EURORDIS
Rare Diseases Europe

Q&A ON FABRAZYME AND REPLAGAL SHORTAGES

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Frequently asked questions from patients and responses prepared by their organisations

New treatment recommendations were released by the European Medicines Agency regarding the medical management of Fabrazyme shortage. These recommendations can be found here:
http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/07/WC500094245.pdf

You can find a letter sent to physicians by Genzyme explaining the situation in several European languages on the website of the Fabry International Network here:
http://www.fabryintnetwork.com/home/navigatie2/events-and-meeting

If you have questions left unanswered by this document, you can contact your doctor and your local group (list at the end of this document).

Q&A on Fabrazyme shortage

CONTACT YOUR LOCAL PATIENT ORGANISATION TO LEARN MORE

IF YOU HAVE QUESTIONS REGARDING YOUR TREATMENT WITH FABRAZYME OR REPLAGAL, THIS DOCUMENT IS INTENDED TO PROVIDE YOU WITH SOME RESPONSES AND IN ANY CASE DO NOT HESITATE TO CONTACT YOUR DOCTOR.

WHAT ARE THERE RISKS WHEN REDUCING FABRAZYME DOSE? 1 | one

Patients who were put on a reduced Fabrazyme dose reported positive or negative. The reduced dose is typically 0.3 mg/kg every other week instead of 1 mg/kg every other week. In the absence of complete assessment these reports can only be considered as anecdotal.

In particular, MPS Society UK conducted a survey among its 200 members affected with Fabry disease, of which 94 responded. Some reported symptoms after reducing the dose were:

- Fabry disease occurrences
- Extreme tiredness
- Return of gastro-intestinal symptoms
- Depression

WHAT IF I RECEIVE LESS THAN 0.3 MG/KG EVERY OTHER WEEK? 2|two

Although this is not the recommended dose, some patients may receive this low dose based on a medical decision and on their health status. However this dose should prescribed to solve the product shortage. If you are proposed a Fabrazyme treatment with less than 0.3 mg/kg every other week, ask your doctor why he or she doesn't prescribe Replagal instead.

I WAS TOLD TO STRICTLY ADHERE TO MY TREATMENT 3|three

"Since I have started my treatment for Fabry disease, both my doctor and my patient organisation have insisted that I should adhere to the infusion every other week, at the prescribed dose. Now firstly I had to lower the dose to a third, which disturbed me, and now I am being told I have to stop treatment because there is not enough supply. I am lost."

Both for Fabrazyme and Replagal, the treatment consists in infusions every second week, continuously. The quantity of each product is different, as the 2 enzymes are not identical. The current situation is exceptional. Both your doctor and your support group are right to insist on the importance to take the treatment as prescribed, life long. When the supply shortage will resume, all patients should be treated optimally again, with the appropriate dose and infusion frequency.

SHOULD I VISIT MY DOCTOR AS USUAL? 4|four

No, you should visit your doctor every two months as you need closer monitoring. This applies either if you are on a reduced dose Fabrazyme or if you switch to Replagal recently.

The European Medicines Agency recommends:

> ***ALL PATIENTS, ESPECIALLY THOSE WITH ADJUSTED DOSE REGIMENS, SHOULD BE UNDER CLOSE CLINICAL SURVEILLANCE. A MEDICAL EXAMINATION, INCLUDING ALL RELEVANT CLINICAL PARAMETERS, SHOULD BE PERFORMED EVERY TWO MONTHS. DOCTORS ARE IN PARTICULAR ADVISED TO MONITOR THE PLASMA GL-3 OR URINARY GL-3 LEVELS, AS FOR THE MOMENT THE GL-3 LEVEL IS THE MOST SENSITIVE PARAMETER.***

When visiting your doctor, schedule the next visit before leaving, in the next 2 months. If no visit can be organised within this timeframe, contact your local patient organisation.

I AM NOT WELL AFTER REDUCING THE FABRAZYME DOSE? 5 | five

As the current Fabrazyme supply is too low to put you back on the full dose, the European Medicines Agency now recommends all patients who are not well with a reduced Fabrazyme dose to be switched to Replagal.

Patients who switched from Fabrazyme to Replagal may experience unpleasant reactions (see below), but in general the switch is well tolerated and health status remains stable. Some patients even reported improvement such as:

- Tiredness and gastro-intestinal symptoms after reducing Fabrazyme dose disappeared when switched to Replagal
- 10 patients reported that Replagal is much less time consuming, Fabrazyme requires 90 minute infusion whereas Replagal requires 40 minute infusion
- "I have benefited as I am no longer ill after treatment which means a lot to me."
- "Since switching to Replagal I have much more energy than when I was on Fabrazyme"
- "Easier to prepare as does not need reconstituting".

