NHDP Clofazimine Experience

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David Scollard, M.D., Ph.D.
Barbara Stryjewska, M.D.
Jacqueline Lea, R.Ph.

Department of Health & Human Services
Health Resources & Services Administration
Healthcare Systems Bureau
National Hansen’s Disease Programs
Non-HD shipments in 2011:

567 Shipments to 187 sponsors in 40 states (including D.C).

TOTAL: 106,000 caps
Standard Treatment Regimen in U.S.

**Tuberculoid** (Paucibacillary, PB)
- Dapsone 100 mg/d
- Rifampin 600 mg/d

1 Year

**Lepromatous** (Multibacillary, MB)
- Dapsone 100 mg/d
- Rifampin 600 mg/d
- Clofazimine 50 mg/d

2 Years
WHO Regimen for HD in Adults

Each blister pack contains treatment for 4 weeks.

**PB adult treatment:**

- **Once a month:** Day 1
  - 2 capsules of rifampicin (300 mg X 2)
  - 1 tablet of dapsone (100 mg)

- **Once a day:** Days 2-28
  - 1 tablet of dapsone (100 mg)

**Full course:** 6 blister packs.

**MB adult treatment:**

- **Once a month:** Day 1
  - 2 capsules of rifampicin (300 mg X 2)
  - 3 capsules of clofazimine (100 mg X 3)
  - 1 tablet of dapsone (100 mg)

- **Once a day:** Days 2-28
  - 1 capsule of clofazimine (50 mg)
  - 1 tablet of dapsone (100 mg)

**Full course:** 12 blister packs.
Some side effect reported in 381/1948 (20%) HD patients. Standard dose = 50 mg daily

Clofazimine Side Effects in 381 HD Patients.
NHDP, 2006-2011
Uneven hyperpigmentation and photosensitivity during Clofazimine treatment
Clofazimine Pigmentation is Reversible
Anti-inflammatory effect in HD

Balagon M, Saunderson PR, Gelber RH. Does clofazimine prevent erythema nodosum leprosum (ENL) in leprosy? A retrospective study, comparing the experience of multibacillary patients receiving either 12 or 24 months WHO-MDT. Lepr Rev. 2011 Sep;82(3):213-21.
Cebu Skin Clinic, Leonard Wood Memorial Center for Leprosy Research, Cebu, Philippines.

### Table 2. Characteristics of ENL reactions in each group

<table>
<thead>
<tr>
<th></th>
<th>One year MDT</th>
<th>Two years MDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases with ENL</td>
<td>N = 60</td>
<td>N = 36</td>
</tr>
<tr>
<td>Clinical diagnosis of severe ENL: n (%)</td>
<td>55 (92%)</td>
<td>14 (39%)</td>
</tr>
<tr>
<td>Total duration of ENL in weeks:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>49.7</td>
<td>12.4</td>
</tr>
<tr>
<td>Range</td>
<td>8–125</td>
<td>3–44</td>
</tr>
<tr>
<td>Duration &gt;20 weeks: n (%)</td>
<td>48 (80%)</td>
<td>8 (22%)</td>
</tr>
<tr>
<td>Average number of episodes per patient</td>
<td>2.9</td>
<td>2.4</td>
</tr>
<tr>
<td>Average duration of each episode</td>
<td>17 weeks</td>
<td>5.3 weeks</td>
</tr>
<tr>
<td>Total dose of prednisolone (gm) given:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>10.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Range</td>
<td>0.0–34.7</td>
<td>0.1–4.2</td>
</tr>
<tr>
<td>Cases given &gt;2 gm prednisolone: n (%)</td>
<td>51 (85%)</td>
<td>5 (14%)</td>
</tr>
</tbody>
</table>

- Screening -- Clofazimine inhibits T cell-receptor–mediated signaling → IL-2
- Clofazmine blocked the Kv1.3 K+ channel → perturbation of Ca++ channel → inactivation of calcineurin-NFAT pathway
Obtaining Clofazimine from the NHDP

Background: Late 2002, NHDP conferred with reps. from FDA Drug Shortage, Novartis, CDC and WHO to agree upon a process for continuing availability of clofazimine in the U.S.

