Unituxin®
(dinutuximab)
Injection

Education for parents and caregivers

Understanding your child's treatment with dinutuximab

Antibody therapy for pediatric high-risk neuroblastoma

UNITUXIN® (dinutuximab) INJECTION, FOR INTRAVENOUS USE

Indication

Unituxin is used to treat children with high-risk neuroblastoma who have had some success with prior first-line treatments. Granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA) are part of the treatment regimen with Unituxin.

Important Safety Information for Unituxin

Boxed WARNING

- Serious Infusion Reactions
  - Unituxin can cause serious and potentially life-threatening infusion reactions. These include excess fluid in tissue, noisy or difficult breathing, a feeling of narrowing in the throat, rash, and low blood pressure.
  - Tell your healthcare professional right away if you notice any of the following on the day of, or the day after, the infusion: facial or lip swelling, rash, difficulty breathing, lightheadedness, or dizziness. Patients who experience severe infusion reactions should stop receiving treatment with Unituxin.
- Neurotoxicity
  - Unituxin causes serious neurologic adverse reactions including severe neuropathic pain (nerve pain) and peripheral neuropathy (weakness, pain and/or numbness in hands, feet, legs or arms).
  - Severe neuropathic pain occurs in the majority of patients. Pain medication given prior to, during, and for 2 hours following treatment can help manage the pain.
  - Tell your healthcare professional about severe or worsening pain and signs and symptoms of neuropathy such as numbness, tingling, burning, or weakness experienced during treatment with Unituxin. Depending on the severity of pain, patients may need to stop treatment.

Please see Important Safety Information on pages 2 to 8 and Full Prescribing Information, including Boxed WARNING, for UNITUXIN in the pocket.

CONTRAINDICATIONS

Patients who are allergic to dinutuximab should not take Unituxin.

WARNINGS AND PRECAUTIONS

Serious Infusion Reactions

- In a clinical study, 35 (26%) patients taking Unituxin experienced severe (Grade 3 or 4) infusion reactions. Serious infusion reactions included swelling of the face and upper airway, difficult or abnormal breathing, bronchospasm, rash and hives, and low blood pressure. Urgent intervention included blood pressure support, bronchodilator therapy, corticosteroids, infusion rate reduction, infusion interruption, or permanent discontinuation of Unituxin.
- Infusion reactions generally happen during or within 24 hours after treatment with Unituxin. Tell your healthcare professional right away if you notice any signs or symptoms of serious infusion reactions, including facial or lip swelling, rash, difficulty breathing, lightheadedness, or dizziness, that occur during or within 24 hours following infusion. Your healthcare professional will decide whether treatment should be stopped temporarily or permanently.

Neurotoxicity

- ***Pain:***
  - Your healthcare professional will administer medication before, during, and after treatment to help manage pain. Tell your healthcare professional right away about any severe or worsening pain.
  - In a clinical study, 114 (85%) patients taking Unituxin experienced pain despite pre-treatment with pain medicine including morphine sulfate infusion. Severe (Grade 3) pain occurred in 68 (51%) patients taking Unituxin compared to 5 (5%) patients who were not taking Unituxin. Pain typically occurred during the Unituxin infusion and was most commonly reported as stomach pain, generalized pain, pain in the arms or legs, back pain, nerve pain, muscle and bone pain of the chest, and joint pain.
  - If severe pain is experienced, your healthcare professional may reduce the speed at which Unituxin is given. Unituxin may be stopped if pain is not adequately controlled through medical intervention.