ARE THERE RISKS TO SWITCH TO REPLAGAL? 6 | six

Patients who were switched to Replagal reported positive or negative effects after the switch. In the absence of complete assessment these reports can only be considered as anecdotal.

In particular, MPS Society UK conducted a survey among its 200 members affected with Fabry disease, of which 94 responded. Some reported reactions after switching to Replagal were:

- Shortage of breath after 30 min of infusion and getting worse each time (in this case it was decided to stop treatment until Fabrazyme becomes available again)
- Occurrence of a stroke
- Fabry disease symptoms such as pain
- Not feeling as well and having to visit family doctor more often than usual
- Pins and needles as well as burning sensation in lower legs and arms
- Tiredness, recurrence of stomach problems
- Collapse

IS THIS SITUATION AFFECTING THE WHOLE WORLD? 7 | seven

The tight Fabrazyme supply applies to every country in the world and affects all commercial formulations but not all clinical trials. In Europe guidance to physicians is supplied by the regulatory authority (European Medicines Agency www.ema.europa.eu).

WHO MAKES THESE TREATMENT RECOMMENDATIONS? 8 | eight

The Committee of Human Medicinal Products (CHMP) at the European Medicines Agency is the committee of experts that decides on the authorisation to place new medicines on the market. It also reviews adverse reactions reported once a medicine is on the market, and decides on what to do when shortage of a medicine occurs. It is composed of experts of all European Member States and can invite external experts to participate in the scientific discussions.

The CHMP largely consulted with both Fabrazyme and Replagal manufacturers through conference calls, meetings, written questions and answers. In its communication to the public and healthcare professionals, the CHMP consulted with patient representatives and has been in close contact with them since the beginning of the shortage.

MY PHYSICIAN IS ON HOLIDAY AT THE MOMENT 9|nine

"How can I arrange to change my treatment?"

If you are not able to discuss the rearrangement of your treatment supply or your infusion dates with your hospital team or homecare service, then you should contact your local patient group for advice. Your local patient representative should be able to give you a contact at the local Genzyme or Shire office that should be able to help.

I HAD TO FIGHT FOR REIMBURSEMENT OF THERAPY. 10|ten

"I'm afraid that switching will weaken my argument with insurance. What do you advise me?"

The recommendation to switch to Replagal is based only on the tight supply of Fabrazyme. If you have problems accessing Replagal, you should contact your local patient group.

I JUST STARTED MY TREATMENT WITH FABRAZYME. 11|eleven

"Is it then recommended to switch to Replagal? "

Yes, the guidelines cover all patients. No new treatment should be initiated using Fabrazyme, until further notice. Patients who started recently with Fabrazyme for the first time should now switch to Replagal.

WHAT WILL HAPPEN TO ME IF I DETERIORATE? 12|twelve

Not only on a reduced dose of Fabrazyme but also on Replagal?

The progression of Fabry disease is usually very slow in the adult population but it is variable from one person to the next. It is recommended that your physician monitors your situation every other month. Full dose Fabrazyme is now used only for a limited number of patients who have no other option than this one and who are deteriorating. In this case, your physician will need to contact Genzyme to discuss your treatment accordingly.

IS THERE ENOUGH REPLAGAL FOR ALL? 13| thirteen

"If all patients are switched to Replagal, is there a risk that the Replagal supply becomes to short for the entire treated population?"

As many patients are switching from Fabrazyme to Replagal, the demand for Replagal is increasing. If your doctor or your pharmacist explains to you that there are difficulties obtaining Replagal, you should inform your local patient group. This risk is carefully followed by Shire who manufactures Replagal, and by regulatory authorities.

In a letter sent on 24 August 2010 to patient organisations, Shire, producer of Replagal, explains that the company is providing Replagal to 80% of Fabry patients in Europe and needs to limit the number of patients

treated with this product as they have now reached the maximum number of patients they can provide with Replagal.

WHAT ARE THE RESTRICTIONS ON ACCESS TO REPLAGAL? 14|fourteen

- For patients who are treated with Replagal, nothing will change.
- A waiting list is established for patients who wish to switch from Fabrazyme to Replagal between now and the end of 2010. Urgent medical needs will be addressed by doctors to the company.
- During 2011, Shire will provide Replagal to 250-350 additional patients worldwide
- In 2012, a new manufacturing facility should increase Replagal supply and no more restrictions will be applied on this product.

