

Clofazimine Update

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Why Clofazimine?

- Key part of a more efficacious, all oral regimen
- Better side effect profile than other agents
- Generally very well tolerated

Common CFZ Side-Effects > 1%

- Skin
 - Darkening 75-100%
 - Dryness / scaliness 8-28%
 - Rash / itching 1-5%
- GI
 - Nausea 40-50%
 - Vomiting, constipation, diarrhea, pain less common
- Ocular – discoloration and dryness
- Other discoloration – urine, feces, sweat

Uncommon CFZ Side-Effects <1%

- Hepatitis, hepatomegaly, jaundice, bowel obstruction
- Decreased vision
- Dizziness, fatigue, neuralgia
- Depression
- Lab abnormalities: elevated Tbili, ALT, hypokalemia

CFZ, prolonged QT Interval and Torsades de Pointes

Cases of Torsades de Pointes with QT prolongation have been reported in patients receiving dosage regimens containing higher than 100 mg daily dose of LAMPRENE or in combination with QT prolonging medications.

For QT prolongation and Torsades de Pointes cases, the patient must remain under medical surveillance. In all these patients, monitor electrocardiograms (ECGs) for QT prolongation and cardiac rhythm disturbances [see Dosage and Administration (2.1)].

QT prolongation has also been reported in patients who were receiving LAMPRENE with bedaquiline at the recommended dosage regimen for each drug. Monitor ECGs if LAMPRENE is coadministered to patients receiving bedaquiline, and discontinue LAMPRENE if clinically significant ventricular arrhythmia is noted or if the QTcF interval is 500 ms or greater. If syncope occurs, obtain an ECG to detect QT prolongation.

Clofazimine Challenges

- Not FDA approved for TB
 - Requires a research study proposal
 - Proposal must be approved by an Institutional Review Board
 - FDA Single Patient Investigational New Drug (SPIND) approval for EACH patient
 - Request CFZ from manufacturer (Novartis)
 - Novartis Letter of Agreement (LOA) is required
 - Novartis LOA likely unacceptable to governmental agencies and will require coordination with agency legal counsel

NOTE: Took me over 9 months to complete the process.

