Helping your family understand and face CLN2 disease

The information included in this brochure is based on expert recommendations about caring for children with CLN2 disease. It contains resources, information, and useful tips to help you make a meaningful difference for a child with CLN2 disease.

This brochure is meant to support you and serve as a guide as you learn more about CLN2 disease. It is important to work closely with your doctor to find the right healthcare team and treatments for your child.

CLN2 disease-specific language, which may require further explanation, is used in this brochure. For educational purposes, these terms are highlighted in purple throughout the brochure, and definitions can be found on page 7.

BIOMARIN®

What is CLN2 disease?

CLN2 disease is a rare genetic disorder that affects children[1,2]

This disease is:

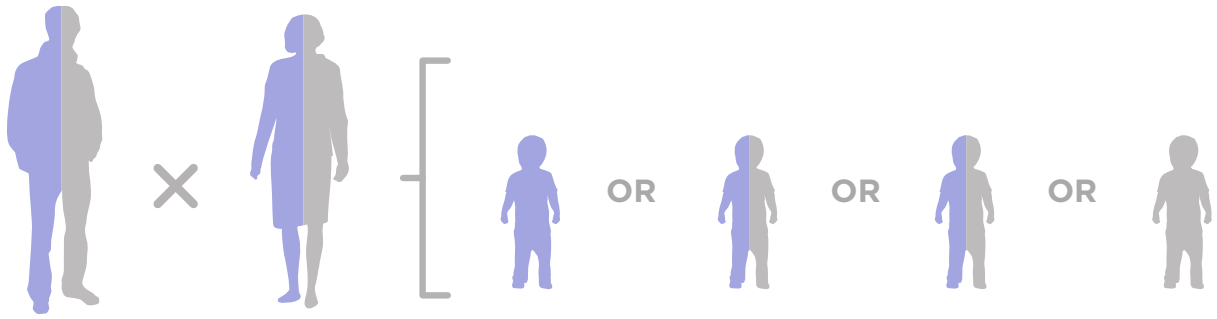
- Named after the *CLN2* gene, which is mutated in CLN2 disease[2]
- One of the most common forms of neuronal ceroid lipofuscinosis (NCL)[2]
  - NCLs are a group of disorders that are also known as Batten disease[3]
- Previously known as late-infantile NCL (LINCL), meaning that for most children, symptoms begin between the ages of 2 and 4[2]

CLN2 disease is an inherited disease that is passed down through families. Children with CLN2 disease are born with this condition, even though it may take months or years before they start showing signs. Diagnosis can be confirmed either through genetic or enzymatic testing.[2,4]

CLN2 disease is referred to as an autosomal recessive disorder[2]:

- Everyone has two copies of the *CLN2* gene (also called *TPP1* gene). In people with CLN2 disease, both inherited genes (one from each parent) have mutations
- Parents of a child with CLN2 disease have a mutation in one of their *CLN2* genes
- Parents are carriers of the genetic mutation, which means they are healthy but can pass on the mutation to their children
- If both parents carry the mutation and have a child, there is a
  - 25% chance that the child will inherit both mutations and be affected by CLN2 disease and experience symptoms
  - 50% chance that the child will be healthy, but they will also carry one mutation for CLN2 disease
  - 25% chance that the child will not carry any mutation for CLN2 disease and will not have CLN2 disease

WHEN BOTH PARENTS CARRY THE MUTATED FORM OF THE GENE, EACH OF THEIR CHILDREN HAS A 25% CHANCE OF BEING AFFECTED BY CLN2 DISEASE[2,5]



