimine) 100 mg once a month under supervision + 50 mg twice a week as self-medication + rifampicin 300 mg once a month under supervision + dapsone 25 mg once a day as self-medication.

Treatment of children below 10 years of age is possible only if dapsone tablets of 25 mg are commercially available.

Patients with erythema nodosum leprosum (ENL)

Adults and children: If the patient develops ENL, treatment with rifampicin and dapsone should be continued as before, and the dosage of clofazimine increased to 200 to 300 mg daily, given under medical supervision. These high daily doses should not be given for longer than 3 months (see section WARNINGS AND PRECAUTIONS). The dose of clofazimine should be

gradually reduced, first to 100 mg twice daily for 12 weeks and then to 100 mg once daily for a further 12 to 24 weeks.

Drug-resistant tuberculosis (DR-TB)

Dosage:

For the treatment of pulmonary DR-TB as part of the WHO shorter or conventional treatment regimen, Lamprene is administered in adults and children as follows:

Adults and adolescents:

- For adults weighing at least 30 kg, the recommended dosage is 100 mg/day.
- For adults weighing less than 30 kg, the recommended dosage is 50 mg/day.

Children (less than 12 years of age):

- For children weighing at least 30 kg, the recommended dosage is 2-5 mg/kg/day, not exceeding 100 mg/day.
- For children weighing less than 30 kg, the recommended dosage is 2-5 mg/kg/day, not exceeding 50 mg/day. If a dose lower than 50 mg/day is required, the 50 mg dose can be given every other day.

Treatment regimen:

Lamprene is used as part of the WHO recommended conventional treatment regimen (18 to 24 months) for the treatment of pulmonary drug-resistant tuberculosis (MDR-TB/XDR-TB) or as part of the WHO shorter treatment regimen (9-12 Months), only for patients with rifampicin resistant or multi-drug resistant tuberculosis (RR-/MDR-TB).

Lamprene must always be used as part of combination regimen with other effective anti-tuberculosis (anti-TB) drugs. The treatment regimen and duration of treatment should follow the WHO treatment guidelines. It is recommended to refer to the latest WHO treatment guidelines for DR-TB for the current dosage regimen recommendation.

Directly observed therapy (DOT) may be appropriate for DR-TB treatment as per local guidelines.

Dosing in special populations

Patients with concomitant HIV infection:

Information from HIV-positive and immune-compromised leprosy patients and TB indicates that the response to clofazimine, including treatment of leprosy reactions, is not altered, and that no dose adjustments are required in these patients.

Renal impairment

There are no data available in patients with renal impairment. Clofazimine may be used in patients with mild to moderate renal impairment. However, caution should be exercised while administering clofazimine to patients with severe renal impairment.

Hepatic impairment

There are no data available in patients with hepatic impairment. Clofazimine should not be administered to patients with hepatic impairment unless the benefit clearly outweighs the risk (see section CLINICAL PHARMACOLOGY).

Method of administration

Lamprene should be taken with a meal or with a glass of milk to ensure maximum absorption.

CONTRAINDICATIONS

Known hypersensitivity to clofazimine or to any of the excipients of Lamprene.

WARNINGS AND PRECAUTIONS

Patient adherence

Lamprene should never be used as monotherapy for the treatment of leprosy or DR-TB. Clofazimine must be used in combination with other drugs according to the dosing regimens described in section DOSAGE REGIMEN AND ADMINISTRATION for the treatment of leprosy and DR-TB.

Multidrug therapy is necessary to prevent the emergence of drug resistance. Patients should be informed of the importance of adherence with the prescribed drug regimen in order to prevent drug resistance. Irregularity in administration of medication and poor adherence can lead to delayed and incomplete cure, rendering the patient a source of contamination.

In leprosy patients poor adherence to treatment can ultimately result in the development of disabilities and deformities. Whenever possible, efforts should be made to ensure that non-adhering patients receive adequate assessment, health education and supervised treatment.

Patients should be trained to recognize the signs and symptoms of reactions and relapses following completion of treatment, and should be made aware of the importance of immediately reporting the earliest manifestations of these signs to the relevant health centers.

Lepra reactions

The WHO generally recommends not interrupting MDT during lepra reactions. Please refer to section DOSAGE REGIMEN AND ADMINISTRATION for Lamprene dosing in patients who develop ENL (erythema nodosum leprosum) reactions. Some data indicate a trend towards reduction in the frequency and severity of ENL in MB leprosy patients treated with MDT. This trend may be attributed to the anti-inflammatory properties of clofazimine. Nevertheless,

temporary, unexplained increases in the reporting of reversal reactions have also been observed in MB leprosy patients, usually during the first year of treatment with MDT. Lepra reactions usually respond satisfactorily to standard anti-inflammatory therapy (prednisolone).

Accumulation of clofazimine

The deposition of large amounts of clofazimine in the intestinal mucosa causes irritation, leading to gastrointestinal disturbances (e.g. abdominal pain [sometimes intermittent], nausea, vomiting and diarrhea) usually with mild forms, but sometimes with more severe clinical manifestations. Clofazimine has heterogeneous distribution throughout the body and a slow elimination rate, accumulating mainly in fatty tissue, the reticuloendothelial system (macrophages, histiocytes and spleen), and the skin. Adverse reactions to clofazimine are mainly linked to its uptake by tissue and organs. Because of this, the use of high doses for long periods should be avoided. After prolonged administration in high doses, clofazimine may accumulate in various organs, body fluids and tissues as crystals. Among the viscera, the jejunum has the highest drug deposition, closely followed by the spleen. If crystals are deposited in the mesenteric lymph nodes and/or histiocytes at the lamina propria of the jejunal mucosa, this may lead to intestinal obstruction. Fatalities have been reported following gastrointestinal side effects. If gastrointestinal symptoms develop during treatment, the dosage should be reduced or the interval between doses prolonged. Symptoms may slowly regress on withdrawal of the drug.

In the event of persistent diarrhea or vomiting, the patient should be hospitalized.

Skin discoloration

Physicians should be aware that skin discoloration due to clofazimine may result in depression (isolated cases of depression with suicide have been reported). Patients should be warned that Lamprene may cause discoloration of the conjunctiva, lacrimal fluid, sweat, sputum, urine, feces, nasal secretions, semen and breast milk, and reddish to brownish-black discoloration of the skin. Patients should be told that discoloration of the skin, although reversible, may take several months or years to disappear after the end of therapy with Lamprene.

Torsades de pointes and QT prolongation

Cases of Torsades de Pointes with QT prolongation have been reported in patients receiving clofazimine at doses higher than usually recommended or in combination with QT-prolonging medications, and therefore caution is required in the treatment of these patients (see section INTERACTIONS). Patients receiving clofazimine at doses higher than usually recommended or in combination with QT-prolonging medications should have regular ECGs performed to monitor for QT prolongation and cardiac rhythm disturbances.

Interactions

As clofazimine is predicted to be a moderate to strong inhibitor of CYP3A (CYP3A4 and CYP3A5) substrates, caution should be exercised while co-administering clofazimine with drugs which are CYP3A substrates (see Section INTERACTIONS).

Driving and using machines

Dizziness, visual acuity reduced, nausea, fatigue and headache have been reported on Lamprene therapy. Patients experiencing such adverse reactions should not drive a vehicle or operate machines.

ADVERSE DRUG REACTIONS

Summary of the safety profile

The safety profile of Lamprene is similar when used in leprosy and DR-TB.

Tabulated summary of adverse drug reactions

Adverse drug reactions (Table 2) are listed according to system organ classes in MedDRA. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. In addition, the corresponding frequency category using the following convention (CIOMS III) is also provided for each adverse drug reaction: *very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), including isolated reports.*

Table-2 Summary of adverse drug reactions

Blood and lymphatic system disorders	
Very rare:	Lymphadenopathy, splenic infarction, anaemia
Psychiatric disorders	
Very rare:	Depression
Nervous system disorders	
Uncommon:	Headache
Very rare:	Dizziness
Eye disorders	
Very common:	Conjunctival discolouration, corneal pigmentation, tear discolouration
Common:	Visual acuity reduced, dry eye, eye irritation
Uncommon:	Maculopathy, corneal deposits
Respiratory, thoracic and mediastinal disorders	
Very common:	Sputum discoloured
Gastrointestinal disorders	
Very common:	Nausea, vomiting, abdominal pain, diarrhoea, faeces discoloured
Uncommon	Gastroenteritis eosinophilic, decreased appetite
Very rare:	Intestinal obstruction, gastrointestinal haemorrhage, abdominal discomfort, abdominal pain upper, constipation
Hepatobiliary disorders	
Very rare	Hepatitis, blood bilirubin increased, jaundice, aspartate aminotransferase increased
Skin and subcutaneous tissue disorders	
Very common:	Sweat discolouration, skin discolouration, hair colour changes, ichthyosis, dry skin
Common:	Rash, pruritus

Uncommon:	Photosensitivity reaction, dermatitis acneiform
Very rare:	Dermatitis exfoliative
Renal and urinary disorders	
Very common:	Chromaturia
General disorders and administration site conditions	
Uncommon:	Fatigue
Very rare:	Pyrexia
Investigations	
Common:	Weight decreased
Uncommon:	Blood sugar increased

Note: Depression has been reported due to skin discoloration, and drug related isolated cases of suicides have been reported. Reddish to brownish-black discoloration of the skin and leprous lesions, particularly in fair-skinned patients at sites exposed to light, and discoloration of the hair are reversible, although in the case of the skin it may take several months or years to disappear after the end of treatment. Corneal pigmentation (subepithelial corneal brownish pigmented lines) is due to crystal deposits. It is reversible on discontinuation of Lamprene. Some of the adverse reactions to clofazimine are mainly linked to its uptake by tissue and organs (see section WARNINGS AND PRECAUTIONS).