WHY DID THE FABRAZYME SHORTAGE OCCUR? 15|fifteen

As explained by the European Medicines Agency in its press releases; the supply shortage is "caused by the shutting down of Genzyme's production site for Fabrazyme (agalsidase beta) in Allston Landing, in the United States of America in June 2009, because a viral contamination (calicivirus of the type Vesivirus 2117) required sanitisation of the bioreactors. The virus is not known to cause disease in humans, but it may affect the quantity, but not the quality, of the enzymes produced in the bioreactors. An in-depth investigation of the cause of the contamination is ongoing".

HOW LONG WILL THIS SITUATION LAST FOR? 16|sixteen

As of 28 July 2010, Fabrazyme manufacturer cannot commit to a date when Fabrazyme production will resume to sufficient levels. When the problem was first identified in 2009, it was first thought that the shortage should not last for more than one year. However, new difficulties have postponed the date when Fabrazyme production would come back to normal, and no prediction can be made on when this will happen.

Replagal supply will be also limited until 2012, when a new facility will start producing the product.

SHALL I PROPOSE MY DOCTOR TO CHANGE TREATMENT? 17|seventeen

Or should I wait this initiative to come from him/her?

The recommendations from the European Medicines Agency apply to all patients in Europe. It is not likely that Fabrazyme stocks are available at your hospital pharmacy, so if the proposal to switch to Replagal has not been made already, you can be proactive and contact your specialist doctor to do so. This would ensure the switch to Replagal in the best conditions, as you should not wait for your Fabrazyme treatment to be interrupted to organise a switch to Replagal.

WHERE CAN I CONTACT MY LOCAL PATIENT GROUP? 18 | eighteen

Please see below the list of local Fabry patient organisations (click on the text in blue):

Belgium	BOKS	Contact or visit: www.boks.be
Denmark	Fabry.dk	Contact or visit: www.fabry.dk
Finland	Suomen Fabry-yhdistys	Contact or visit: www.ms-liitto.fi
France	Association des Patients - Maladie de Fabry	Contact or visit: www.apmf-fabry.org
	Vaincre les Maladies Lysosomales	Contact or visit: www.vml-asso.org
Germany	Morbus Fabry Selbsthilfegruppe MFSH e.V.	Contact or visit: www.fabry-selbsthilfegruppe.de
Italy	Gruppo Italiano Pazienti Fabry (O.N.L.U.S)	Contact or visit: www.fabryonlus.org
	Italian Association of Anderson-Fabry Patients	Contact or visit: www.aipaf.org
Lithuania		Contact
Netherlands	Fabry Support & Informatie Groep Nederland	Contact or visit: www.fabry.nl
Norway	Fabry Pasientforening, Norge	Contact or visit: www.fabry.no
Slovakia		Contact
Spain	Associacion MPS	Contact or visit: http://mpsesp.org
Sweden	Patientföreningen för Fabrysjuka i Sverige	Mail to or visit: www.fabry.se
Switzerland	FabrySuisse	Contact or visit: www.fabrysuisse.ch
United Kingdom	MPS Society UK	Contact or visit: www.mpssociety.co.uk

Other parts of the world

Australia & New Zealand	Fabry Support Group Australia	Contact or visit: www.fabry.com.au
Brazil	Wanderlei Cento Fante	Contact or visit: www.fabry.org.br
Canada	Canadian Fabry Association	Contact or visit: www.fabrycanada.com
South Africa		Contact or visit: www.gaucherssa.co.za
United States of America	Fabry Support and Information Group	Contact or visit: www.fabry.org

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ABOUT EURORDIS

The European Organisation for Rare Diseases (EURORDIS) represents more than 433 rare disease organisations in 43 different countries, covering more than 4,000 distinct rare diseases. It is therefore the voice of the 30 million patients affected by rare diseases throughout Europe.

EURORDIS is a non-governmental patient-driven alliance of patient organisations and individuals active in the field of rare diseases, dedicated to improving the quality of life of all people living with rare diseases in Europe. It is supported by its members and by the French Muscular Dystrophy Association (AFM), the European Commission, and corporate foundations and the health industry. EURORDIS was founded in 1997. Further details concerning EURORDIS and rare diseases are available at: www.eurordis.org

YOUR COMMENTS

If you have comments on this document, or if you would like to share your experience during the Fabrazyme and now Replagal supply shortages, please send an email to: eurordis@eurordis.org