WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

[*]https://extranet.who.int/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

1. NAME OF THE MEDICINAL PRODUCT

[TB364 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 100 mg clofazimine.

Excipients with potential clinical effect

Each capsule contains about 20 mg of soybean oil, 48 mg glycerin, 0.0073 mg methylparaben and 0.0041 mg propylparaben.

3. PHARMACEUTICAL FORM

Soft capsules.

[TB364 trade name] is a brown opaque, oval soft capsule, the capsules are plain and have no markings. They are filled with brick red to brown suspension. Note. The capsules are to be swallowed whole, see section 4.2 How to take [TB364 trade name].

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[TB364 trade name] is indicated in combination with other tuberculosis medicines for the treatment of drug-resistant tuberculosis due to *Mycobacterium tuberculosis*.

Treatment regimens should follow the most recent WHO treatment guidelines, supplemented by other authoritative guidelines.

4.2 Posology and method of administration

Posology

Adults and adolescents weighing at least 46 kg

The usual dose is 1 capsule (100 mg) once daily.

Children and adolescents weighing less than 46 kg

The usual dose in children is 2–5 mg/kg daily, up to a maximum dose of 100 mg daily.

[TB364 trade name] is not suitable for infants weighing less than 5 kg and a formulation with a lower amount of clofazimine should be chosen. For children weighing 5 kg to less than 24 kg, [TB364 trade name] may be given **2–3 times a week** (see table below) but use of a formulation containing a lower amount of clofazimine is preferred.

Child's weight	**Number of capsules**
5 to less than 10 kg*	1 capsule on **2 days each week** (for example on Mondays and Fridays)
10 to less than 24 kg	1 capsule on **3 days each week** (for example on Mondays, Wednesdays and Fridays)
24 to less than 46 kg	1 capsule once daily
* For infants weighing less than 10 kg, it is recommended that an expert in paediatric drug-resistant TB be consulted.	

† Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

Special populations

Patients with renal impairment

No dose adjustment is required in patients with renal impairment.

Patients with hepatic impairment

[TB364 trade name] should be used with caution in patients with severe hepatic impairment, and the dose may need to be adjusted (see section 4.4).

Method of administration

[TB364 trade name] should be taken with food, because food increases the absorption (see section 5.2). The capsules should be swallowed whole with water.

Missed dose and vomiting after a dose

It is important that the patient takes the medicine regularly as prescribed. Missing doses can increase the risk of resistance to [TB364 trade name] and reduce its effectiveness.

If the patient vomits within 1 hour of taking [TB364 trade name], the patient should take an extra dose. If vomiting occurs more than an hour after taking the dose, the patient does not need to take an extra dose and can take the next dose as usual when it is due.

Treatment interruption to manage side effects

If, because of side effects, the 6-month or modified 9-month regimen comprising [TB364 trade name] is interrupted for more than 7 consecutive or for non-consecutive days up to a total of 4 weeks, the treatment duration should be extended to make up for the missed doses. If the interruption is longer, appropriateness of the treatment should be re-evaluated.

4.3 Contraindications

Hypersensitivity to clofazimine or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Abdominal obstruction and other gastrointestinal reactions

Clofazimine may accumulate in various organs as crystals, including the mesenteric lymph nodes and histiocytes at the lamina propria of the intestinal mucosa, spleen and liver. Deposition in the intestinal mucosa may lead to intestinal obstruction. Splenic infarction, gastrointestinal bleeding, and death have been reported. If a patient complains of pain in the abdomen, nausea, vomiting, or diarrhoea, initiate appropriate medical investigations and consider discontinuing the drug.

QT interval prolongation

Using clofazimine with drugs that prolong the QT interval may cause additive QT prolongation and lead to torsade de pointes:

- anti-TB drugs: fluoroquinolones, bedaquiline and delamanid; and
- ancillary and common drugs: azole antifungals, macrolides, metoclopramide, efavirenz, furosemide, hydrochlorothiazide, citalopram, escitalopram, methadone, antiarrhythmics

Whenever possible, an ECG should be obtained before starting treatment, and, if needed, during treatment. Serum potassium, calcium, and magnesium should be measured at the start of treatment and corrected if abnormal. Electrolytes should be monitored if the QT interval is prolonged.

