ABSTRACT: This article reviews the chemistry, pharmacology, spectrum of activity, pharmacokinetics, clinical efficacy in leprosy and Mycobacterium avium complex (MAC) infection, adverse effects, drug interactions, and special considerations of clofazimine. The drug is active in vivo against M. leprae and in vitro against MAC. In addition, it possesses anti-inflammatory and immunosuppressive properties. Clinical studies support the efficacy of clofazimine as a part of multidrug therapy in treating leprosy. It also appears to reduce the incidence and severity of erythema nodosum leprosum reactions that often occur during the treatment of leprosy. Efficacy in treating MAC infection in patients with AIDS is not well documented, despite the use of clofazimine in combination with other agents. A few patients have responded symptomatically and by clearing their mycobacteremia, although there is no evidence that mortality is reduced. Clofazimine is well tolerated, at least when doses ≤100 mg/d are used. Adverse reactions include discoloration of the skin, self-limiting gastrointestinal intolerance, severe and life-threatening abdominal pain and organ damage due to clofazimine crystal deposition, and asymptomatic discoloration of the eye. Clofazimine should be considered for formulary inclusion.


CLOFAZIMINE HAS BEEN USED in the treatment of leprosy (Mycobacterium leprae) since 1962. Because of the rarity of this disease in the US, clofazimine was available only as an orphan drug until recently. The current AIDS epidemic has led to the frequent occurrence of opportunistic infections. One of the most commonly encountered pathogens, found in 50 percent or more of AIDS patients at autopsy, is the M. avium complex (MAC). Clofazimine is used, in combination with other agents, in the treatment of MAC in AIDS patients. In this article, current knowledge regarding clofazimine is reviewed.

Chemistry

Clofazimine is a substituted iminophenazine bright red dye. Its chemical name is 3-(p-chloroanilino)-10-(p-chlorophenyl)-2,10-dihydro-2-(isopropylimino)phenazine (Figure 1). Its molecular weight is 473.4. Commercially available capsules of clofazimine contain micronized drug suspended in an oil-wax base. Clofazimine is insoluble in water, sparingly soluble in ethanol, and readily soluble in benzene.

Pharmacology

MECHANISM OF ACTION AND RESISTANCE

The mechanism of action of clofazimine is not fully understood, but appears to involve binding to mycobacterial DNA, primarily at the guanine base. This inhibits template function of the DNA strand, resulting in growth inhibition.

Clofazimine has been noted to possess both anti-inflammatory and immunosuppressive effects. This adds to its utility in treating leprosy by helping to control erythema nodosum leprosum (ENL) reactions, although corticosteroids frequently are required for severe cases (see Clinical Efficacy section). Detrimental effects due to the immunosuppressive properties of clofazimine, if any, in AIDS patients have not been investigated.

Any resistance of M. leprae to clofazimine is difficult to detect, because the bacillus cannot be grown in vitro. Instead, it must be evaluated in vivo using a mouse foot-pad model, in which mice are fed clofazimine 0.001-0.0001% in their diet. Clofazimine resistance has been reported in a single patient, but in vivo studies were unable to differentiate resistance from a normal variant wild strain. Clofazimine-resistant MAC strains have not been reported.

SPECTRUM OF ACTIVITY

Because M. leprae cannot be grown in vitro, susceptibility testing and development of therapeutic alternatives have been hampered. Fortunately, M. leprae may be grown in vivo, and the development of a mouse foot-pad model has shown that clofazimine 0.001-0.0001% in the diet is able to inhibit growth of the organism. Although mycobacterial killing apparently begins immediately, it cannot be detected in the mouse foot-pad model for about 50 days. Determination of the activity of clofazimine is further confounded by the fact that M. leprae is an intracellular organism, and clofazimine is distributed unevenly in the body.

MAC may be grown in vitro, and minimum inhibitory concentrations (MIC) range from 0.1 to 10 μg/mL. The majority of MICs are ≤2 μg/mL. Susceptibility of the isolate varies according to the test media in which it is grown. The lower the pH of the test media, the higher the MIC. These investigators found that the MIC increased from 0.188 to 4.0 μg/mL as the pH of the broth was decreased from 6.8 to 5.0.
Despite low MIC values for clofazimine against MAC, killing curve studies have failed to demonstrate a significant reduction in colony-forming units. This is not surprising since minimum bactericidal concentrations (MBC) have been shown to be 32-fold or greater than the MIC. In some cases, the MIC to MBC ratio has been as high as 1:256. Therefore, tolerance appears to occur with clofazimine.

