

Dear CFA Members,

We wanted to contact you with some recent developments for Fabrazyme which is manufactured by Genzyme. As many of you already know there has been a worldwide shortage of Fabrazyme that started in the summer of 2009. Replagal (manufactured by Shire) is the other ERT treatment for Fabry Disease.

Many of us that are on Fabrazyme had a number of half doses in late summer 2009. Since then the Canadian patients have been receiving Fabrazyme at full dose as a part of the Canadian Fabry Disease Initiative (CFDI) Study. Genzyme has been working over the last year to rebuild Fabrazyme to full production and to rebuild the supplies of Fabrazyme. Unfortunately, Genzyme has experienced another manufacturing interruption which in turn has worsened the already critical worldwide supply shortage.

As a result, there is not enough Fabrazyme for all of the Canadian patients at full dose. Thankfully, there are already plans in place to ensure that all Fabry patients on ERT continue to receive infusions. We are very fortunate in Canada that both ERT treatments, Replagal and Fabrazyme, are approved and in use. We are also very fortunate that our doctors, clinicians, the drug companies and our home care nurses all work collaboratively to ensure treating patients is the first priority. A part of that plan is that many of us that are on Fabrazyme will be switching to Replagal for a period of time. Shire has assured us that they have more than sufficient supplies of Replagal to treat all the patients that switch products during this time. We understand that Fabry patients already on Replagal are not affected by these changes.

You will be receiving a letter from your doctor with further information on your particular situation. We are attaching a letter from Dr. West that explains much of the current situation. As discussed in his letter there will be some logistical matters that need to be completed before we can switch products. We encourage all patients to discuss their situation with their doctors so they fully understand the options and best course of action for themselves.

This situation underscores the need for treatment alternatives like Replagal and Fabrazyme. We wish Genzyme a speedy recovery to full production so that Fabry patients worldwide have access to both of these life saving treatments at the full dose.

In the meantime, we have every confidence that everyone is working to ensure we all receive our ERT on time (or with only a very short delay).

Thanks and take control of your health.

Darren Bidulka, President / Président  
Canadian Fabry Association / L'association Canadienne de Fabry  
#416 - 9319 University Crescent  
Burnaby, BC, V5A 4Y5  
Cell 604-512-9770



**Dalhousie University**  
**Department of Medicine**  
5<sup>th</sup> Floor, Dickson Building  
5820 University Avenue  
Halifax, NS B3H 1V8  
Phone: (902) 473-2099  
Fax: (902) 473-2675



May 14, 2010

Dear patient,

As you may have already heard, there has been a severe disruption in the worldwide supply of Fabrazyme<sup>®</sup> enzyme therapy for Fabry disease. This started in the summer of 2009, and has unfortunately become increasingly worse since. Up to now, the CFDI has been able to arrange adequate supply of Fabrazyme at full dose for all patients in this study. Genzyme Canada notified the CFDI researchers on Tuesday May 11, 2010, that the supply of Fabrazyme in Canada was severely reduced effective immediately with only enough drugs for about 12 or so patients. This shortage of Fabrazyme affects all patients in Canada regardless of age, sex or whether their drug is paid for by the CFDI or by private insurance. While Genzyme Corporation has indicated that the supply of Fabrazyme may increase by the fall of 2010, this is far from certain as the supply has been steadily decreasing over the past year. The shortage of Fabrazyme will not close the CFDI study which continues to provide enzyme therapy for Canadians.

While this lack of notice has left us little time to prepare for this problem, we are doing everything possible to ensure that there is an ongoing supply of full dose enzyme for all patients who would benefit from such therapy. Our number one goal is to provide enzyme replacement therapy to patients with Fabry disease in Canada. There are several options for patients on Fabrazyme in Canada. A partial dose of Fabrazyme is not adequate long term as some patients have worsened during this treatment. The CFDI researchers recommend switching to Replagal<sup>®</sup> enzyme which is the only other licensed product in Canada for treatment of Fabry disease. This move is supported by the Research Ethics Board, which oversees the CFDI study as well as the other financial sponsors of the CFDI study (provincial governments and Shire HGT). There is an adequate supply of this Replagal for all Fabry patients and it is secure. This enzyme is infused over 40 minutes every two weeks. Infusion reactions are less common with this enzyme than with Fabrazyme. We will be arranging for all patients to be switched to Replagal as soon as possible. As one can imagine, switching over 60 patients across Canada to a new drug on short notice may result in some delays in infusions and possibly even a few missed infusions over the next 4 weeks until sufficient resources are in place. I ask for your patience with us as we correct a problem not of our making. Before switching to the new drug, patients will be asked to sign a consent form and all will need to have several blood and urine tests completed. Once all patients have been successfully switched to Replagal, then the CFDI researchers will determine the best way to use the very small supply of Fabrazyme that we have left in Canada.

You should be aware that there are several other Fabry disease studies operating in Canada right now with other researchers. You might be eligible for enrollment in one of these studies and if interested

you should contact your Fabry specialist to discuss this further. Please do not hesitate to contact your regional study coordinator or Fabry specialist if you have questions or concerns.

Alternately, you may contact the national office of the CFDI study in Halifax, Nova Scotia, if you have concerns (Kaye LeMoine, National Coordinator, Toll free (877) 998-9797; Dr Michael West, Principal Investigator, (902) 473-4023).

Sincerely yours,

Dr. Michael L. West  
Chair  
Scientific committee  
CFDI Study  
Professor  
Division of Nephrology  
Department of Medicine  
Dalhousie University  
Halifax NS



### **Investigations at time of Switch from Fabrazyme to Replagal**

The following investigations **MUST** take place prior to the first agalsidase alfa infusion:

1. ECG
2. Bloodwork - CBC, electrolytes including Total CO<sub>2</sub> or bicarbonate, urea, creatinine, glucose
3. Urine - Urinalysis and Urine Protein/Creatinine Ratio, Urine for Gb<sub>3</sub> collected on filter paper for Dr. Auray-Blais, Sherbrooke QC
4. Anti-agalsidase antibody tests – one for Shire HGT and another for CFDI

If your patient has been in to your clinic within the past 30 days and had all of these investigations done within this time frame then only the blood samples for Industry antibodies and the CFDI antibodies need to be drawn.

The date of the first Replagal infusion must be carefully recorded.

May 2010