The following may increase the risk for QT prolongation:

- history of torsade de pointes,
- personal or family history of congenital long QT syndrome,
- history of or ongoing hypothyroidism,

- ongoing bradyarrhythmia,
- heart failure or structural heart disease,
- QT-interval as corrected by the Fridericia method (QTcF) greater than 450 ms (confirmed by repeat electrocardiogram),
- serum calcium, magnesium, or potassium levels below the lower limits of normal.

The use of the combination of moxifloxacin with bedaquiline and clofazimine (three drugs that strongly prolong the QT interval) in the tuberculosis treatment-regimen should be avoided.

Concomitant use with medicines, other than those in the treatment regimen, that may prolong the QT interval should be avoided if possible during treatment.

[TB364 trade name] and all other QT-prolonging medicines in the regimen should be discontinued if clinically significant ventricular arrhythmia is noted or if the QTcF interval is 500 ms or greater. For children weighing less than 20 kg, consider reducing the dose of clofazimine. If syncope occurs, an ECG should be obtained to check for QT interval prolongation.

Skin and body fluid discoloration and other skin reactions

Clofazimine causes orange-pink to brown-black discoloration of the skin, as well as discoloration of the conjunctivae, tears, sweat, sputum, urine and faeces. Advise patients that skin discoloration is likely and it may take several months or years to reverse after treatment ends. Advise patients to avoid the sun and to use strong sunscreens.

Other skin reactions associated with clofazimine therapy include ichthyosis, dry skin and pruritus.

Psychological effects of skin discoloration

Skin discoloration due to clofazimine therapy has been reported to result in depression and suicide. Monitor patients for depression or suicidal ideation during [TB364 trade name] therapy.

Liver function

Clofazimine is partially metabolised by the liver. [TB364 trade name] should be used with caution in patients with hepatic impairment. Serum liver enzymes (ALT, ALP, AST, GGT) should be monitored throughout treatment. Patients should also be monitored for symptoms and signs of hepatotoxicity (such as fatigue, anorexia, nausea, jaundice, dark urine, liver tenderness and hepatomegaly) during treatment.

Excipients

[TB364 trade name] contains soybean oil. People allergic to peanut or soya should not use this medicinal product.

[TB364 trade name] also contains glycerin, which may cause headache, stomach upset and diarrhea.

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

4.5 Interaction with other medicinal products and other forms of interaction

QT prolongation and torsade de pointes have been reported in patients receiving clofazimine together with other medicines that prolong the QT interval; see section 4.4 (QT interval prolongation). Concomitant use with medicines, other than those in the treatment regimen, that may prolong the QT interval should be avoided if possible during treatment.

Effects of clofazimine on other medicines

Clofazimine inhibits CYP3A4/5 in laboratory tests. Concomitant use of [TB364 trade name] with medicines that are substrates of CYP3A4/5 may raise blood concentrations of these medicines and increase the risk of adverse effects. Monitor for adverse effects of these medicines when used concomitantly with [TB364 trade name].

4.6 Fertility, pregnancy and breastfeeding

Women of childbearing potential

Pregnancy should be avoided in women treated with clofazimine. Adequate contraceptive measures should be taken during treatment and for at least 4 months after stopping treatment with [TB364 trade name].

Pregnancy

[TB364 trade name] can be used during pregnancy after fully considering the woman's individual circumstances. Although information is limited, successful pregnancy outcomes have been recorded after the use of clofazimine as part of a combination regimen for treating drug-resistant tuberculosis.

The skin of infants born to pregnant mothers who had received clofazimine during pregnancy is pigmented at birth. Limited data is available regarding the reversibility of discoloration. Based on previous observations, discoloration gradually faded over the first year.

Studies in animals have shown reproductive toxicity (see section 5.3).

Tuberculosis can be particularly dangerous in pregnancy and should be managed with effective treatment. The decision on treatment during pregnancy should take into account the grave danger of tuberculosis to the patient and the fetus as well as the possibility of harm to the fetus. Close monitoring during and after pregnancy is important to ensure that any concerns are dealt with promptly

Breast-feeding

Clofazimine passes into breast milk, giving it a pink colour. Clofazimine might increase skin pigmentation in nursing infants.

Breast-feeding infants may be at slight risk of adverse effects of clofazimine but there is insufficient information on the nature and frequency of such effects in the infant.

A decision must be made whether to discontinue breast-feeding or to discontinue or interrupt [TB364 trade name] therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effects [TB364 trade name] on human male or female fertility.