INTERACTIONS

Dapsone

Lamprene appears to have no important effects on the pharmacokinetics of dapsone, although a transient increase in the urinary excretion of dapsone occurred in a few patients. Limited data suggesting that dapsone inhibits the anti-inflammatory activity of Lamprene have not been confirmed. If leprosy-associated inflammatory reactions develop in patients being treated with dapsone and Lamprene, it is still advisable to continue treatment with both drugs.

Rifampicin

Clofazimine reduces rifampicin absorption in leprosy patients, increasing the time it takes for the peak serum concentration to be reached and prolonging the elimination half-life. Total exposure (AUC) of rifampicin was not affected, so this interaction is unlikely to be clinically significant.

Isoniazid

In patients receiving high doses of clofazimine (300 mg daily) and isoniazid (300 mg daily), elevated concentrations of clofazimine were detected in plasma and urine, although skin concentrations were found to be lower.

Interaction with QT prolonging drugs

Cases of Torsades de Pointes with QT prolongation have been reported in patients receiving clofazimine in combination with QT prolonging medications. Caution is recommended when

clofazimine is administered with other drugs (e.g: bedaquiline, fluoroquinolones) with known QT interval prolonging potential (see Section WARNINGS AND PRECAUTIONS).

Effects of clofazimine on CYP3A (CYP3A4 and CYP3A5) substrates:

No clinical drug interaction studies have been performed with CYP3A substrates.

Clofazimine inhibits the CYP3A enzyme *in vitro*. Based on PBPK modeling results, clofazimine is predicted to be a moderate to strong CYP3A inhibitor. Hence, caution should be exercised with the concomitant administration of clofazimine and CYP3A substrates (e.g.: simeprevir, tipranavir, delamanid, lercanidipine, simvastatin, lovastatin).

Effects of other drugs on clofazimine:

In a healthy volunteer study of a combination regimen including clofazimine, cycloserine, ethionamide, para-aminosalicyclic acid, and pyridoxine, the C_{max} and T_{max} values of clofazimine were similar to those reported in other studies where clofazimine was administered alone, suggesting no major effects of these drugs on the pharmacokinetics of clofazimine.

In patients with pulmonary TB, where clofazimine was dosed alone and in combination with bedaquiline, pyrazinamide and pretomanid, the C_{max} and AUC values of clofazimine were similar between the groups suggesting no major effects of these drugs on the pharmacokinetics of clofazimine.

PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL

Pregnancy

Risk summary

It is generally considered that the benefits of MDT (including Lamprene) in the treatment of leprosy during pregnancy outweigh any potential risk, and since leprosy is exacerbated during pregnancy, the WHO recommends that treatment with MDT be continued during pregnancy.

Experience with Lamprene in pregnancy is limited. Clofazimine crosses the placenta, and skin discoloration has been observed in neonates.

Animal studies revealed no evidence of teratogenicity but adverse effects on the fetus were noted at high dosages.

Animal data

No teratogenic effect was observed in the offspring of rodents and rabbits treated during pregnancy with clofazimine at oral doses of up to 50 mg/kg/day and 15 mg/kg/day, respectively. In the mouse, there were signs of fetotoxicity (e.g. retardation of fetal skull ossification) at a dose (50 mg/kg/day) considered sufficiently in excess of the human dose.

Lactation

The benefits of MDT treatment in lactating mothers clearly outweigh the risks, therefore the WHO recommends that treatment be continued during lactation.

Clofazimine passes into the breast milk, and skin discoloration may occur in the infant.

Females and males of reproductive potential

Infertility

There was some evidence of impaired fertility in one study in female rats receiving clofazimine 50 mg/kg/day (see section NON-CLINICAL SAFETY DATA).

Overdosage

Please refer to the Torsades de pointes and QT prolongation subsection in the WARNINGS AND PRECAUTIONS section.

No specific data are available on the treatment of overdose with Lamprene. In cases of acute overdose, symptomatic treatment may be given as required.

CLINICAL PHARMACOLOGY

Mechanism of action (MOA)

Lamprene is thought to exert its anti-mycobacterial effect through multiple mechanisms.

The primary mechanism of action for the antimicrobial activity of clofazimine can be postulated through its membrane-directed activity, including the bacterial respiratory chain and ion transporters. Intracellular redox cycling, involving oxidation of reduced clofazimine, leads to the generation of antimicrobial reactive oxygen species (ROS), superoxide-hydrogen peroxide (H_2O_2).

Secondly, interaction of clofazimine with membrane phospholipids results in the generation of antimicrobial lysophospholipids, which promote membrane dysfunction, resulting in interference with K^+ uptake. Both mechanisms result in interference with cellular energy metabolism by disrupting ATP production.

The third proposed mechanism of action is binding preferentially to mycobacterial deoxyribonucleic acid (DNA) with particular affinity to guanine bases and inhibiting mycobacterial replication and growth.

Clofazimine also displays an anti-inflammatory effect, which may contribute to the efficacy of Lamprene in controlling ENL reactions.

Anti-inflammatory activity of clofazimine is primarily through inhibition of T lymphocyte activation and proliferation. Clofazimine may indirectly interfere with the proliferation of T cells by promoting the release of ROS and E-series prostaglandins (PGs), especially PGE2 from neutrophils and monocytes.

Clofazimine may also exert anti-mycobacterial activity by its effect on tissue macrophages, which are the main targets of infection as well as immune response in TB. Clofazimine has a tendency to concentrate selectively in cells of the reticuloendothelial system, which are the main targets of mycobacterial infection, and this enables it to deliver its action at the intended target. This selective accumulation of clofazimine in macrophages is also believed be involved in the drug's anti-inflammatory properties.

Clofazimine has shown apoptosis inducing properties in activated macrophages, which may be responsible for both anti-inflammatory as well as antibacterial actions of the drug. Clofazimine has been shown to inhibit MtSerB2, a phosphatase produced by *M. tuberculosis* that is believed to help the pathogen to evade the host's immune response. The immunosuppressive properties of clofazimine may be either detrimental of beneficial in TB therapy. The immunosuppressive activity may contribute explain to the lack of early bactericidal activity, but later may contribute to the eradication of slow growing persistent pathogens.

Pharmacodynamic properties (PD)

Leprosy:

The major role of the dapsone-clofazimine component of the MDT regimen for MB leprosy is to ensure elimination of spontaneously occurring rifampicin-resistant mutants (estimated to be less than or equal to 10^4 organisms in an untreated patient with lepromatous leprosy). Daily treatment with dapsone-clofazimine alone for 3 months killed more than 99.999% of viable *Mycobacterium leprae*, suggesting that all spontaneously occurring rifampicin-resistant mutants are likely to be eliminated by 3 to -6 months of treatment with the dapsone--clofazimine component of the MDT regimen.

In humans, clofazimine exerts a bacteriostatic and weak bactericidal effect on *Mycobacterium leprae* (*M. leprae*, Hansen's bacillus). Clofazimine appears to bind preferentially to mycobacterial DNA and inhibit mycobacterial replication and growth.

The minimum inhibitory concentration of clofazimine for *M. leprae* in mouse tissue has been estimated at between 0.1 and 1 microgram per gram; uneven tissue distribution precludes a more accurate estimate. In patients with lepromatous leprosy, the overall antibacterial effect of Lamprene is comparable to that of dapsone. However, the onset of antimicrobial activity of Lamprene is slow, and can only be demonstrated after about 50 days of therapy.