**Pharmacokinetics**

The pharmacokinetic parameters of clofazimine are summarized in Table 1. Clofazimine is slowly and incompletely absorbed from the gastrointestinal (GI) tract following oral administration. Bioavailability, when administered as a microcrystalline suspension in an oil-wax base (the commercially available preparation), has been reported to average 70 percent. When it first was developed and administered as coarse crystals, bioavailability was only 20 percent. Absorption of clofazimine also has been reported to have an inverse relationship to dose. Mathur et al. found that bioavailability fell from 62.5 percent following 100 mg to 42.6 percent after 600 mg. However, there was little difference between 300, 400, and 600 mg in bioavailability. Following a single dose of 200 mg, the maximum serum concentration (C_{max}) averages 0.47 mg/L. Administration with food increases the C_{max} by 28 percent (0.60 mg/L). The median time to reach maximum serum concentration is 12 hours in the fasting state, but shortened to 8 hours following administration with a meal. The area under the serum concentration versus time curve is also increased following administration with a meal, from 18 to 29.1 mg * hour/L.

Multiple-dose administration of 100 mg has been reported to produce a serum concentration of 0.7 mg/L two hours after administration, with the concentration increasing to 1.0 mg/L (300 mg) and 1.4 mg/L (400 mg) following higher doses. The volume of distribution of clofazimine has not been determined, probably because an intravenous form does not exist. Similarly, the type and extent of protein binding of clofazimine has not been studied. However, autopsies in several patients taking various doses of clofazimine for variable lengths of time have been performed, providing a great deal of information on tissue distribution (Table 2). Because MAC infection occurs in many tissues and fluids, adequate distribution of clofazimine to these sites may be important in eliciting a therapeutic response. At autopsy, many tissues were noted to be abnormally stained yellow, orange, red, or brown. Because clofazimine is highly lipophilic, it distributes primarily into fatty tissues in the reticuloendothelial system. Heavy deposits of crystals are often noted in the intestine, liver, and macrophages of the lymph nodes. Clofazimine apparently crosses the placenta and also distributes into breast milk.

Clofazimine undergoes very little metabolism, with less than one percent recovered as metabolites in the urine in a 24-hour period. Three urinary metabolites have been identified, but it is unknown whether they are pharmacologically active. Up to 50 percent of an administered dose has been recovered in the stool. Most likely, this represents unab sorbed drug and biliary excretion. A very small amount is eliminated in sebum and sweat.

The elimination half-life of clofazimine has not been fully characterized in a carefully designed study. There appears to be an initial elimination phase with a half-life of seven to ten days. This is followed by a much longer elimination period, probably resulting from release of the drug from fatty tissues and the reticuloendothelial system, with a half-life of approximately 70 days. Following administration of 50 mg/d for eight days, a steady-state concentration is not achieved. Computer simulation indicates that at least 30 days would be required to approach steady-state. These authors postulate that steady-state could be approached more quickly by giving higher loading doses at the beginning of therapy.

The effect of various disease states on the pharmacokinetics of clofazimine have not been studied. Similarly, the effect of peritoneal and hemodialysis are unknown.

### Clinical Efficacy

A summary of studies evaluating the clinical efficacy of clofazimine in leprosy and MAC is shown in Table 3.

#### LEPROSY

Clofazimine has been approved by the Food and Drug Administration (FDA) for the treatment of lepromatous leprosy, including dapsone-resistant strains and disease complicated by ENL, or type 2, reactions. Prior to the first use...
of clofazimine in 1962 for the treatment of leprosy, single
drug therapy with dapsone was considered the regimen of
choice. However, as dapsone resistance and treatment fail-
ures began to be reported, other drugs began to be evalu-
ated in the 1970s. This eventually led to the recommenda-
tion by the World Health Organization, in 1982, that all lep-
romatous leprosy patients be treated with multidrug ther-
apy. Multidrug therapy consists of dapsone, rifampin and
clofazimine.