Animal studies indicate effects of clofazimine on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Vision problems, dizziness, and fatigue have been reported during treatment with clofazimine. Patients should be instructed that if they experience these symptoms they should avoid potentially hazardous tasks such as driving and operating machinery.

4.8 Undesirable effects

Tabulated list of adverse reactions

The following undesirable effects have been recorded mainly with the use of clofazimine in the treatment of leprosy. Reliable information on frequency of undesirable effects in the treatment of tuberculosis is not available.

The following reactions are common:

Eye disorders

burning, conjunctival and corneal pigmentation due to clofazimine crystal deposits, diminished vision, dryness, irritation, itching

Cardiac disorders

QT prolongation

Gastrointestinal disorders

abdominal and epigastric pain, diarrhoea, gastrointestinal intolerance, nausea, vomiting

Skin and subcutaneous tissue disorders

ichthyosis and dryness, orange, pink to brown-black discoloration of the skin (75 to 100% of the patients) within a few weeks of treatment, rash and pruritus

Other

discoloration of urine, faeces, sputum, sweat; elevated blood sugar, elevated erythrocyte sedimentation rate (ESR)

The following reactions are less frequent:

Eye disorders

maculopathy (bull's eye retinopathy)

Gastrointestinal disorders

anorexia, weight loss, enlarged liver, hepatitis, jaundice, bowel obstruction, constipation, eosinophilic enteritis, gastrointestinal bleeding

Nervous system disorders

dizziness, drowsiness, fatigue, giddiness, headache, neuralgia, taste disorder

Psychiatric disorders

depression and suicide secondary to skin discoloration

Skin and subcutaneous tissue disorders

acneiform eruptions, erythroderma, phototoxicity, monilial cheilosis

Investigations

chemistry	elevated levels of albumin, serum bilirubin, and aspartate aminotransferase (AST), hypokalaemia
haematology	eosinophilia

Other

anaemia, bone pain, cystitis, oedema, fever, lymphadenopathy, splenic infarction, thromboembolism, vascular pain

Reporting of suspected adverse reactions

Health care providers are asked to report adverse reactions that may be linked to a medicine, to the marketing authorisation holder, or, if available, to the national reporting system. Reports of suspected adverse reactions to a medicine are important for the monitoring of the medicine's benefits and risks.

4.9 Overdose

No specific data are available on the treatment of overdosage with clofazimine. In case of overdose, supportive symptomatic treatment should be initiated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimycobacterials, ATC Code J04BA01

Clofazimine is an antimycobacterial drug.

Mechanism of action
Clofazimine may interfere with the proton-motive force and bacterial ATP production by membrane interaction with the respiratory chain or phospholipids. The delayed activity might therefore be due to the need to saturate the lipid-rich bacterial membrane, the time needed to disrupt the proton-motive force and/or the need to deplete energy stores before antimicrobial activity is observed.

Mechanisms of resistance
There is no cross-resistance with rifampicin or dapsone.

5.2 Pharmacokinetic properties

The absorption characteristics of [TB364 trade name] have been determined after administration of single capsules (100 mg clofazimine) in healthy volunteers in the fed state as follows:

Pharmacokinetic variable	**Mean value* (± standard deviation)**
Maximum concentration (C_{max})	162 ± 88 ng/mL
Area under the curve (AUC_{0-72h}), a measure of the extent of absorption	3227 ± 1263 ng·h/mL
Time to attain maximum concentration (t_{max})	6.15 ± 2.56 h

* Arithmetic mean

Pharmacokinetics of Clofazimine

The pharmacokinetics of [TB364 trade name] have not been studied in patients with tuberculosis. Data in the table below are based on the use of clofazimine in patients with leprosy. Clofazimine pharmacokinetic parameters in patients with tuberculosis may differ from those in leprosy patients.