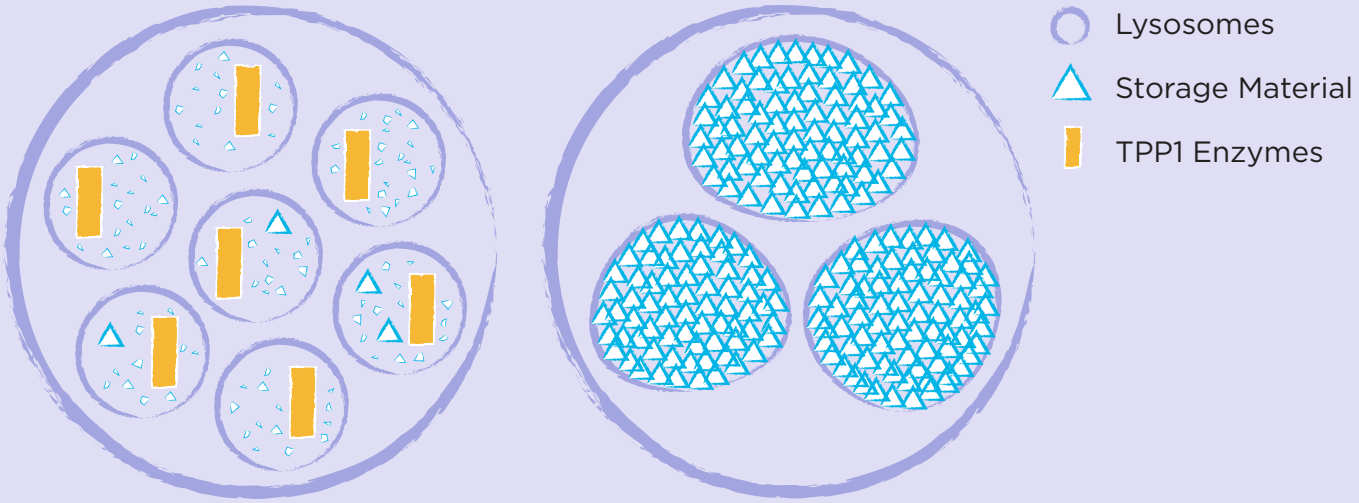
What is CLN2 disease? (continued)

CLN2 disease is a type of lysosomal storage disorder that affects cells in the brain[6]

There are lysosomes inside every cell. Lysosomes contain enzymes that break down material in the cell. One of these enzymes is called tripeptidyl-peptidase 1, or TPP1.[6]

The TPP1 enzyme is missing or not working properly in children with CLN2 disease. When this enzyme isn't working correctly, certain materials build up in the lysosomes of cells, particularly cells in the brain and the eyes.[3,7]

CLN2 DISEASE IS ASSOCIATED WITH A BUILD-UP OF MATERIALS INSIDE BRAIN CELLS[3]



HEALTHY CELL

In healthy brain cells, lysosomes use TPP1 to break down materials.[6]

CLN2 CELL

In CLN2 disease, the lysosome can't use TPP1 to break down materials. Instead, the lysosome stores materials. This build-up of materials is associated with damaging brain cells.[3,6]

Over time, cells stop functioning normally. As this happens, the symptoms of CLN2 disease (for example, language delay, seizures, loss of movement, and visual impairment) appear.[3]

How can I provide the best care for my child?

Children with CLN2 disease can experience a range of symptoms[8]

These symptoms may require specific types of care. Based on expert recommendations for the treatment of CLN2 disease, a child with CLN2 disease may be referred to see a variety of healthcare professionals, each specialising in a particular area.

There are a number of ways to optimise care for your child, which includes managing key symptoms of CLN2 disease, including seizures, movement disorders, nutritional concerns, and pain.

Seizure management[8]

Your doctor may use medications to manage seizures, one of the most common symptoms of CLN2 disease. There are many anti-epileptic drugs (AEDs) available to help manage seizures. However, some AEDs may be more effective than others in the treatment of seizures that are related to CLN2 disease. It is important to work closely with your doctor to find the right AEDs for your child.

