Disclaimer: The information provided here should NOT be used as a substitute for seeking professional medical diagnosis, treatment, or care. You should NOT rely on any information in these pages to replace consultations with qualified health professionals. The information presented in this document comes from Friedreich's Ataxia medical professionals trying to be helpful to FA families who may be considering use of medication for FA that has not been approved by regulatory authorities (off-label use). Although this information has been reviewed by a number of physicians expert in FA, we do not offer this information as medical advice, but rather as thoughtful reflections you might want to consider, along with your own team of medical professionals.

FRIEDREICH'S ATAXIA PATIENT GUIDE TO OFF-LABEL DRUG USE

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As research in FA has advanced, new potential treatments are emerging. These new treatments come from two general categories. One category is "new" drugs/compounds – "new" meaning never tried in patients. These are compounds created or discovered in the laboratory and not currently on the market or available. The second category is "existing" drugs or compounds – "existing" meaning that these drugs or compounds were developed and approved for use in other diseases or these are naturally occurring compounds that may be marketed as dietary supplements. This document deals with issues raised by "existing" compounds that, based on laboratory or clinical research, also appear to show a potential to be helpful in FA. Even though an "existing" compound may show benefit in laboratory, case report, or small patient studies, thorough evaluation and properly conducted trials need to be done to seek approval of that "existing" drug or compound for use in FA. Use of "existing" drugs for FA when such approval has not been obtained or evaluated is called "off-label drug use". The option of off-label drug use is becoming visible and we want the FA patient community to be informed and aware of the risks and limitations of off-label drug use.

Points to Consider in Off-Label Use of Drugs

The use of marketed drugs or medications that have not been specifically reviewed, tested and approved by regulatory agencies ("off-label use") in individuals with Friedreich's Ataxia can be very dangerous. All drugs have side-effects that can cause harm, including increasing risk of death. Drugs come to the marketplace after a rigorous development and testing process, and a formal review and approval process by a regulatory body (in the United States this is the Federal Drug Adminstration). When drugs are approved, they are approved at specific dosages for specific indications or conditions. The side-effects that are reported with the drug are only those that were documented in the experimental treatment groups so additional adverse side-effects may be found when individuals with other disorders use the drug. Once a drug is approved, physicians use best clinical practice and their medical judgment when prescribing drugs to treat patients, which usually is prescribing the drug for the approved indication. Physicians, however, may and sometimes do prescribe the drug for use in other indications.

Why might a physician prescribe a drug for off-label use?

1. The mechanism of action of the drug might suggest that it would be beneficial to a patient who is not responding to other treatment options.
2. Individual studies or case reports may suggest benefit for other indications when there is preclinical or laboratory studies that suggest an "existing" drug might have benefit in FA. However, pre-clinical or laboratory studies that suggest potential benefit of a drug rarely translates to benefit in patients. The cellular and animal models used in laboratory testing have limitations and do not closely replicate the human disease. Also, the experience with many disorders has shown that drug candidates identified in laboratory studies usually do not show the same benefit when delivered to patients.

Off-label use impact on clinical trials?
When a physician is prescribing a drug to treat a patient, this is not considered research or a study – this is medical management and decisions made are solely between the patient and the physician. Patients should discuss with their physician the risks and benefits of any drug being considered for treatment and plans for monitoring the drug and its possible effects, good or bad, on the patient.

Properly designed clinical trials are absolutely necessary to fully evaluate risks and benefits of a drug for each indication or disease. Using unapproved or off-label medications outside a clinical trial can increase risks to patients and can impede the process of thoroughly evaluating the medication for the new treatment.

All serious adverse events (such as hospitalization, disability, life-threatening event or death) that occur while a patient is taking a drug must be reported by the physician. If a patient is taking a drug off-label and he/she experiences a serious adverse event it is possible that this could have a negative impact on implementation of controlled clinical studies of the drug. Even if the drug did not cause the serious adverse event but there is lack of sufficient evidence for another cause, the drug will be implicated and it may affect the success of a complete study.

Drugs may have different side-effects when used in different disorders. One cannot assume that the side-effects reported when the drug was approved will apply when the drug is used for a different indication or use. Also, the dosage and/or administration (pill, injection, etc) of the drug may need to be adjusted for optimal usage.

Properly controlled clinical trials in patients with FA are essential to determine:

1. The proper dosage of the drug
2. Whether or not the drug biologically acts in people the way it did in laboratory and animal models
3. If there are any clinical benefits
4. If the drug is safe
5. Who responds to the drug

Establishing the drug as standard of care increases access of the new treatment to patients.
When drugs are prescribed off-label the insurance provider may not cover the cost of the drug. Most insurers will require evidence that the drug treats or has benefit to the disorder being treated. FARA is working with FA researchers, clinicians, pharmaceutical companies and government agencies to advocate that well-designed clinical trials are initiated to fully evaluate these potential treatments. While this process is slow, the safety issues and ramifications of adverse events could have dramatic effects on the implementation and pace of future treatment advances.

What can be done now to support and facilitate upcoming treatment trials?
Join the FARA patient registry - www.curefa.org/registry
This patient registry is used by researchers and pharmaceutical companies for notification and recruitment of FA patients for clinical drug trials.

Visit a FA Clinical Network site and participate in clinical research.
FA Clinical Network - http://www.curefa.org/network.html
The Collaborative Clinical Research Network in Friedreich's Ataxia (CCRN in FA) is an international network of clinical research centers that work together to advance treatments and clinical care for individuals with Friedreich's ataxia. The network collaborates with pharmaceutical companies, government agencies and other research centers and the patient community to facilitate clinical research and trials needed to identify new therapies. At each clinical research center there is a team of researchers, physicians and health care providers dedicated to FA. Many of the network sites have

a variety of important research studies that patients can participate in such as assessment of clinical measures, quality of life studies, biomarker studies and clinical trials. The link above provides you with additional information and a list of network sites.

For questions and discussion about this guide contact Paul Konanz, FAer parent, at pkonanz@comcast.net or call 707-795-3293.

SPECIFIC OFF-LABEL GUIDES:
EPO (Erythropoietin): Patient Guide / Physician's Guide

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