No cross-resistance occurs with dapsone and rifampicin, probably because clofazimine has a different mode of action. *M. leprae* resistant to clofazimine have been reported only in isolated cases.

DR-TB

The MIC of clofazimine against drug susceptible as well as single drug-resistant, multidrug-resistant and extensively drug resistant TB strains ranges from <0.0625 µg/mL to > 1 µg/mL. The majority [84.7% (95% CI: 69.5%, 93.1%)] of the tested strains have a reported MIC value of ≤ 0.5 µg/mL for clofazimine.

Clofazimine does not show cross-resistance with isoniazid or rifampin. *In vitro* resistance to clofazimine in *mycobacterium tuberculosis* has been mapped to mutations in the transcriptional

regulator Rv0678 which results in the upregulation of MmpS5-MmpL5, an efflux pump. These mutants show cross-resistance to bedaquiline. Two additional mutations (Rv1979c and Rv2535c) have also been associated with clofazimine resistance *in vitro*; however, the mechanism and clinical relevance of these mutations is yet to be determined

Pharmacokinetic properties (PK)

Absorption

Clofazimine is absorbed relatively slowly. Bioavailability of clofazimine from the micronized suspension in an oil-wax base (such as that of Lamprene capsules) is up to 70% after a dose of 100 mg, and decreases with higher doses. The time to reach peak plasma concentration (median time) of clofazimine decreases from 12 to 8 hours under fed conditions relative to the fasted state. Administering the drug with food increases the bioavailability in terms of AUC (area under the concentration-time curve) by about 60%, and tends to accelerate the absorption rate. After administration of a single oral dose of 200 mg clofazimine with a morning meal, mean (±SD) peak plasma concentrations of 0.41 (±0.14) micrograms per mL (861 (±289) pmol/g) were measured in healthy volunteers. When clofazimine is taken on an empty stomach, the peak plasma concentration was approximately 20% lower.

After repeated administration of clofazimine to leprosy patients in daily doses of 50 mg and 100 mg, mean trough concentrations of 0.27 and 0.43 micrograms / mL (580 pmol/g and 910 pmol/g), respectively, were measured after 42 consecutive days. Steady-state concentrations were not reached within this time period. The accumulation ratios after 50 and 100 mg daily doses of clofazimine on day 42 were 9.88 and 11.61, respectively. The estimated time to reach steady-state plasma concentration after a 50 mg daily dose in leprosy patients was 70 days.

Distribution

Clofazimine is strongly lipophilic and accumulates mainly in fatty tissue and in macrophages of the reticuloendothelial system. After long-term treatment, clofazimine has been detected in the following organs, tissues and body fluids: subcutaneous fat, mesenteric lymph nodes, bile and gall bladder, adrenals, spleen, small intestine, liver, muscle tissue, bones, and skin. Clofazimine does not appear to cross the intact blood-brain barrier.

Clofazimine crosses the placenta and passes into the breast milk in sufficient quantities to cause discoloration of the milk.

Clofazimine bound to the alpha- and beta-lipoproteins in serum, particularly the beta-lipoproteins, and the binding was saturable at approximately 10 microgram/mL (21141 pmol/g) concentrations. Binding to gamma-globulin and albumin was negligible.

Biotransformation/Metabolism

Information on the metabolism of clofazimine is limited. Three metabolites, two of which are glucuronides, have been identified in urine.

Elimination

Clofazimine is eliminated slowly from the plasma. The mean elimination half-life of the unchanged substance following a single dose of 200 mg in healthy volunteers was 10.6 (±4.0) days. After repeated administration of 50 mg and 100 mg daily to leprosy patients, the elimination half-life was about 25 days.

Unchanged clofazimine is excreted via the bile mainly in the feces. Within 3 days on average, 35% of the dose is recovered in feces. No more than 0.4% of the dose is found in the urine as unchanged clofazimine after 24 hours. Urinary metabolites account for about 0.6% of the daily dose.

Special populations

No data is available on the effects of renal or hepatic dysfunction, or of age, on the pharmacokinetics of clofazimine.

CLINICAL STUDIES

No recent clinical trials have been conducted by Novartis with Lamprene

NON-CLINICAL SAFETY DATA

Carcinogenicity and mutagenicity

Long-term carcinogenicity studies in animals have not been conducted with clofazimine. No mutagenic activity was detected in the Ames test but there is some evidence of clastogenic potential in mice.

Reproductive toxicity

For reproductive toxicity, see section PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL.

There was some evidence of impaired fertility in one study in female rats receiving clofazimine 50 mg/kg/day (from 9 weeks before mating until weaning); the number of offspring was reduced and there was a lower proportion of implantations. Lower doses (5 and 25 mg/kg/day) had no such effects.

Incompatibilities

None known.

Storage

See folding box.

Lamprene should not be used after the date marked "EXP" on the pack.

Lamprene must be kept out of the reach and sight of children.

Manufacturer:

See folding box.

International Package Leaflet

Information issued: May 2018

® = registered trademark

Novartis Pharma AG, Basel, Switzerland

MODELLO 10-1 **Allegato 10**

AL MINISTERO DELLA SALUTE
USMAF-SASN di Lazio, Marche, Umbria, Abruzzo e Molise
UNITÀ TERRITORIALE DI ROMA CIAMPINO

Richiesta di importazione di medicinali ai sensi del D.M. 11/02/1997.

Il sottoscritto Medico curante Dr. _____

residente in _____ prov. _____ via _____

tel. _____ iscritto nell'Albo dell'Ordine dei Medici-Chirurghi di _____

al n. _____ codice regionale _____

operante presso il Reparto / Divisione di _____

dell'Ospedale/ASL _____

chiede di importare dall'estero il seguente medicinale:

Principio/i attivo/i: Clofaziminum
Nome commerciale: Lamprene
Forma farmaceutica: capsule
Dosaggio specialità: 50 mg
Nella quantità di nr.: _____ confezioni contenenti nr. 100 unità di farmaco cadauna
Prodotto dalla ditta: Catalent Germany Eberbach GmbH
Titolare estero AIC: Novartis Pharma AG
Precisa che tale medicinale è regolarmente registrato nel Paese di provenienza: Svizzera
Per il trattamento di: _____
Tale medicinale è indispensabile per la cura del Sig. (solo iniziali o codice): _____
Affetto da: _____
Motivo per cui viene richiesta la scorta di reparto*: _____

_____

Dichiara altresì che il farmaco:

- non ha valida alternativa terapeutica con altri medicinali registrati in Italia;
- non contiene sostanze stupefacenti o psicotrope;
- non è un emoderivato;
- verrà impiegato sotto la propria diretta responsabilità, dopo aver ottenuto il consenso informato scritto del paziente o, in caso di minori o incapaci, di chi esercita la patria potestà;
- che le generalità del paziente ed i documenti relativi al consenso informato sono custoditi presso il medico curante per la durata prevista dalla normativa vigente;
- in caso di richiesta per scorta, che il quantitativo richiesto non supera i 90 giorni di terapia per paziente.

Particolari condizioni di conservazione del medicinale:
Temperatura (es. -20°C, da 2 a 8°C, <25°C, <30°C, nessuna indicazione): temperatura ambiente

Altro: _____

Luogo e data: _____

_____
Il Dirigente del Servizio Farmaceutico
Timbro e firma leggibile per esteso

_____
Il Medico Curante
Timbro e firma leggibile per esteso

**Da compilare solo in caso di richiesta di importazione per costituire una scorta di reparto*

Olga Marletta <omarletta@arnasgaribaldi.it>

Dottssa Marletta
04.09.2020

Fwd: OFFERTA ARNAS GARIBALDI LAMPRENE CPR. 50 MG.

1 messaggio

barbara.busa@libero.it <barbara.busa@libero.it> 3 settembre 2020 15:21
Rispondi a: barbara.busa@libero.it
A: omarletta <omarletta@arnasgaribaldi.it>

REPUBBLICA ITALIANA
A.R.N.A.S. GARIBALDI
CATANIA
SETTORE FARMACO E PRONTO SOCCORSO
- 4 SET. 2020
PROT. N° 4494
ARRIVO

Dottssa Barbara Busà
Dirigente Farmacista
ARNAS Garibaldi Catania

Inviato da Libero Mail per iOS

——— Messaggio inoltrato ———
Da: Farmaceutica Internazionale Italiana - Claudio Pallotta <commerciale@finternazionale.it>
A: barbara.busa@libero.it <barbara.busa@libero.it>
Data: giovedì 3 settembre 2020, 11:37 +0200
Oggetto: OFFERTA ARNAS GARIBALDI LAMPRENE CPR. 50 MG.