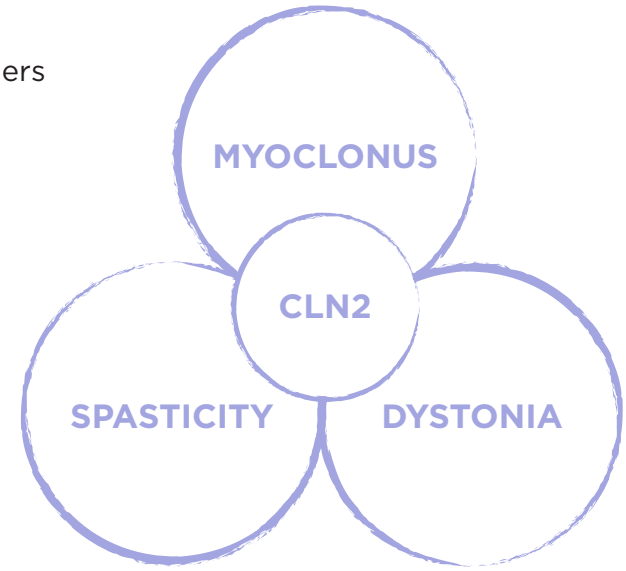
The goal of CLN2 seizure management should be to control seizures and minimise disabling or life-threatening seizures. Your doctor will work to find the medication(s) and dosage that best control seizure activity with minimal side effects.

Medication(s) should be reevaluated periodically. It is possible that medication(s) that worked well in the past may no longer work as well for your child.

Movement disorder management

Three of the most common movement disorders associated with CLN2 disease are[2,9]:

1. **Myoclonus**—a sudden, uncontrolled twitching of muscles[10]
2. **Dystonia**—uncontrolled muscle contractions[11]
3. **Spasticity**—increased muscle tone or muscle stiffness that interferes with movement or speech[12]



Experts agree that treatment should focus on reducing how often your child experiences these symptoms, lessening the severity of these symptoms, and preventing or relieving any pain children may experience.[8]

Certain medications and physical therapy may be used to help manage movement disorders. Your doctor may even recommend support equipment (an ankle brace) or items designed to adjust body posture (special pillows, a neck support, or a vest). Talk to your doctor about any movement disorder symptoms your child may be experiencing. You can work together to find a treatment that will best address your child's movement disorder symptoms.[8]

How can I provide the best care for my child? (continued)

Nutritional management

As CLN2 disease progresses, certain feeding and digestive issues may occur, including[2,7,8]:

- Swallowing difficulties
- Reflux (stomach acid flowing back into the food pipe, or oesophagus)
- Constipation

When caring for a child with CLN2 disease, it is important to keep them in good nutritional status, prevent deficiencies, and make sure they maintain an appropriate growth rate. Achieving these goals may require supplementing their diet with formula, vitamins, and minerals. To prevent constipation, it is important to include an appropriate amount of water and fibre in your child's diet, and consider medications that may help relieve this symptom.[8]

As swallowing difficulties increase, managing your child's secretions will become very important. Your doctor will recommend treatments and help you develop the right plan for your child.[8]

You and your doctor should discuss your child's nutritional status and any feeding abilities or restrictions you encounter. Together, you can identify potential issues and ways they can be addressed, such as special diets and other methods of feeding.[8]

Pain management[8]

CLN2 disease includes a range of symptoms, some of which may cause pain. The most common causes of pain are:

- Contractions/dystonia
- Spasticity/positioning problems
- Gastrointestinal (GI) symptoms such as reflux or constipation

As parents or caregivers, you play an important role in pain assessment. Your ability to read your child's reactions and/or signals can help your doctor find the cause of pain and treat painful symptoms appropriately. Sometimes, finding the cause of pain may take time and careful evaluation of different parts of the body may be required. Once the cause of pain has been identified, your doctor will provide recommendations for addressing any pain your child may experience.

How can I provide the best care for my child? (continued)

Incorporate physical therapy to address specific skills and symptoms[8]

Experts agree that children with CLN2 disease can benefit from physical therapy that has been adapted for the specific challenges they face. Talk to your doctor about developing a physical therapy plan specialised for CLN2 disease. Physical and occupational therapy should be started early to help your child maintain abilities for as long as possible.

