



National Tay-Sachs & Allied  
Diseases Association, Inc.

Friday, OCTOBER 16, 2015

## NTSAD Monthly Research Review

### What is Pyrimethamine?

This drug is approved for treating malaria, and has also been found to have an effect on other diseases such as toxoplasmosis, a life-threatening parasitic infection. It has also been used as an **off-label** therapy for Tay-Sachs (Late Onset and Juvenile). Pyrimethamine is based on **pharmacological chaperone technology**.

In the July issue of NTSAD's Research Review we wrote:

In 2009, NTSAD funded an investigator-sponsored clinical trial at Hospital for Sick Children and NYU for the treatment of Late Onset Tay-Sachs with pyrimethamine (PYR) led by Drs. Joe Clarke and Ed Kolodny. The results were published in 2011.

The study concluded that leukocyte Hex A activity is enhanced in vivo by treatment with PYR. However, future studies were needed to assess protocol, including dosage, and perform related biochemical studies. An Israeli team of researchers performed similar studies and recently published their results. While they also found that PYR increase Hex A activity in LOTS patients, "the observed increase is repeatedly transient and not associated with discernible beneficial neurological or psychiatric

### 21st Century Act Passes



The 21st Century Cures Act passed in the House this past summer. An important part of the act addresses affordable accessibility to potential treatments. Drugs like Daraprim that have an off-label use should be more affordable as sometimes these are an individual's only option for any kind of treatment.

The Act passed thanks to the people whose shouts and letters made a difference. The efforts of NTSAD's advocacy partners - NORD, the EveryLife Foundation and the Rare Disease Legislative Advocates - keep us posted on rare disease legislation that can have a profound impact on all of us as treatments are researched and hopefully brought to market.

effects."

\* Click [here](#) to read the published paper about the pyrimethamine studies conducted in 2011.

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## What's the Story with Daraprim?

This drug (also known by its generic name, pyrimethamine) has been in the **news** recently with the extreme price increase from \$13.50 a pill to \$750 after the pharmaceutical company producing it was bought by another company. It has caught the attention of the NY Attorney General and presidential candidate Hillary Clinton.

The sudden increase in price will have a profound effect on the treatment of patients suffering from these illnesses, and for those who use pyrimethamine for **off-label use** for Late Onset or Juvenile Tay-Sachs.\*

See the **sidebar** for how patients and patient groups like NTSAD can have a voice when legislation is brought before the House and Senate that can impact drug costs for orphan drug therapies.

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## What is off-label use?

It is when physicians treat their patients using treatments approved for other uses but not officially approved for use for their particular disorder. The National Organization for Rare Disorders (NORD) writes on their website:

People with rare diseases often have difficulty being reimbursed for the care they receive because that care is "off-label" and may not be covered by health insurance. This financial burden can be an enormous strain on patients and families, especially when the cost of off-label treatments runs very high.

Another drug that has an off-label use is miglustat (also

Now, NTSAD has been asked to get involved in the advocacy for the Senate phase called the **Innovation for Healthier Americans**. Stay tuned for future announcements about how you can play a role in getting the Act approved!

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## 2015 Day of Hope



The **Fifth Annual Day of Hope** is still going strong. To date over \$27,000 has been raised in the last month! There are still a few events happening in the coming weeks.

Visit [www.NTSAD.org](http://www.NTSAD.org) to see if there is one near you.

It's never too late to give to research.

**Make your gift here!**

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## Late Onset Natural History Studies

**National Institutes of Health (NIH)**  
National Human Genome Research  
Institute  
Bethesda, Maryland  
*GM1 or GM2 gangliosidosis*  
(*Infantile, Juvenile, Late Onset*)

**Mass General Hospital (MGH)**  
Boston, Massachusetts  
*Late Onset Tay-Sachs, Late Onset*

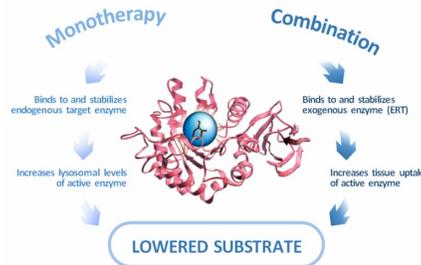
known as Zavesca) which is a potential substrate reduction therapy for the lysosomal storage disorders. Read the **NTSAD's Subcommittee on Experimental Therapies** paper on substrate reduction therapy [here](#).

**University of Minnesota (UMN)**  
Clinical and Translational  
Science Institute  
Minneapolis, Minnesota  
*Infantile/Juvenile/Late Onset Tay-Sachs or Sandhoff diseases*

## What is a Pharmacological Chaperone?

### Pharmacological chaperone technology

involves the use of small molecules that selectively bind to and stabilize proteins in cells, leading to improved protein folding and trafficking, and increased activity. In lysosomal storage disorders, the target protein is an enzyme that works in the **lysosome** to break down substrate. Due to genetic mutations, lysosomal enzymes may be misfolded and unstable, which may hamper the protein's ability to be trafficked through the cell.



In lysosomal storage disorders, the binding of the pharmacological chaperone to the active site of the misfolded **protein** in the **endoplasmic reticulum (ER)** of the cell helps the protein fold into its correct three-dimensional shape. Stabilization of the protein allows the protein-chaperone complex to pass through the quality control system of the ER. The protein-chaperone complex is then properly trafficked from the ER, through the Golgi apparatus, to the lysosome, which is the protein's final destination. Once in the lysosome, the pharmacological chaperone is displaced from the active site of the protein. This allows the protein, which is biologically active, to break down the natural **substrate** in the lysosome."

\* **Definition** borrowed from *Amicus Therapeutics*

For more information about these studies, contact Diana, Director of Family Services, [here](#).

## Are you on Facebook and Twitter?



Like **NTSAD's Facebook page** and follow [@susanr Kahn](#) for new developments in therapies, science, genetic testing, patient advocacy, and more.

## What Questions Do You Have about Research?

We want to hear from you and address any topics or answer any questions you may have about research. Our Research Initiative Committee is a group of knowledgeable friends who are ready to tackle the tough questions and address the topics that are meaningful to you. Send Diana an email [here](#) with your ideas for next month's issue for November 13, 2015.

**national tay-sachs & allied diseases association**

susan kahn, executive director ([skahn@ntsad.org](mailto:skahn@ntsad.org))

joan lawrence, development director ([joan@ntsad.org](mailto:joan@ntsad.org))

diana pangonis, family services director ([diana@ntsad.org](mailto:diana@ntsad.org))

ingrid miller, office manager ([ingrid@ntsad.org](mailto:ingrid@ntsad.org))

becky benson, conference coordinator ([becky@ntsad.org](mailto:becky@ntsad.org))

alison perkus, development associate ([alison@ntsad.org](mailto:alison@ntsad.org))

2001 beacon street

suite 204

boston, ma 02135

(617) 277-4463

[www.NTSAD.org](http://www.NTSAD.org)

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