Buongiorno, faccio seguito alla Sua richiesta ed allego alla presente offerta per il farmaco descritto in oggetto.

A disposizione per eventuali chiarimenti porgo cordiali saluti.

Si precisa che, vista l'emergenza sanitaria attualmente in corso a livello internazionale, potrebbe essere bandita l'esportazione di medicinali da parte di qualsiasi Paese Estero.

FARMACEUTICA INTERNAZIONALE ITALIANA S.r.l. SI AVVALE SOLO ED ESCLUSIVAMENTE DI GROSSISTI E/O DITTE PRODUTTRICI CON REGOLARE AUTORIZZAZIONE ALLA VENDITA

E/O PRODUZIONE DEI FARMACI RICHIESTI. SI SPECIFICA CHE TALI CARATTERISTICHE SI EVINCONO DA DOCUMENTAZIONE UFFICIALE RICHIESTA AGLI ORGANI COMPETENTI DI CONTROLLO.

FARMAVELIA INTERNAZIONALE ITALIANA

Claudio Pallotta

Corso Marconi n° 26

28883 – GRAVELLONA TOCE (VB) - ITALIA

Tel. 0323/86.55.57

Fax: 0323/84.52.67

e-mail: commerciale@finternazionale.it

pec: farminternaz@pec.it

3 allegati

LAMPRENE CPR. 50 MG. NOVARTIS FRANCIA.pdf
38K

DICHIARAZIONE RESPONSABILITA' LAMPRENE CPR. 50 MG. NOVARTIS FRANCIA.pdf
426K

OFFERTA ARNAS GARIBALDI LAMPRENE CPR. 50 MG.pdf
111K

Dénomination du médicament

LAMPRENE 50 mg, capsule molle

(Clofazimine)

Encadré

Veuillez lire attentivement cette notice avant de prendre ce médicament car elle contient des informations importantes pour vous.

· Gardez cette notice. Vous pourriez avoir besoin de la relire.

· Si vous avez d'autres questions, interrogez votre médecin ou votre pharmacien.

· Ce médicament vous a été personnellement prescrit. Ne le donnez pas à d'autres personnes. Il pourrait leur être nocif, même si les signes de leur maladie sont identiques aux vôtres.

· Si vous ressentez un quelconque effet indésirable, parlez-en à votre médecin ou votre pharmacien. Ceci s'applique aussi à tout effet indésirable qui ne serait pas mentionné dans cette notice. Voir rubrique 4.

Que contient cette notice ?

1. QU'EST-CE QUE LAMPRENE 50 mg, capsule molle ET DANS QUELS CAS EST-IL UTILISE ?

Classe pharmacothérapeutique : Médicaments pour le traitement de la lèpre - code ATC : J04BA01

Ce médicament est un antibiotique.

Il appartient à la famille des antilépreux. Il permet de détruire certaines bactéries appelées mycobactéries.

Dans quels cas est-il utilisé ?

Ce médicament est utilisé en association avec deux autres médicaments (la dapsone et la rifampicine) pour traiter la lèpre (maladie de Hansen).

La lèpre est une infection de longue durée provoquée par une bactérie et qui touche les nerfs, la peau, l'intérieur de la bouche, du nez, des oreilles et les parties génitales.

Ce médicament est également utilisé pour traiter l'érythème noueux lépreux (apparition de nodules rouges sur la peau s'accompagnant de fièvre et d'un malaise général).

Vous devez vous adresser à votre médecin si vous ne ressentez aucune amélioration ou si vous vous sentez moins bien.

2. QUELLES SONT LES INFORMATIONS A CONNAITRE AVANT DE PRENDRE LAMPRENE 50 mg, capsule molle ?

Ne prenez jamais LAMPRENE 50 mg, capsule molle :

· Si vous êtes allergique à la clofazimine ou à l'un des autres composants contenus dans ce médicament, mentionnés dans la rubrique 6.

· Si vous êtes allergique à l'arachide ou au soja car ce médicament contient de l'huile de soja.

Avertissements et précautions

Ce médicament contient du parahydroxybenzoate d'éthyle sodé et du parahydroxybenzoate de propyle sodé et peut provoquer des réactions allergiques.

Adressez-vous à votre médecin ou pharmacien avant de prendre LAMPRENE 50 mg, capsule molle

· si vous avez une maladie grave du foie ou des reins.

· en cas de coloration anormale de votre peau et de vos cheveux avec un impact sérieux sur votre qualité de vie ce qui vous rend dépressif.

· en cas de troubles de la vision (vision floue ou autre trouble).

· si vous avez des troubles digestifs, ces effets indésirables pouvant parfois avoir des conséquences fatales. Dans ce cas, votre médecin pourra réduire votre dose ou espacer les prises.

· si vous développez des signes tels qu'une diarrhée ou des vomissements persistants. Dans ce cas, votre médecin pourra vous hospitaliser.

La substance active de LAMPRENE est rouge et peut entraîner une coloration anormale de la peau, de la sueur, des larmes, des urines, des expectorations, du sperme ou du lait maternel, des cheveux et des fèces dans les semaines qui suivent le début du traitement. Cette coloration rougeâtre à brun foncé disparaîtra à l'arrêt du traitement, cependant le retour à la couleur initiale pourra prendre plusieurs mois ou années.

Si cette coloration vous rendait dépressif, consultez votre médecin.

LAMPRENE peut provoquer des troubles du rythme cardiaque (allongement de l'intervalle QT, torsades de pointe) lorsqu'il est utilisé à des doses supérieures aux doses recommandées ou en même temps que certains médicaments connus pour donner des troubles du rythme cardiaque. Dans ces situations, votre médecin vous demandera de faire régulièrement un électrocardiogramme afin de dépister un éventuel trouble du rythme cardiaque.

Enfants et adolescents

Se référer à la section posologie.

Chez les enfants de moins de 10 ans, le traitement n'est possible que si la dapsone est disponible sur le marché en comprimés de 25 mg.

Autres médicaments et LAMPRENE 50 mg, capsule molle

Informez votre médecin ou pharmacien si vous prenez, avez récemment pris ou pourriez prendre tout autre médicament.

LAMPRENE 50 mg, capsule molle avec des aliments et boissons

Sans objet.

Grossesse et allaitement

Si vous êtes enceinte ou que vous allaitez, si vous pensez être enceinte ou planifiez une grossesse, demandez conseil à votre médecin ou pharmacien avant de prendre ce médicament.

Grossesse

La clofazimine (substance active contenue dans LAMPRENE) traverse la barrière placentaire. Si vous êtes enceinte ou si vous envisagez de l'être, vous ne devez prendre ce médicament que si votre médecin le décide.

Si vous découvrez que vous êtes enceinte pendant le traitement, consultez votre médecin car lui seul peut juger de la nécessité de le poursuivre.

Allaitement

La clofazimine (substance active contenue dans LAMPRENE) passe dans le lait maternel. Par conséquent, vous devez éviter d'allaiter pendant votre traitement.

Seul votre médecin est à même de vous prescrire LAMPRENE en période d'allaitement.

Conduite de véhicules et utilisation de machines

Soyez très prudent. Ne pas conduire sans l'avis d'un professionnel de santé.

Ce médicament peut provoquer une baisse de la vue, des troubles de la vue de jour et de nuit, des troubles du champ visuel, une somnolence, des nausées ce qui peut diminuer votre vigilance. Si vous ressentez l'un de ces effets, il est déconseillé de conduire un véhicule ou d'utiliser une machine.

LAMPRENE 50 mg, capsule molle contient de l'huile de soja, du parahydroxybenzoate d'éthyle sodé et du parahydroxybenzoate de propyle sodé

médecin ou pharmacien en cas de doute.

Posologie

Dans le traitement de la maladie de Hansen (Lèpre), ce médicament vous sera prescrit en association avec 2 autres médicaments qui agissent sur cette infection : la dapsone et la rifampicine.

Votre médecin déterminera la dose que vous devez prendre en fonction de votre âge et de votre poids.

A titre indicatif, la posologie usuelle recommandée par l'Organisation Mondiale de la Santé (OMS), est la suivante :

Adultes (à partir de 15 ans) :

· *Lamprène (clofazimine)* : 300 mg/1 fois par mois (J1) sous surveillance + 50 mg/j (de J_2 à J_{28}),

· *rifampicine* : 600 mg/1 fois par mois (J_1) sous surveillance,

· *dapsone* : 100 mg/j (de J_1 à J_{28}).

Utilisation chez les enfants et les adolescents

Enfants de 10 à 14 ans :

· *Lamprène (clofazimine)* : 150 mg/1 fois par mois (J_1) sous surveillance + 50 mg un jour sur deux (de J_2 à J_{28}),

· *rifampicine* : 450 mg/1 fois par mois (J_1) sous surveillance,

· *dapsone* : 50 mg/j (de J_1 à J_{28}).