- FDA determined CLO medically necessary for leprosy; occasionally used in MDR TB
- NHDP agreed to sponsor IND for leprosy
  (Novartis allows NHDP to reference their Master Drug File)
- All other uses will require single-patient use IND
- **No-one was willing to sponsor IND for MDR TB**
- NHDP serves as supplier on behalf of FDA for single patient IND’s issued
- FDA classifies clofazimine as Investigational
  > Use requires IND application and IRB approval
  > CDC provides national IRB for Clofazimine for HD patients
  > Some universities will not delegate this and require their IRB to review
- For non-HD use, clinician must contact FDA for individual IND
- Once approved, FDA sends e-mail to Catherine Crnko (NHDP) with the Physician’s name, IND Number, & shipping information
- This email is forwarded to the NHDP Pharmacy (J. Lea) for processing
ANNUAL REPORT FORM
Due April 15 each year

CLOFAZIMINE USE IN THE LONG-TERM TREATMENT OF LEPROSY
Fax to 225-756-3806 or email to mainer@hrs.gov
Original to be kept in chart

1. Date of report: ____________________________

2. Patient's name (Last, First, Middle): ____________________________

3. Date of birth: ____________________________

4. Patient's disease classification (circle one):
   a) lepromatous leprosy (LL)
   b) borderline-lepromatous (BL)
   c) mid-borderline (BB)
   d) indeterminate (I)
   e) borderline-tuberculoid (BT)
   f) tuberculoid (TT)

5. Other diagnoses (circle all that STILL apply):
   a) Known or suspected erythema nodosum leprosum (ENL)
   b) Known or suspected dapsone-resistant Hansen's disease (HD)
   c) Intolerance of other HD medication: ___________ (list)
   d) Cranial nerve involvement: ___________ (list)
   e) Other Nerve involvement: ___________ (list)

6. Other leprosy related drugs added during the past year: _____Yes _____No
   If yes, please specify:
   _____ Dapsone (DDS, Avlosulfone)
   _____ Rifampin (Rimactane®; Rifadin®)
   _____ Minocycline
   _____ Ofloxacin
   _____ Thalidomide
   _____ Prednisone
   _____ Clarithromycin
   _____ Other: ____________________________

7. Bacterial Index (BI) on most recent skin scraping or biopsy: _________

8. Response to Clofazimine (circle one):
   a) Good, no intolerances
   b) Good, minor hyperpigmentation
   c) Good, tolerable hyperpigmentation
   d) Fair, unacceptable hyperpigmentation
   e) Poor (intolerance of antibiotic)
   f) Unknown
   g) Lost to follow-up

9. Other Clofazimine-related problems (circle any appropriate):
   a) Nausea
   b) Bowel motility problems
   c) Dry eyes
   d) Dry skin
   e) Pruritus
   f) Other abnormality: ___________________________ (list)

10. Is patient still on therapy? _____ Yes _____ No
    (Date Discontinued and Why: ____________________________)

Clinical Investigator Signature ____________________________ Date ____________________________

Revised March 2010
# Investigational Drug Accountability Record

(please use this form to inventory your clinical supplies)

## Name of Institution and Investigator:

Drug Name, Strength and Dosage Form: Clofazimine 50 mg capsules (Novartis Lamprène)

| FDA IND #67,033 | Protocol Title: Clofazimine Use in the Long-Term Treatment of Leprosy, Phase III |
| CDC IRB #5811   |                                                                                     |

A three-month supply, defined as 90-100 days [as multiples of one-hundred-pill bottles of Clofazimine 50 mg capsules, as needed] may be dispensed to the patient at each visit.

<table>
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<tr>
<th>Line No.</th>
<th>Date</th>
<th>Patient ID</th>
<th>Dose</th>
<th>Quantity Dispensed</th>
<th>Quantity Received</th>
<th>Lot Number</th>
<th>Balance</th>
<th>Recorder's Initials</th>
<th>Date Returned</th>
<th>Quantity Returned</th>
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<td>Issued</td>
<td>by NHDP Pharmacy</td>
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<td>F0005A EXP 3/14</td>
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</table>

**Order Request:** Please send __________ Clofazimine 50 mg capsules.

(Up to a 3 month supply may be ordered)
Contact Information

David M. Scollard, M.D., Ph.D
DScollard@hrsa.gov

Barbara M. Stryjewska, M.D.
Bstryjewska@hrsa.gov

Jacqueline Lea, R.Ph.
JLea@hrsa.gov

Renee Painter
RPainter@hrsa.gov

Catherine Crnko
CCrnko@hrsa.gov

National Hansen’s Disease Programs
1770 Physicians Park Drive
Baton Rouge, LA  70816
1-800-642-2477
www.hrsa.gov/hansens