Prior to the recommendation for multidrug therapy, Ah-
rens et al. compared dapsone and clofazimine as single agents
in a multicenter, double-blind trial. A total of 94 patients
were allocated to receive clofazimine 100 mg or dapsone 50
mg twice weekly and followed for 48 weeks. The incidence
and rate of clinical, bacteriologic, and histopathologic re-
sponse in the two groups was equivalent. Of importance,
twice as many patients in the dapsone group experienced at
least one ENL reaction.19

Multidrug therapy comprising dapsone, rifampin, and clo-
fazimine has now been evaluated in several open, noncom-
parative trials. Tiwari et al. evaluated multidrug therapy in 58
institutionalized patients over a two-year period. Multibacill-
ary leprosy was treated with a 14-day induction regimen of ri-
fampin 600 mg/d, dapsone 100 mg/d, and clofazimine 100
mg/d. This was followed by a maintenance regimen of rifamp-
in 600 mg once a month, dapsone 100 mg/d, and clofazo-
mine 100 mg every other day plus 300 mg once monthly.
Most patients required between 6 and 18 months to become
bacteriologically negative on this regimen.20

Katoch et al. have reported their four-year follow-up experi-
ence with 56 patients treated with multidrug therapy
that included clofazimine. Smears for acid-fast bacilli were
negative within four years in the majority of patients. Skin
lesions regressed in all patients during the first year. Bacil-
lemia, which was present in 53 percent of patients at the
start of therapy, had cleared in all patients by 2/4 years. All
patients completed 42 months of follow-up, but only 24 pa-
ients completed 48 months. The authors postulated that
multidrug therapy may lead to long-term cures with rela-
tively short durations of therapy.21

In a comparison of two different multidrug therapy regi-
imens, Chattopadhyay et al. randomized patients to receive
either clofazimine 100 mg every other day plus 300 mg
monthly, or ethionamide 375 mg/d, in combination with ri-
fampin 600 mg/d for three weeks followed by 600 mg/mo
and dapsone 100 mg/d. Of 61 patients entering the study, 53
(31 receiving clofazimine) completed the two-year treat-
ment period. Clinical improvement was based on a scoring
system involving color, degree of infiltration, sensory loss,
and involvement of peripheral nerves. Clinical improve-
ment occurred more quickly in the first month in the ethi-
onamide group; however, no difference was noted at later
time points. More patients became bacteriologically nega-
tive (25.8 vs. 4.5 percent) in the clofazimine group by the
end of the study. The incidence of ENL reactions was lower
in the clofazimine arm of the study (30 vs. 50 percent). The
results of this study favor clofazimine over ethionamide as
the third drug in multidrug therapy.22

Because leprosy requires long-term therapy, patient
compliance is a significant issue. It has led to the perceived
need for monthly "supervised" doses of rifampin and clo-
fazimine. Ellard et al. undertook a compliance study in 488
patients receiving multidrug therapy by monitoring urine
samples to detect clofazimine and dapsone. They reported
that more than 90 percent of their patients collected at least
90 percent of their medication from the clinic during the
first two years of treatment. Urine tests indicated that 72
percent of the patients had taken their prescribed clofazo-
mine and 78 percent took their dapsone.28

ENL reactions may complicate treatment of leprosy in up
to 50 percent of patients during the first year.4,7 The most
common manifestations are fever, malaise, and tender,
erythematous skin nodules. Severe reactions may be ac-
 companied by joint swelling, orchitis, albuminuria, neuri-
tis, iritis, epistaxis, and lymphadenopathy; hospitalization
is often necessary in these cases. Corticosteroids and tha-