Enfants de moins de 10 ans :

· *Lamprène (clofazimine):* 100 mg/1 fois par mois (J_1) sous surveillance + 50 mg 2 fois par semaine,

· *rifampicine* : 300 mg/1 fois par mois (J_1) sous surveillance,

· *dapsone* : 25 mg/j.

Chez les enfants de moins de 10 ans, le traitement n'est possible que si la dapsone est disponible sur le marché en comprimés de 25 mg.

Cependant, des rythmes d'administration autres que celui préconisé par l'OMS, sont possibles.

Se conformer strictement à l'ordonnance de votre médecin.

Dans le traitement de l'érythème noueux lépreux le dosage de la clofazimine doit être augmenté à 200-300 mg par jour, sous surveillance médicale. Ces doses journalières élevées ne devraient pas être prescrites plus de 3 mois. La dose de clofazimine doit être diminuée progressivement, d'abord à 100 mg deux fois par jour pendant 12 semaines, puis à 100 mg une fois par jour pendant 12 à 24 semaines supplémentaires.

Mode d'administration

Ce médicament est à prendre par voie orale.

Vous devez prendre la capsule de préférence au cours d'un repas ou avec un verre de lait.

Durée du traitement

Vous devrez prendre ce médicament, associé à deux autres médicaments (la dapsone et la rifampicine) pendant au moins 12 mois.

Pour être efficace, cet antibiotique doit être utilisé régulièrement aux doses prescrites, et aussi longtemps que votre médecin vous l'aura conseillé.

La disparition de la fièvre, ou de tout autre symptôme, ne signifie pas que vous êtes complètement guéri.

L'éventuelle impression de fatigue, n'est pas due au traitement antibiotique mais à l'infection elle-même. Le fait de réduire ou de suspendre votre traitement serait sans effet sur cette impression et retarderait votre guérison.

Si vous avez pris plus de LAMPRENE 50 mg, capsule molle que vous n'auriez dû

Ne prenez pas de dose double pour compenser la dose que vous avez oublié de prendre.

Si vous arrêtez de prendre LAMPRENE 50 mg, capsule molle

Sans objet.

Si vous avez d'autres questions sur l'utilisation de ce médicament, demandez plus d'informations à votre médecin ou à votre pharmacien.

4. QUELS SONT LES EFFETS INDESIRABLES EVENTUELS ?

Comme tous les médicaments, ce médicament peut provoquer des effets indésirables, mais ils ne surviennent pas systématiquement chez tout le monde.

Allergie : En raison de la présence d'huile de soja, ce médicament peut provoquer une réaction allergique telle que l'urticaire. Il peut provoquer également un malaise brutal avec une baisse importante de la tension artérielle (choc anaphylactique). Si l'un de ces effets survient, arrêtez le médicament et contactez immédiatement votre médecin.

Les effets indésirables suivants surviennent très fréquemment :

Effets sur la peau

· Chez les personnes à peau claire, une coloration rougeâtre à brun foncé de la peau en particulier sur les zones découvertes et sur les lésions, modification de la couleur des cheveux.

· Chez les personnes à peau noire, cette coloration peut prendre une couleur gris-noire.

Ces troubles disparaissent à l'arrêt du traitement, mais souvent la coloration de la peau ne disparaît complètement que plusieurs mois voire plusieurs années après l'arrêt du traitement. Dans certains cas, la coloration de la peau peut être définitive.

· Une sécheresse de la peau, qui peut s'accompagner parfois d'un décollement de la peau (squames).

Effets sur les yeux

· Une coloration de certaines parties de l'œil (la conjonctive et/ou la cornée) et des larmes.

Effets digestifs

· Des nausées, vomissements, diarrhées.

· Des douleurs du ventre.

Autres effets

· Une coloration anormale de la sueur, de la salive, des urines et des selles.

Les effets indésirables suivants surviennent fréquemment :

Effets sur la peau

· Des démangeaisons, une éruption sur la peau.

Effets sur les yeux

· Une sécheresse et une irritation des yeux, une baisse de la vue, des troubles de la vision (tels que des troubles de la vue de jour et de nuit, des troubles du champ visuel).

Autres effets

· Une coloration du lait maternel.

· Une perte de poids.

Les effets indésirables suivants surviennent peu fréquemment :

Effets sur les yeux

· Une pigmentation de la macula (zone spécifique de la rétine située au fond de l'œil).

· Une diminution de l'appétit.

Effets sur la peau

· Une réaction excessive de la peau lors d'une exposition au soleil ou aux UV (photosensibilité).

· Des éruptions sur la peau comparables à l'acné.

Effet détecté lors d'une analyse de sang

· Une augmentation du taux de sucre dans le sang.

Effets digestifs

· Une maladie de l'intestin par dépôts de cristaux dans la muqueuse digestive.

Les effets indésirables suivants surviennent rarement :

Effets sur le cerveau et les nerfs

· Une somnolence.

· Une fatigue.

Les effets indésirables suivants surviennent très rarement :

Effets sur le cerveau et les nerfs

· Une dépression due à la coloration de la peau.

Autres effets

· Un lymphœdème (gonflement d'une partie du corps dû à une accumulation de liquide lymphatique).

· Des troubles sévères du rythme cardiaque.

· Une atteinte de la rate.

· Une diminution importante du taux de certains globules blancs (granulocytes) dans le sang.

Les effets indésirables suivants ont une fréquence qui n'est pas connue :

Effets digestifs

· Un arrêt du transit intestinal (occlusion intestinale).

· Une gêne abdominale.

· Des douleurs abdominales hautes.

Effets sur la peau

· Une maladie sévère de la peau.

Autres effets

· Une acidité élevée dans le sang.

· Une coloration des crachats.

La pigmentation de la cornée (pigmentation brune sous-épithéliale) est due à des dépôts de cristaux. Ce trouble est réversible à l'arrêt du traitement.

Déclaration des effets secondaires

Si vous ressentez un quelconque effet indésirable, parlez-en à votre médecin ou votre pharmacien. Ceci s'applique aussi à tout effet indésirable qui ne serait pas mentionné dans cette notice. Vous pouvez également déclarer les effets indésirables directement via le système national de déclaration : Agence nationale de sécurité du médicament et des produits de santé (ANSM) et réseau des Centres Régionaux de Pharmacovigilance - Site internet: www.ansm.sante.fr

Tenir ce médicament hors de la vue et de la portée des enfants.

N'utilisez pas ce médicament après la date de péremption indiquée sur la boîte. La date de péremption fait référence au dernier jour de ce mois.

A conserver à une température ne dépassant pas 25°C.

Conserver le flacon soigneusement fermé, à l'abri de l'humidité.

Ne jetez aucun médicament au tout-à-l'égout ou avec les ordures ménagères. Demandez à votre pharmacien d'éliminer les médicaments que vous n'utilisez plus. Ces mesures contribueront à protéger l'environnement.

6. CONTENU DE L'EMBALLAGE ET AUTRES INFORMATIONS

Ce que contient LAMPRENE 50 mg, capsule molle

· La substance active est :

Clofazimine..... 50,00 mg

pour une capsule molle

· Les autres composants sont :

Le butylhydroxytoluène, l'acide citrique anhydre, le propylèneglycol, l'huile de colza, la lécithine de soja, un mélange de cires (cire d'abeille, huile de soja hydrogénée, huiles végétales hydrogénées).

Composition de l'enveloppe de la capsule molle : gélatine, glycérol, oxyde de fer noir, oxyde de fer rouge, paraméthoxy-acétophénone, éthylvanilline, parahydroxybenzoate d'éthyle sodé, parahydroxybenzoate de propyle sodé.

Qu'est-ce que LAMPRENE 50 mg, capsule molle et contenu de l'emballage extérieur

Ce médicament se présente sous forme d'une capsule molle.

Chaque boîte contient un flacon de 100 capsules.

Titulaire de l'autorisation de mise sur le marché

NOVARTIS PHARMA S.A.S.

2-4, RUE LIONEL TERRAY

92500 RUEIL-MALMAISON

Exploitant de l'autorisation de mise sur le marché

NOVARTIS PHARMA S.A.S.

2-4, RUE LIONEL TERRAY

92500 RUEIL-MALMAISON

Fabricant

NOVARTIS PHARMA S.A.S.

2-4, RUE LIONEL TERRAY

92500 RUEIL-MALMAISON

Noms du médicament dans les Etats membres de l'Espace Economique Européen

Sans objet.