How to obtain CFZ in Texas Today

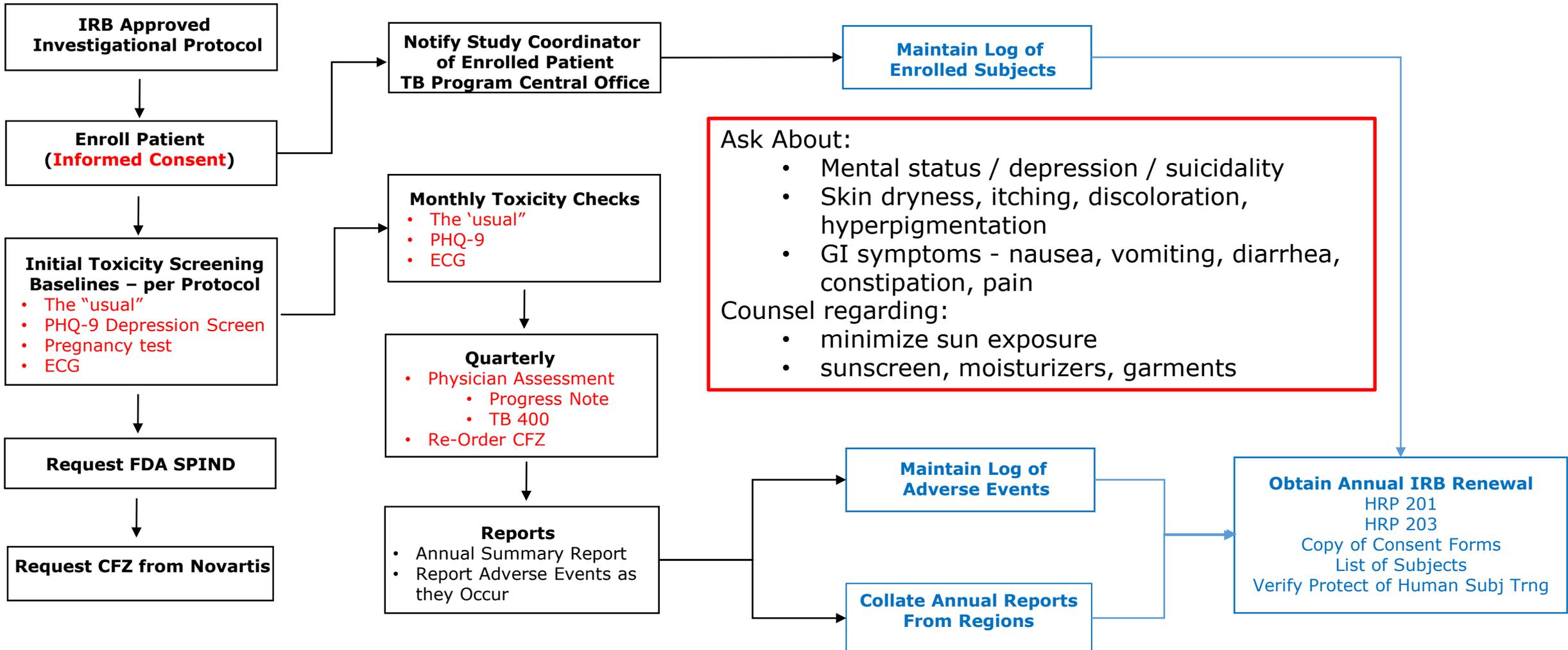
- Inpatient
 - TCID
- Outpatient
 - Regional Health Dept
 - Region 2/3: Dr. Massey
 - Region 9/10: Dr. Boneta
 - Region 11: Dr. Prot and Dr. Boneta – 14 patients enrolled; 13 active
 - Region 8: Dr. Ringsdorf
- Local Health Dept

BACK-UP SLIDES

Clofazimine Work Plan

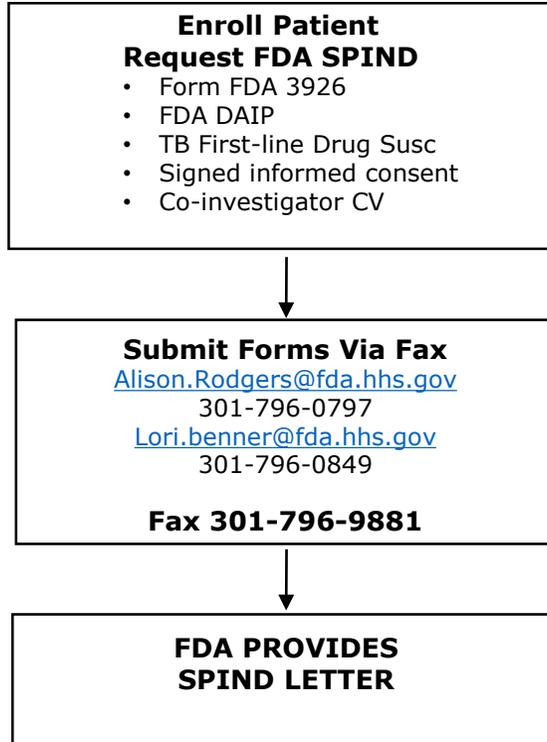
Regional Staff / Co-Investigator

Study Coordinator / Primary Investigator TB Program Office



Clofazimine Drug Ordering

FDA Approval (Regional TB Program)



Novartis Drug Order (Regional TB Program)

DSHS Internal Process (Pharmacy Branch / TB Program)

- Paperwork sent to FDA may have PII so send via fax;
- Paperwork being transmitted to Novartis does not have any PII and can be transmitted via email
- DSHS obtained blanket approval from HHSC Exec Commissioner to accept CFZ donation from Novartis as of 21 August