### Table 3. Summary of Clinical Studies Evaluating the Efficacy of Clofazimine in the Treatment of Leprosy and MAC

<table>
<thead>
<tr>
<th>REFERENCE</th>
<th>PATIENTS ENTERED (n)</th>
<th>PATIENTS COMPLETING (n)</th>
<th>COMPARATIVE DRUG/REGIMEN</th>
<th>CONCURRENT THERAPY</th>
<th>RESPONSE TO THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leprosy</td>
<td>19</td>
<td>94</td>
<td>D</td>
<td>none</td>
<td>Clinical improvement 93% with clofazimine vs. 75% with dapsone; no difference in other measures; twice as many ENL reactions in dapsone group</td>
</tr>
<tr>
<td>20</td>
<td>58</td>
<td>58</td>
<td>none</td>
<td>Ri, D</td>
<td>Clinical response occurred in 46.5% of patients within 6 mo</td>
</tr>
<tr>
<td>21</td>
<td>56</td>
<td>24</td>
<td>none</td>
<td>Ri, D</td>
<td>Clinical response occurred in all patients within 1 y; bacillariemia cleared in all patients within 30 mo</td>
</tr>
<tr>
<td>22</td>
<td>61</td>
<td>53</td>
<td>R, D, E</td>
<td>Ri, D</td>
<td>Clinical response occurred in 69.9% of clofazimine patients, vs. 73.3% in the other group; bacteriologic negativity was 25.8 vs. 4.5%, respectively</td>
</tr>
<tr>
<td>MAC</td>
<td>23</td>
<td>29</td>
<td>none</td>
<td>Rb, E, Et</td>
<td>No patient had an objective response to therapy; mycobacteremia persisted in 92%</td>
</tr>
<tr>
<td>24</td>
<td>13</td>
<td>none</td>
<td>Rb, A, others</td>
<td></td>
<td>Transient clinical improvement in 1 patient; transient negative blood cultures occurred in 7/13, but all relapsed</td>
</tr>
<tr>
<td>25</td>
<td>7</td>
<td>none</td>
<td>Rb, Et, I</td>
<td></td>
<td>Clinical improvement in 6 patients; transient negative blood cultures in 5, sustained in 1; 6 patients died within 1 y</td>
</tr>
<tr>
<td>26</td>
<td>4</td>
<td>none</td>
<td>Rb, I, Et</td>
<td></td>
<td>Clinical improvement occurred in all 4 patents; 2 patients died within 5 mo</td>
</tr>
</tbody>
</table>

A = amikacin; D = dapsone; E = ethionamide; Et = ethambutol; I = isoniazid; MAC = Mycobacterium avium complex; Rb = rifabutin; Ri = rifampin.
MAC IN AIDS PATIENTS

MAC was first recognized as a rare cause of slowly progressive pulmonary infection, usually in elderly men with underlying lung disease. With the advent of the current AIDS epidemic, MAC has been noted frequently, being present at autopsy in 50 percent or more of patients. MAC is more commonly detected in AIDS patients, and because controlled clinical studies are lacking, an immunodeficient in vivo model (the beige mouse) has been developed to help bridge the gap between in vitro testing and clinical efficacy. Using this model, clofazimine 20 mg/kg po has been shown to be more effective than ethambutol and the investigational agent rifabutin (an- samycin). The combination of clofazimine and rifabutin was more effective than any single agent or other combination. Serum concentrations produced by these regimens were not reported, so it is difficult to extrapolate these data to the treatment of human infection. In a follow-up study, the same investigators compared amikacin, clofazimine, and rifabutin, alone and in combination. Although amikacin alone was noted to be quite effective, the combination of clofazimine and amikacin was more active. Endpoints considered in these two studies included mortality, reduction in the number of colony-forming units, and histopathologic examination of the tissues involved. The reader is referred to these articles for a more detailed account.

Mishra and Girdhar reported that 22 of 30 patients with frequent ENL responded to clofazimine in doses up to 300 mg/d. In three of the eight nonresponders, lymphadenopathy developed after clofazimine was begun, so not all patients benefit from its use. Similarly, clofazimine 50–100 mg/d as a part of multidrug therapy has been reported not to affect the incidence of ENL. It is unknown whether this lack of response relates to the low dosage used, the intensive nature of multidrug therapy, or other as yet unidentified factors.

Reversal (type 1) reactions also may occur in leprosy patients. Existing lesions may worsen, and actual nerve damage may occur. Clofazimine does not appear to be beneficial in treating this condition, and in fact may worsen it. Corticosteroids are the drugs of choice for treating type 1 reactions.

MAC was isolated from the blood of 90 percent of the patients, as well as many other sites. Despite combination drug therapy, all 29 patients had evidence of persistent infection. Of 26 patients with initially positive blood cultures, 24 had persistent mycobacteremia. At the time the report was written, 22 of the patients had died (76 percent); in the 17 who received an autopsy, MAC was isolated from at least one site. In addition, fever, malaise, anorexia, and weight loss persisted despite antimycobacterial therapy.

Masur et al. treated 13 mycobacteremic patients with clofazimine 100 mg/d and rifabutin, as well as amikacin and other drugs as guided by susceptibility testing. Duration of therapy ranged from 33 to 530 days. Six of the patients had at least two consecutive negative blood cultures at some point during therapy. Two of these six patients relapsed and developed positive cultures again during therapy. In only one patient was there a clear correlation between conversion to negative cultures and clinically apparent improvement.