La dernière date à laquelle cette notice a été révisée est :

[à compléter ultérieurement par le titulaire]

< {MM/AAAA}>< {mois AAAA}.>

CONSEILS POUR UNE BONNE UTILISATION DES ANTIBIOTIQUES

Les antibiotiques sont efficaces pour combattre les infections dues aux bactéries. Ils ne sont pas efficaces contre les infections dues aux virus.

Aussi, votre médecin a choisi de vous prescrire cet antibiotique parce qu'il convient précisément à votre cas et à votre maladie actuelle.

Les bactéries ont la capacité de survivre ou de se reproduire malgré l'action d'un antibiotique. Ce phénomène est appelé résistance : il rend certains traitements antibiotiques inactifs. La résistance s'accroît par l'usage abusif ou inapproprié des antibiotiques.

Vous risquez de favoriser l'apparition de bactéries résistantes et donc de retarder votre guérison ou même de rendre inactif ce médicament, si vous ne respectez pas :

- la dose à prendre,
- les moments de prise,
- et la durée du traitement.

En conséquence, pour préserver l'efficacité de ce médicament :

1. N'utilisez un antibiotique que lorsque votre médecin vous l'a prescrit.
2. Respectez strictement votre ordonnance.
3. Ne réutilisez pas un antibiotique sans prescription médicale même si vous pensez combattre une maladie apparemment semblable.
4. Ne donnez jamais votre antibiotique à une autre personne, il n'est peut-être pas adapté à sa maladie.
5. Une fois votre traitement terminé, rapportez à votre pharmacien toutes les boîtes entamées pour une destruction correcte et appropriée de ce médicament.

FARMACEUTICA INTERNAZIONALE ITALIANA S.r.l.
Partita I.V.A. 02130320035
Corso Marconi, 26 – 28883 GRAVELLONA TOCE
Tel.0323/86.55.57 - 84.08.05 - Fax 0323/84.52.67 cell.339/13.67.875
e-mail: info@finternazionale.it

Oggetto : OFFERTA ECONOMICA

Alla c.a. Dr.ssa Barbara Busà

Gravellona Toce 3 settembre 2020 Riferimento Cliente Num. 765 A.R.N.A.S. GARIBALDI

Pos.	Nome commerciale	Principio attivo	LOTTO COD C.I.G.	Confezionamento e dosaggio	Ditta produttrice titolare AIC	Paese di origine	Quantità prevista per unità	Prezzo a Voi riservato per cpr. o f.la	Prezzo a Voi riservato per Confezione	Note
1 A	Lamprene	Clofazimina		100 Cpr. 50 mg.	Novartis	Francia/Svizzera		1,0250	102,50	MINIMO D'ORDINE N. 10 CONFEZIONI - SPESE DI TRASPORTO GRATUITE - SCADENZA 02/2023 - TEMPI DI CONSEGNA 8 GIORNI LAVORATIVI CIRCA DALLA DATA DI RICEZIONE DELL'ORDINE
1 B	Lamprene	Clofazimina		100 Cpr. 50 mg.	Novartis	Francia/Svizzera		1,0250	102,50	MINIMO D'ORDINE N. 6 CONFEZIONI - SPESE DI TRASPORTO € 70,00 - SCADENZA 02/2023 - TEMPI DI CONSEGNA 8 GIORNI LAVORATIVI CIRCA DALLA DATA DI RICEZIONE DELL'ORDINE

Spese di imballaggio e trasporto: VEDI NOTE
Spese di sdoganamento: GRATUITE
I.V.A : 10%

I prezzi rimarranno invariati salvo aumenti particolarmente significativi disposti dalla casa madre.

A disposizione per qualsiasi chiarimento in merito, l'occasione ci è gradita per inviarVi i ns. migliori saluti.

Pagamento entro 90 gg. Dalla data emissione Fattura

FARMACEUTICA INTERNAZIONALE ITALIANA S.r.l.
UFFICIO OFFERTE
Daniela Ferroni

Olga Marletta <omarletta@arnasgaribaldi.it>

Richiesta offerta Clofazimina 50mg cpr

6 messaggi

barbara.busa@libero.it <barbara.busa@libero.it> 3 settembre 2020 11:17
Rispondi a: barbara.busa@libero.it
A: "flavio.sestili" <flavio.sestili@profarmaitalia.com>, info <info@profarmaitalia.com>
Cc: omarletta <omarletta@arnasgaribaldi.it>

Si chiede vostra migliore offerta del farmaco in oggetto , si richiedono n. 600 cpr , si prega di dare cortese riscontro entro il lunedì 7 settembre 2000

Dottssa Barbara Busà
Dirigente Farmacista
ARNAS Garibaldi Catania

Inviato da Libero Mail per iOS

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barbara.busa@libero.it <barbara.busa@libero.it> 3 settembre 2020 11:18
Rispondi a: barbara.busa@libero.it
A: Mariangela Li Greci <ligreci@unipharma.ch>, Maria Ilenia Saporito <saporito@unipharma.ch>
Cc: omarletta <omarletta@arnasgaribaldi.it>

[Testo tra virgolette nascosto]

---

barbara.busa@libero.it <barbara.busa@libero.it> 3 settembre 2020 11:20
Rispondi a: barbara.busa@libero.it
A: "Farmaceutica Internaz. Italiana" <ufficio.ordini@finternazionale.it>, omarletta <omarletta@arnasgaribaldi.it>

Si chiede vostra migliore offerta del farmaco in oggetto , si richiedono n. 600 cpr , si prega di dare cortese riscontro entro il lunedì 7 settembre 2020

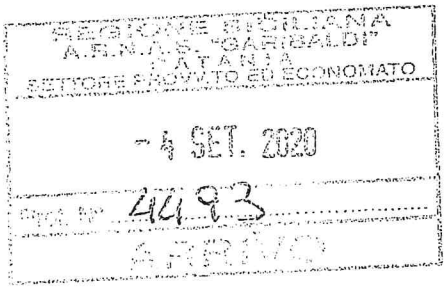
Dottssa Barbara Busà
Dirigente Farmacista
ARNAS Garibaldi Catania
[Testo tra virgolette nascosto]

---

barbara.busa@libero.it <barbara.busa@libero.it> 3 settembre 2020 11:21
Rispondi a: barbara.busa@libero.it
A: Ordini Ottopharma <ordini@ottopharma.com>, info <info@ottopharma.com>, Sales Ottopharma <sales@ottopharma.com>
Cc: omarletta <omarletta@arnasgaribaldi.it>

[Testo tra virgolette nascosto]

Info Ottopharma <info@ottopharma.com> 3 settembre 2020 14:10
A: "barbara.busa@libero.it" <barbara.busa@libero.it>
Cc: omarletta <omarletta@arnasgaribaldi.it>



Buongiorno,

In allegato nostra migliore offerta e scheda tecnica.

Si allega modulo di importazione necessario da allegare all'ordine.

Cordiali Saluti,

Marco.

OTTOPHARMA S.r.l.
Via Novara, 38 - 28021 Borgomanero (NO) | P.IVA - C.F. 02457060032
Tel.+39 0322 255639 | **Tel.** +39 393 8030590 | **Fax** 0322- 060732 | **Mail** info@ottopharma.com | **Web** www.ottopharma.com

Da: barbara.busa@libero.it <barbara.busa@libero.it>
Inviato: giovedì 3 settembre 2020 11:22
A: Ordini Ottopharma <ordini@OTTOPHARMA.COM>; Info Ottopharma <info@OTTOPHARMA.COM>; Sales Ottopharma <sales@OTTOPHARMA.COM>
Cc: omarletta <omarletta@arnasgaribaldi.it>
Oggetto: Richiesta offerta Clofazimina 50 mg cpr

[Testo tra virgolette nascosto]

3 allegati

2209.pdf
201K

MODULO IMPORTAZIONE D.M. 11.02.1997.pdf
227K

Lamprene 50mg o 100mg CPS Novartis Svizzera.pdf
219K

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barbara.busa@libero.it <barbara.busa@libero.it> 3 settembre 2020 15:21
Rispondi a: barbara.busa@libero.it
A: omarletta <omarletta@arnasgaribaldi.it>

Dottssa Barbara Busà
Dirigente Farmacista
ARNAS Garibaldi Catania

Inviato da Libero Mail per iOS

——— Messaggio inoltrato ———
Da: manuel.monopoli@profarmaitalia.com <manuel.monopoli@profarmaitalia.com>
A: <barbara.busa@libero.it>
Data: giovedì 3 settembre 2020, 11:57 +0200
Oggetto: Re:Richiesta offerta Clofazimina 50mg cpr

Buongiorno.
Purtroppo al momento non abbiamo la disponibilità del prodotto.

