Cooley's Anemia FOUNDATION
Leading the Fight Against Thalassemia

www.thalassemia.org

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Dear Patient Community:

As you may know Novartis has announced that this week, the new formulation of deferasirox (Exjade), to be called Jadenu will be available to US patients. Jadenu will be a once daily tablet dose. The dosing is not the same as Exjade dosing because the new tablet format can enter the blood stream more easily. We encourage you to talk to your physician about your questions regarding this new treatment option.

We also wanted to take the opportunity to share with you some advice about topics that have come up to the Foundation and some of the doctors at major treatment centers regarding deferasirox (Exjade) and hope that this information is useful to you in addressing concerns you may have about your current chelation.

Topic One: Requests for increased monitoring of kidney function for patients on Exjade

Background: As many readers know, Novartis added a "boxed warning" to the deferasirox [Exjade] package insert in 2011 to alert prescribers to toxicities noted with the drug since its commercial launch in 2006. These included risk of kidney toxicity, risk of liver toxicity, and gastrointestinal bleeding. The present label for both Exjade and the new tablet formulation JadeNu provide some guidance about monitoring and possible dose modification for changes in urine protein or serum creatinine.

The Medical Advisory Board would like to remind patients and families about a few points concerning kidney function and deferasirox.

Most patients tolerate deferasirox without serious kidney problems. The most common laboratory abnormality is that creatinine rises, but typically remains within the normal range for age, or just above. This is not thought to be a serious problem.

It is important for both prescribers and patients to be aware that even frequent laboratory testing doesn't rule out the possibility of relatively acute changes in kidney function. It is possible that dehydration (to which simple symptoms including vomiting, diarrhea, and fever can contribute) may make kidney changes more likely. Kidney changes are probably more common in elderly patients, and patients with baseline poor kidney function due to age or other problems. In patients for whom deferasirox is very effective, so that the body iron burden falls rapidly, it is possible that the drug becomes relatively more toxic. This underscores the importance of regular monitoring of iron burden, ideally by MRI, to help achieve the correct dosing.

Patients and families should keep in mind that the suggested guidelines about dose reduction or temporary cessation of deferasirox are not rules written in stone or proven to be the perfect cutoffs. Evaluation of each patient should be on an individual basis, taking into account other medical problems if any, iron burden, and history of dosage of deferasirox and other chelators (see issue #2 on the next page as well).

Topic Two: Requests to switch from deferasirox to deferoxamine (Desferal® and generics)

Background: There are now four licensed chelator preparations in the US, deferoxamine (usually given subcutaneously 8-10 hours per night, 5-7 nights per week), deferasirox dissolvable tablets taken daily or divided twice daily, or now available in tablet form and oral deferiprone, given three times a day. Each has its own advantages and disadvantages in various clinical settings. None are free of important side effects in a minority of patients, and each has particular advantages for certain patients but not all. In addition, some patients can get substantial benefits from combination of two chelators, under expert supervision with adequate monitoring for safety and iron removal.

The advent of oral chelation with the launch of deferasirox in 2006 marked a major advance in treatment for patients with thalassemia and other transfusion-related disorders. One unequivocal disadvantage of deferoxamine is the very difficult treatment regimen for any patient, but especially for active young patients. Despite the challenges in administering deferoxamine, some patients are able to use it regularly and effectively, don't mind the nuisance and the needles and may choose not to change to another chelator.

The oral chelators can markedly improve ability of patients to take chelators as recommended. Missed doses of any chelator can mean higher iron burden and risk of iron-related hormone problems, or in the long run, risk of heart disease.

The Medical Advisory Board strongly recommends individualized discussion with prescribers about chelation choices for each individual patient. This typically should be done in a full office visit, weighing thoroughly the pros and cons of switching for any individual patient. Use of these drugs in combination should also be discussed with an expert provider.

With this letter, the Foundation is also again including a reminder to families on advice on Chelation Use and Illness.

We hope you will continue to work with your physician and medical team to voice your concerns and wishes so that we may provide the best care and advice.

Sincerely,

Ellis J. Neufeld, MD PhD
Chair, CAF Medical Advisory Board