Agins et al. have presented a more encouraging picture of MAC treatment. Seven patients with mycobacteremia were treated with clofazimine 100 mg/d in combination with rifabutin, isoniazid, and ethambutol. At least two consecutive negative blood cultures were noted in six patients. In addition, these six patients reported clinical improvement in their symptoms of fever, weight loss, and night sweats. However, all of the patients but one died within one year; the seventh died after 17 months.

Bach has reported his experience in treating MAC infection in four AIDS patients, using the combination of clofaz-
imine, rifabutin, isoniazid, and ethambutol. However, only one of these patients had a positive blood culture prior to therapy, and follow-up cultures were not reported for any of the patients. Clinical improvement was noted in all four patients, although two of them died within five months. Follow-up had only occurred for three and five months in the other two patients. 

It is obvious from these reports that combination therapy, including clofazimine, has been largely ineffective in treating MAC infection in AIDS patients. Controlled, comparative trials are not available, a problem that may persist for some time. New regimens, containing amikacin and ciprofloxacin, are being recommended based on in vitro and in vivo test results. In the meantime, combination therapy appears to provide symptomatic relief to some patients, so it seems reasonable to offer it to them once the potential risks and benefits have been explained.

**Pediatric Considerations**

The safety and efficacy of clofazimine in children under 12 years of age have not been established. However, clofazimine has been used in a small number of children. 

**Adverse Effects**

Most patients treated with clofazimine in a dose ≤100 mg/d tolerate it quite well. Higher doses, especially ≥300 mg/d, may cause severe adverse effects. The most common adverse reactions secondary to clofazimine affect the skin, GI tract, and eye (Table 4). 

**SKIN**

A pink to brownish-black discoloration of the skin is quite common, occurring in nearly all patients receiving the drug. Discoloration is thought to occur because clofazimine is a red dye. The skin usually becomes discolored during the first few weeks of therapy and the discoloration usually disappears within several months after clofazimine is stopped. Discoloration also has been present in neonates at birth if the mother has taken clofazimine during pregnancy. At autopsy, patients who have received clofazimine usually display a red-orange discoloration of many organs and tissues, especially the GI tract and fatty tissues. 

Clofazimine is secreted in sweat, tears, sputum, and other body fluids, making it important to warn the patient to expect a red-brown discoloration. Ichthyosis and dry skin are encountered in up to 75 percent of patients treated with clofazimine. Application of oil, petrolatum, or a 25 percent urea emollient lotion can alleviate this problem. Other rarely occurring adverse reactions involving the skin include rash, pruritus, and exfoliative dermatitis. 

**GI TRACT**

The most serious and limiting adverse effect of clofazimine involves the GI tract. There are two possible syndromes, one occurring early which is self-limited, the other occurring late, which is potentially fatal. The early reaction consists of anorexia, nausea, or diarrhea and probably is due to a local irritant effect of the drug. It responds promptly to reduced dosage or discontinuation of the drug. The late occurring reaction involves anorexia, nausea, vomiting, weight loss, and/or abdominal pain. It usually occurs during long-term therapy with dosages >100 mg/d. Despite discontinuation of clofazimine, the patients may not improve, and a few patients have died. At laparotomy, large deposits of clofazimine crystals in association with congestion of the small bowel mucosa and mesenteric lymph node enlargement have been found. Splenic infarction and eosinophilic enteritis have been associated with this syndrome rarely. 

**THE EYE**

Red-brown discoloration of the cornea, conjunctiva, and lacrimal fluid occurs frequently in patients receiving clofazimine. Slit-lamp examination often reveals clofazimine microcrystals. In addition, small brownish lines or streaks in the cornea have been described during clofazimine therapy. These lines disappear slowly following discontinuation of the drug. To date, clofazimine has not been reported to affect color vision or visual acuity.

**MISCELLANEOUS**

Clofazimine is not mutagenic and has not been reported to be teratogenic. When used in pregnant women, hyperpigmented skin has been noted in the neonate. In addition, a 20 percent neonatal death rate has been reported. Further work has shown reduced estrogen concentrations in women receiving clofazimine. Despite these concerns, clofazimine is quite useful in pregnant women with leprosy and ENL reactions; thalidomide is contraindicated and high-dose prolonged courses of corticosteroids are not desirable. Therefore, the benefits and risks of clofazimine in pregnancy must be carefully weighed in each patient.