Types of therapy[8]

- Physical—training that promotes comfort and extends independence through the use of therapy chairs (exercise their ability to sit upright) and standing devices (support muscle function and the ability to stand). Caregivers can learn exercises and positioning techniques that can be integrated into daily routines
- Occupational—exercises to help children maintain daily skills and activities of daily living
- Speech—early development of alternative communication methods, like symbols and gestures, can help prolong interaction after speech is lost
- Holistic—addresses the whole person (body, mind, and spirit) to decrease possible anxiety, pain, and boredom. Examples of holistic therapy include music classes and swimming

Beyond symptom management, there are other considerations to help support a child with CLN2 disease

EDUCATIONAL AND SOCIAL STRATEGIES CAN POSITIVELY IMPACT LIFE FOR CHILDREN WITH CLN2 DISEASE[8]

Maintaining regular school attendance is extremely valuable for children with CLN2 disease and their families. Children and their families benefit from the social interaction and the continued involvement in the community.

It may become difficult to communicate with your child as language, motor skills, and vision decline. To help you continue communicating with your child, experts suggest early development (when possible) and use of alternative communication methods like symbols and gestures.

Glossary[2,4-7,9-13]

Anti-epileptic drugs (AEDs)
Drugs that can help manage seizures.

Autosomal recessive disorder
A pattern of inheritance where 2 mutated genes (one from each parent) are passed to their child, which then causes a certain disease.

Batten disease
An extremely rare autosomal, recessive, neurodegenerative disorder that begins in childhood. It is named after Dr. Batten, who discovered the disease.

Carrier
Someone who only carries one mutated gene for an autosomal recessive disease, and therefore, does not have the disease.

CLN2 disease
A rare autosomal recessive disorder where lysosomes don't have enough of the TPP1 enzyme to break down materials in cells.

Dystonia
Involuntary muscle contractions that cause repetitive or twisting movements.

Enzyme
Proteins that cause reactions to occur in cells.

Genetic mutation
A permanent alteration to the genetic material in DNA.

Late-infantile
An age range that generally includes toddlers to very young children. This age range is used to describe when signs of a disease typically begin to appear.

Lysosome
Lysosomes are found within cells, and contain enzymes. One of their primary purposes is to recycle particles using enzymes.

Lysosomal storage disorder (LSD)
An inherited disease that is characterised by an abnormal build-up of various materials in lysosomes in the body's cells as a result of a reduced amount of a particular enzyme. Nearly 50 various types of LSD have been identified to date.

Myoclonus
Erratic, jerky contraction of groups of muscles.

Neuronal ceroid lipofuscinoses (NCLs)
A group of rare, genetic, neurodegenerative disorders.

Neurodegenerative
Having a decline or change in brain function.

Progressive disease
A disease that gradually increases in severity.

Spasticity
A condition in which certain muscles are continuously contracted. This contraction causes stiffness or tightness of the muscles.

Tripeptidyl-peptidase 1 (TPP1)
A reduced amount of this enzyme is what causes CLN2 disease.

How can I connect with others?

Connect with a growing community of support and advocacy for CLN2 disease and Batten disease

You are not alone—there are many support resources for families and caregivers of children with CLN2 disease. Caring for a child who has CLN2 disease can be emotionally and physically demanding. That's why finding other parents and professionals to talk to can make the disease easier to manage. If you have a child with Batten disease, these organisations welcome you and want to answer your questions.

Batten Disease Support and Research Association (BDSRA)

The BDSRA is committed to raising funds for research, providing family support services, enhancing education, raising awareness, and advocating for legislative action.

Learn more at www.battens.org.au

Visit www.CLN2family.com.au today for more information about CLN2 disease

This online resource is an additional resource in the CLN2 disease community that provides support for families and caregivers.

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