General	
	Average serum concentration of clofazimine in leprosy patients treated with 100 mg daily was 0.7 µg/mL.
Absorption	
Absorption	Clofazimine absorption ranges from 45 to 62% in leprosy patients
Oral bioavailability	Information not available
Food effect	Median T_{max} of clofazimine decreases from 12 hours to 8 hours under fed conditions relative to the fasted state.
Distribution	
Volume of distribution (mean)	Information not available
Plasma protein binding *in vitro*	Clofazimine is bound to alpha- and primarily to beta-lipoproteins in serum, and the binding was saturable at plasma concentrations of approximately 10 µg/mL. Binding to gamma-globulin and albumin was negligible.
Tissue distribution	Clofazimine is lipophilic and deposits predominantly in fatty tissue and in cells of the reticuloendothelial system. It is taken up by macrophages throughout the body and clofazimine crystals have predominantly been

	found in the mesenteric lymph nodes, adrenals, subcutaneous fat, liver, bile, gall bladder, spleen, small intestine, muscles, bones, and skin. In clinical studies, clofazimine had good penetration in tissue but not in cavities. Target tissue concentrations may be much higher than can be inferred from plasma measurements (except for caseating tissue in a cavity).
Metabolism	
	Limited information. Three clofazimine metabolites were found in urine following repeated oral doses of clofazimine.
Elimination	
Elimination half life	25 days (range 6.5 to 160 days) following repeated oral doses of 50 or 100 mg clofazimine in leprosy patients.
Excretion	After a single dose of 300 mg clofazimine, elimination of unchanged clofazimine and its metabolites was negligible in a 24-hour urine collection. Part of the ingested drug recovered from the faeces may represent excretion via bile. A small amount is also eliminated in the sputum, sebum, and sweat.
Drug interactions *(in vitro*)	Clofazimine inhibits the metabolism of CYP2C8, CYP2D6, CYP3A4/5 drug substrates.

No information on the pharmacokinetics of clofazimine in paediatric patients is available.

5.3 Preclinical safety data

Genotoxicity
In mutagenicity studies clofazimine was found negative in an Ames test. There is some evidence of clastogenic potential in mice.

Carcinogenicity
Long-term carcinogenicity studies in animals have not been conducted with clofazimine.

Toxicity to reproduction
Impaired female fertility (reduced number of offspring and lower proportion of implantations) was observed in one study in rats receiving clofazimine (from 9 weeks before mating until weaning) at 50 mg/kg/day. No non-clinical data on male fertility are available.

In a rat study using 25 times the usual human dose of clofazimine, there was a reduction in the number of offspring and fewer implantations. Clofazimine was not teratogenic in rats and mice at 50 mg/kg/day or in rabbits at 15 mg/kg/day. Nursing mice developed an increase in bone marrow chromosome abnormalities attributed to clofazimine in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule fill:

Soybean oil
Canola oil
Hydrogenated vegetable oil
White beeswax
Lecithin
Butylated hydroxytoluene

Capsule shell:

Gelatin
Glycerin
Ethyl vanillin
Black iron oxide
Red iron oxide
Methylparaben
Propylparaben

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

HDPE bottle

[TB364 trade name] is available in a white HDPE bottle containing 100 capsules. It also contains 1g silica gel stick and closed with white low density polyethylene cap.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. SUPPLIER

Dong-A ST Co. Ltd.

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8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

TB364

9. DATE OF PREQUALIFICATION

26 January 2021

10. DATE OF REVISION OF THE TEXT

March 2026

References

General reference sources for this SmPC include:

WHO consolidated guidelines on tuberculosis. Module 4: treatment and care. Geneva: World Health Organization; 2025. Licence: CC BY-NC-SA 3.0 IGO. Available at: https://tbksp.who.int/en/node/2952 [accessed 22 September 2025]

WHO operational handbook on tuberculosis. Module 4: treatment and care. Geneva: World Health Organization; 2025. Licence: CC BY-NC-SA 3.0 IGO. Available at: https://tbksp.who.int/en/node/3011 [accessed 22 September 2025]

WHO operational handbook on tuberculosis. Module 5: management of tuberculosis in children and adolescents. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0IGO Available at: https://tbksp.who.int/en/node/1981 [accessed 25 November 2025]

FDA label Lamprene: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/019500s014lbl.pdf [accessed 22 September 2025]

Further references relevant to sections of the SmPC include:

Section 4.6 and 5.3

Das RK, Roy B: Evaluation of genotoxicity of clofazimine, an antileprosy drug, in mice in vivo. I. Chromosome analysis in bone marrow and spermatocytes. Mutat Res 241:161-8, 1990.

Stenger et al., cited by Shepard TH: Catalog of teratogenic agents, 7th ed., Baltimore, Johns Hopkins University Press, 1989, p 96.

Venkatesan K, Mathur A, Girdhar A, Girdhar BK: Excretion of clofazimine in human milk in leprosy patients. Lepr Rev 68:242-6, 1997.

Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products