Saluti
Manuel Monopoli

ProFarma Italia
PROFARMA Italia
Divisione Vendite
manuel.monopoli@profarmaitalia.com
mob. +39 366 4049597

Da : barbara.busa@libero.it
A : "flavio.sestili" flavio.sestili@profarmaitalia.com,"info" info@profarmaitalia.com
Cc : "omarletta" omarletta@arnasgaribaldi.it
Data : Thu, 03 Sep 2020 12:17:38 +0300
Oggetto : Richiesta offerta Clofazimina 50mg cpr

Si chiede vostra migliore offerta del farmaco in oggetto , si richiedono n. 600 cpr , si prega di dare cortese riscontro entro il lunedì 7 settembre 2000
[Testo tra virgolette nascosto]

OttoPharma

CERTIFIED SYSTEM IQS ISO 9001

CERTIFIED SYSTEM IQS

AZIENDA CERTIFICATA
BUONE PRATICHE DI DISTRIBUZIONE MEDICINALI (BDP)
CERTIFIED COMPANY
GOOD DISTRIBUTION PRATICES MEDICINAL PRODUCTS (GDP)

Spett.le

ARNAS GARIBALDI

PIAZZA SANTA MARIA
DI GESU' 5
95124 CATANIA CT

PROPOSTA DI FORNITURA

N°	Data	Pagina	Cliente
2209	**03/09/20**	**1**	**71**

Spedizione	Porto
A MEZZO CORRIERE	**FRANCO**

Cod. Pag.	Modalità Pagamento	Consegna
1	**60 GG BONIFICO D.F.**	

Codice Articolo	Descrizione Articolo	UM	Quantità	Prezzo Unitario	Prz.Confezione
FAR0512	LAMPRENE 50MG 100CPR	CF	1	1,32	132,00
	(CLOFAZIMINA)				
	SPESE TRASPORTO				15,00
	PRODUTTORE:NOVARTIS				
	PROVENIENZA:SVIZZERA				
	CONSEGNA: 7-10 GG LAVORATIVI				
	Tutti i prezzi sono da				
	intendersi I.V.A. 10% esclusa				
	Spese di importazione:				
	GRATUITE				
	>> LA PRESENTE OFFERTA SI				
	INTENDE VALIDA FINO AL				
	31/12/2020 <<				
	**Salvo aumenti disposti dalla				
	Ditta produttrice				

GLI ORDINI ANDRANNO INOLTRATI A: E-MAIL: ordini@ottopharma.com in alternativa FAX: 0322-060732

OTTOPHARMA S.r.l.
Sede Operativa: Via Italia, 14 – 28045 Invorio (NO) Tel: 0322/255639 Fax: 0322/060732 - P.IVA - C.F. 02457060032
| www.ottopharma.com | info@ottopharma.com

Allegato
AL MINISTERO DELLA SALUTE
USMAF-SASN LOMBARDIA, PIEMONTE E VALLE D'AOSTA
UNITA' TERRITORIALE TORINO CASELLE

Richiesta di importazione di medicinali ai sensi del D.M. 11/02/1997.

Il sottoscritto Dr. .....
Residente in..... via .....
tel.....iscritto nell'Albo dell'Ordine dei Medici-Chirurghi di ..... al n..... cod. regionale.....
..... chiede di importare il medicinale (contenente il seguente/i principio/i attivo/i):.....
nome commerciale: .....
forma farmaceutica .....
nella quantità di numero ..... confezioni contenenti .....
di farmaco cadauna. prodotto dalla ditta: ..... (specificare il nome dell'azienda)
Precisa che tale medicinale è regolarmente registrato nel Paese di provenienza: .....
per il trattamento di .....
Tale medicinale è indispensabile per la cura del Sig. (iniziali o codice) .....
affetto da: .....
Motivo per cui viene richiesta la scorta di reparto****.....

Dichiara altresì che il farmaco:

- non ha valida alternativa terapeutica con altri medicinali registrati in Italia;
- non contiene sostanze stupefacenti o psicotrope;
- non è un emoderivato;
- verrà impiegato sotto la propria diretta responsabilità, dopo aver ottenuto il consenso informato scritto del paziente;
- che le generalità del paziente ed i documenti relativi al consenso informato sono custoditi presso il medico curante per la durata prevista dalla normativa vigente.

Particolari condizioni di conservazione del medicinale:
Temperatura (es. -20°C, da 2 a 8°C, < 25°, <30°, nessuna indicazione): .....
Altro: .....

Luogo e data _____

_____
Timbro e firma leggibile del medico

_____
Timbro e firma leggibile del Servizio Farmaceutico

****Da compilare solo in caso di scorta reparto

NOVARTIS

Drug Regulatory Affairs

LAMPRENE®

(clofazimine)

50 or 100 mg capsules, soft

International Package Leaflet

Lamprene®

Clofazimine

COMPOSITION AND PHARMACEUTICAL FORM

Each soft capsule contains 50 or 100 mg of micronized clofazimine suspended in an oil-wax base.

For excipients, see section EXCIPIENTS.

Certain dosage strengths may not be available in all countries.

INDICATIONS

Lamprene, employed in combination with Rimactane® (rifampicin) and dapsone, serves as treatment for multibacillary (MB) forms of leprosy, with positive skin smear (lepromatous (LL), borderline lepromatous (BL), mid-borderline (BB) leprosy) or all cases clinically diagnosed as multibacillary with more than 5 skin lesions, as well as erythema nodosum leprosum (ENL).

Multidrug therapy (MDT) is necessary in order to prevent the emergence of resistant strains of Mycobacterium leprae. Note that MDT calendar blister packs and bulk Lamprene capsules for management of ENL reactions can be obtained free of charge from the WHO.

DOSAGE AND ADMINISTRATION

For the treatment of leprosy the WHO recommends the following regimens:

Multibacillary leprosy (LL, BL, BB)

	Dapsone	Rifampicin (Rimactan)	Clofazimine (Lamprene)
Adults and adolescents (50-70 kg)	100 mg daily	600 mg once a month under supervision	50 mg daily AND 300 mg once a month under supervision
Children (10-14 years)	50 mg daily	450 mg once a month under supervision	50 mg on alternate days AND 150 mg once a month under supervision

Children <10 years: The dose should be adjusted appropriately, for example, Lamprene 100 mg once a month under supervision + 50 mg twice a week as self-medication + Rimactane® (rifampicin) 300 mg once a month under supervision + dapsone 25 mg once a day as self-medication.

This triple combination should be given for 12 months.

Erythema nodosum leprosum (ENL)

Adults and children: If the patient develops ENL, the treatment with rifampicin and dapsone should be continued as before, and the dosage of Lamprene raised to 200-300 mg daily, given under medical supervision. These high daily doses must not be given for longer than 3 months.

Method of Administration

To ensure maximum absorption Lamprene should be taken with meals or with milk.

CONTRAINDICATIONS

Known hypersensitivity to clofazimine or to any of the excipients of Lamprene.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Lamprene should never be used alone for the treatment of leprosy. Multidrug therapy is necessary to prevent the emergence of drug resistance.

Warnings

After prolonged administration in high doses, clofazimine may accumulate in tissue, e.g. the wall of the small bowel, and precipitate. Enteropathy may develop if crystals are deposited in the lamina propria of the jejunal mucosa and the mesenteric lymph nodes, sometimes leading to intestinal obstruction. If gastrointestinal symptoms develop during treatment, the dosage should be reduced or the interval between doses prolonged. Symptoms may slowly regress on withdrawal of the drug.

In the event of persistent diarrhoea or vomiting, the patient should be hospitalised.

Precautions

Leprosy patients suffering repeatedly from abdominal pains and diarrhoea, as well as those with liver or kidney damage, should if possible not be treated with Lamprene. If treatment is necessary, these patients should be kept under medical supervision.

Daily doses of >100 mg Lamprene should be given for as short a time as possible (<3 months) and only under close medical supervision.

Physicians should be aware that skin discoloration due to Lamprene may result in depression (two cases of depression with suicide have been reported). Patients should be warned that Lamprene may cause discoloration of the conjunctiva, lacrimal fluid, sweat, sputum, urine, faeces, nasal secretions, semen, breast milk and reddish to brownish-black discoloration of the skin. Patients should be told that discoloration of the skin, although reversible, may take several months or years to disappear after the end of therapy with Lamprene.

INTERACTIONS

Dapsone

Lamprene seems to have no important effects on the pharmacokinetics of dapsone, although a transient increase in the urinary excretion of dapsone occurred in a few patients. Preliminary data suggesting that dapsone inhibits the anti-inflammatory activity of Lamprene have not been confirmed. If leprosy-associated inflammatory reactions develop in patients being treated with dapsone and Lamprene, it is still advisable to continue treatment with both drugs.