**Drug Interactions**

In six male leprosy patients who received a single dose of rifampin 600 mg in conjunction with clofazimine (dose not specified), a statistically significant reduction in the rate of rifampin absorption and time to reach maximum serum concentration was noted. Bioavailability was not affected, so this interaction is unlikely to be significant. In a mul-
multple-dose study, clofazimine had no effect on rifampin pharmacokinetic parameters. 31 Similarly, three multiple-dose studies have failed to detect any effect of clofazimine on dapsone pharmacokinetics in leprosy patients. 32-34 In contrast, isoniazid has a significant effect on clofazimine pharmacokinetics. In seven of ten leprosy patients receiving clofazimine 300 mg/d, concomitant isoniazid-reduced clofazimine tissue concentrations were measured by biopsy. In addition, serum clofazimine concentrations and urinary excretion were increased through this interaction. The authors postulated that isoniazid mobilized a tissue depot of clofazimine, resulting in more drug in the blood and less in the tissues. 34

Summary

Clofazimine has been approved by the FDA for the treatment of leprosy. It is particularly useful in preventing or treating leprosy patients with frequent or severe ENL reactions. Because leprosy is rarely encountered in the US, this may not comprise its largest area of use here.

The current AIDS epidemic, in which MAC is frequently encountered, has provided a different role for clofazimine. Although the overall experience in treating MAC infection in AIDS patients with clofazimine combined with other agents has not been favorable, it is clear that some patients respond by clearing their mycobacteremia and becoming asymptomatic. Thus, it seems appropriate to make the drug available to these patients. Ongoing studies, using in vivo test systems, may produce a combination of drugs, including clofazimine, which is very active against this difficult infection. A great deal of work must yet be done to clarify this issue. Because of clofazimine's long elimination half-life and uneven tissue distribution pattern, alternative dosing strategies may be possible which maximize its therapeutic potential while minimizing adverse reactions.

Clofazimine should be added to formularies at institutions that are involved in the treatment of either leprosy or AIDS. It also should be available on an outpatient basis. Cost is not a major concern, as a 100-mg dose is approximately the same as a bedtime dose of a histamine H2-receptor antagonist. There are no therapeutic equivalents to clofazimine, and it is particularly useful as a component of multidrug therapy.

The technical assistance of Vanessa Petersen in the preparation of this manuscript is greatly appreciated.

References

34. GANGADHARAM PRJ, PERUMAL VK, PODAT PAT, NESAVALU L, ISEMAN MD. In vivo activity of amikacin alone or in combination with clofazimine or rifabutin or both against acute experimental Mycobac-
El fármaco tiene actividad in vivo contra M. leprae, y en vitro contra M. avium complex. Además posee propiedades antiinflamatorias e inmunosupresoras. La absorción de clofazimina a través del trayecto gastrointestinal es lenta e incompleta. Su eliminación es en gran medida en la forma intacta por la orina y en las heces fecales. Los estudios clínicos apoyan la efectividad de clofazimina como parte del régimen de múltiples medicamentos que se utilizan en el tratamiento de lepra. El fármaco también parece reducir la incidencia y severidad de la reacción de eritema nodoso leproma que ocurre comúnmente en el tratamiento de esta condición. La efectividad en el tratamiento de MAC en pacientes con SIDA no está muy bien documentada. Algunos pacientes han demostrado una mejora disminuyendo la sintomatología, al igual que se ha logrado erradicar la micobacteria, pero no se ha alterado la mortalidad. Clofazimina ha sido bien tolerada en dosis de hasta 100 mg/día. Efectos adversos incluyen decoloración de la piel y de los ojos, intolerancia gastrointestinal, dolor abdominal severo, y daño a órganos secundarios a la deposición de cristales del fármaco. Aunque clofazimina se había utilizado en el tratamiento de lepra desde 1962, el número de estos casos eran limitados. La epidemia de SIDA ha llevado al uso frecuente del fármaco, ya que uno de los patógenos que más comúnmente causa infecciones oportunistas en esta condición es M. avium complex. Clofazimina se utiliza frecuentemente en combinación con otros agentes antinfectivos para el tratamiento de esta condición en pacientes con SIDA. Se necesitan estudios comparativos controlados que evalúen el tratamiento de esta infección que es tan difícil de tratar.