Rifampicin

Clofazimine reduces rifampicin absorption in leprosy patients, increasing the time it takes for peak serum concentration to be reached and prolonging the elimination half-life. Bioavailability was not affected, so this interaction is unlikely to be clinically significant.

Isoniazid

In patients receiving high doses of clofazimine (300 mg daily) and isoniazid (300 mg daily), elevated concentrations of clofazimine were detected in plasma and urine, although skin concentrations were found to be lower.

PREGNANCY AND LACTATION

Pregnancy

No mutagenic activity was detected in the Ames test and in cytogenic tests in patients treated with Lamprene. No teratogenic effect was observed in rabbits or rats given clofazimine doses 8 and 25 times the usual human dose, respectively. However, with doses 12 to 25 times those given to humans, retardation of fetal skull ossification and fetotoxicity were observed in mice.

Experience with Lamprene in pregnancy is limited. Clofazimine crosses the placenta, and skin discoloration in neonates has been observed. Lamprene should be used during pregnancy only if the potential benefit justifies the risk to the fetus. Since leprosy is exacerbated during pregnancy, the WHO recommends that treatment with Lamprene should be continued during pregnancy.

Lactation

Clofazimine passes into the breast milk, and skin discoloration may occur in the infant. Lamprene should be administered to a breast-feeding woman only if clearly indicated.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Dizziness, decreased visual acuity, fatigue and headache have been reported under Lamprene therapy. Patients experiencing such adverse reactions should not drive a vehicle or operate machines.

UNDESIRABLE EFFECTS

Adverse reactions (Table 1) are ranked in descending order of frequency, as follow: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000) very rare (< 1/10,000), including isolated reports.

Table 1

Blood and lymphatic system disorders	
Very rare:	Lymphadenopathy, splenic infarction, anaemia
Psychiatric disorders	
Very rare:	Depression
Nervous system disorders	
Uncommon:	Headache
Very rare:	Dizziness
Eye disorders	
Very common:	Conjunctival discolouration, corneal pigmentation, tear discolouration
Common:	visual acuity decreased, dry eyes, eye irritation
Uncommon:	Maculopathy, corneal deposits
Respiratory, thoracic and mediastinal disorders	
Very common:	Sputum discoloured
Gastrointestinal disorders	
Very common:	Nausea, vomiting, abdominal pain, diarrhoea, faeces discoloured
Uncommon	Gastroenteritis eosinophilic, anorexia
Very rare:	Intestinal obstruction, gastrointestinal haemorrhage, abdominal discomfort, abdominal pain upper, constipation
Hepatobiliary disorders	
Very rare	Hepatitis, blood bilirubin increased, jaundice, aspartate aminotransferase increased
Skin and subcutaneous tissue disorders	
Very common:	Sweat discolouration, skin discolouration, hair colour changes, ichthyosis, dry skin
Common:	Rash, pruritus
Uncommon:	Photosensitivity reaction, dermatitis acneiform
Very rare:	Dermatitis exfoliative
Renal and urinary disorders	
Very common:	Chromaturia
General disorders and administration site conditions	
Uncommon:	Fatigue
Very rare:	Pyrexia
Investigations	
Common:	Weight decreased
Uncommon:	Blood sugar increased

Note: Depression was reported to be due to skin discolouration and two suicides were reported. Reddish to brownish-black discoloration of the skin and leprous lesions, particularly in fair-skinned patients at sites exposed to light, and discoloration of the hair are reversible, although in the case of the skin it may take several months to disappear after the end of treatment. The corneal pigmentation (subepithelial corneal brownish pigmented lines) is due to crystal deposits. It is reversible on discontinuation of Lamprene.

OVERDOSE

No specific data are available on the treatment of overdose with Lamprene. In cases of acute overdose the stomach should be emptied by inducing vomiting or performing gastric lavage, and symptomatic treatment should be given as required.

PHARMACODYNAMICS

Clofazimine exerts in man a bacteriostatic and weakly bactericidal effect on *Mycobacterium leprae* (M. leprae, Hansen's bacillus). Its precise mechanism of action against mycobacteria remains to be elucidated. Clofazimine appears to bind preferentially to mycobacterial DNA and inhibit mycobacterial replication and growth.

No cross-resistance occurs with dapsone and rifampicin, probably because clofazimine has a different mode of action. *M. leprae* resistant to clofazimine have been reported only in isolated cases.

The minimum inhibitory concentration of clofazimine for *M. leprae* in mouse tissue has been estimated at between 0.1 and 1 microgram per gram; uneven tissue distribution precludes a more accurate estimate. In patients with lepromatous leprosy, the overall antibacterial effect of Lamprene is comparable to that of dapsone. However, the onset of antimicrobial activity of Lamprene is slow and can only be demonstrated after about 50 days of therapy.

Clofazimine also displays an anti-inflammatory effect, which may contribute to the efficacy of Lamprene in controlling ENL reactions.

PHARMACOKINETICS

Absorption

Clofazimine is absorbed relatively slowly. Bioavailability of clofazimine from the micronised suspension in an oil-wax base is up to 70% after a dose of 100 mg, and decreases with higher doses. Peak plasma concentrations of the unchanged active substance are reached 8 to 12 hours after a single oral dose. Administering the drug with food increases bioavailability in terms of AUC (area under the concentration-time curve) by about 60% and tends to accelerate the absorption rate. After administration of a single oral dose of 200 mg clofazimine with breakfast, mean (±SD) peak plasma concentrations of 861 (±289) pmol/g were measured in healthy volunteers. When clofazimine is taken on an empty stomach, the peak plasma concentration was approximately 20% lower.

After repeated administration of clofazimine to leprosy patients in daily doses of 50 mg and 100 mg, mean morning trough concentrations of 580 pmol/g and 910 pmol/g, respectively, were measured after 42 consecutive days. Steady-state concentrations were not reached within this time period.

Distribution

Clofazimine is strongly lipophilic and accumulates mainly in fatty tissue and in macrophages of the reticuloendothelial system. After long-term treatment, clofazimine has been detected in the following organs and tissues and body fluids: subcutaneous fat, mesenteric lymph nodes, bile and gall bladder, adrenals, spleen, small intestine, liver, muscle tissue, bones, and skin, but never in the brain. Clofazimine does not appear to cross the intact blood-brain barrier.

Clofazimine crosses the placenta and passes into the breast milk in sufficient quantities to colour the milk.

Biotransformation

Information on the metabolism of clofazimine is limited. Three metabolites, two glucuronides, have been identified in urine.

Elimination

Clofazimine is eliminated slowly from the plasma. The mean elimination half-life of the unchanged substance following a single dose of 200 mg in healthy volunteers was 10.6 (±4.0) days. After repeated administration of 50 mg and 100 mg daily to leprosy patients, the elimination half-life was about 25 days.

Unchanged clofazimine is excreted via the bile mainly in the faeces. Within 3 days on average, 35% of the dose is recovered. No more than 0.4% of the dose is found in the urine as unchanged clofazimine after 24 hours. The urinary metabolites account for about 0.6% of the daily dose.

Characteristics in patients

No data is available on the effects of renal or hepatic dysfunction, or of age on the pharmacokinetics of clofazimine.

PRECLINICAL SAFETY DATA

Long-term carcinogenicity studies in animals have not been conducted with clofazimine. No mutagenic activity was detected in the Ames test. No primary teratogenic effect was observed in the offspring of rats and rabbits treated during pregnancy with clofazimine in doses of up to 50 mg/kg/day and 15 mg/kg/day, respectively. However, there was evidence of fetotoxicity in mice at doses of 50 mg/kg/day, and fetal skull ossification was somewhat delayed.

EXCIPIENTS

Butylated hydroxytoluene (E 321); sodium salt of ethyl hydroxybenzoate (E215); sodium salt of propyl hydroxybenzoate (E 217); p-methoxy acetophenone; propylene glycol; rapeseed oil; soybean lecithin; hydrogenated soybean oil; partially hydrogenated vegetable oils; beeswax; gelatin; glycerol 85%; citric acid anhydrous; ethylvanillin; black iron oxide, red iron oxide (E172).

INCOMPATIBILITIES

None known.

STORAGE

Protect from moisture, store below 25°C.

Lamprene should not be used after the date marked "EXP" on the pack.

INSTRUCTIONS FOR USE AND HANDLING

Note: Lamprene should be kept out of the reach and sight of children.

Manufacturer:

See folding box.

International Package Leaflet

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Novartis Pharma AG, Basel, Switzerland