Important Safety Information for Unituxin (continued)

- ***Peripheral Neuropathy:***
  - Symptoms of neuropathy (may include numbness, tingling, burning), or weakness. Report any signs or symptoms of neuropathy immediately to your healthcare provider.
  - In a clinical study, severe (Grade 3) peripheral sensory neuropathy occurred in 2 (1%) patients and severe peripheral motor neuropathy occurred in 2 (1%) patients taking Unituxin compared to zero patients who were not taking Unituxin.
  - Treatment with Unituxin may need to be permanently discontinued in patients with Grade 2 peripheral motor neuropathy, Grade 3 sensory neuropathy that interferes with daily activities for more than 2 weeks, or Grade 4 sensory neuropathy.
- ***Neurological Disorders of the Eye:***
  - Neurological disorders of the eye can be serious. Tell your healthcare professional immediately if you experience blurred vision, sensitivity to light, drooping of the upper eyelid, double vision, optic disc swelling, or fixed or unequal pupil size as these can be signs and symptoms of a neurological disorder of the eye. Patients who experience neurological disorders of the eye may need to have the Unituxin dose reduced or permanently stopped.
  - In clinical studies, neurological disorders of the eye experienced by 2 or more patients treated with Unituxin included blurred vision, sensitivity to light, dilated pupils, an inability to move the eyelid, fixed or unequal pupils, optic nerve disorder, drooping of the eyelid, and swelling.
- ***Prolonged Urinary Retention:***
  - Urinary retention (inability to completely empty the bladder) that persists for weeks to months after stopping opioids has occurred in patients treated with Unituxin. Report to your healthcare provider persistent urinary retention that does not resolve after having stopped opioid therapy. If you experience prolonged urinary retention, your healthcare professional will decide whether treatment should be stopped.

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- ***Transverse Myelitis:***
  - Transverse myelitis has occurred in patients treated with Unituxin. Symptoms may include weakness, tingling or burning sensation, reduced sensation, or inability to control urine. Report signs or symptoms of transverse myelitis immediately to your healthcare provider. Your healthcare professional will determine if you have transverse myelitis and stop treatment as necessary.
- ***Reversible Posterior Leukoencephalopathy Syndrome (RPLS):***
  - RPLS is swelling in the back part of the brain. It has occurred in patients treated with Unituxin. Symptoms may include severe headache, high blood pressure, change in vision, feeling drowsy or tired, or seizures (fits). Report signs or symptoms immediately to your healthcare provider. Unituxin may be stopped in patients with signs and symptoms of RPLS.

Capillary Leak Syndrome

- Capillary leak syndrome is a potentially life-threatening condition in which fluid and proteins leak out of tiny blood vessels and flow into surrounding tissue. This leads to dangerously low blood pressure. If severe capillary leak syndrome is experienced, the speed at which Unituxin is given may need to be interrupted, reduced, or permanently stopped.
- Signs and symptoms of capillary leak syndrome include swelling of the arms, legs, and other parts of the body; shock; lightheadedness; weakness; fatigue; nausea; and rapid drop in blood pressure. Immediately report any signs or symptoms of capillary leak syndrome to your healthcare professional.
- In a clinical study, severe (Grades 3 to 5) capillary leak syndrome occurred in 31 (23%) patients taking Unituxin and in no patients who were not taking Unituxin.

Low Blood Pressure

- In a clinical study, 22 (16%) patients taking Unituxin experienced severe (Grade 3 or 4) low blood pressure. Fluids will be given by your healthcare professional prior to treatment with Unituxin. Blood pressure should be watched closely during Unituxin treatment. Tell your healthcare professional right away if you experience any changes in breathing, dizziness or lightheadedness, fainting, or dehydration (symptoms may include unusual thirst, urinating less often than usual, dark colored urine, dry skin, or tiredness). Patients who get low blood pressure may need to have the speed at which Unituxin is given reduced or permanently stopped.

Important Safety Information for Unituxin (continued)

Infection

- In a clinical study, 17 (13%) patients experienced severe (Grade 3 or 4) bacteremia that required urgent intervention, and 24 (18%) patients experienced sepsis. Closely monitor for signs and symptoms of systemic infection such as fever or tiredness. Tell your healthcare professional if you notice any signs of an infection.
- Patients who develop systemic infection will need to temporarily stop treatment with Unituxin until the infection resolves.

Bone Marrow Suppression

- Patients taking Unituxin may have slow blood clotting. This is due to a lowering of the number of platelets in the blood. Unituxin may also cause low red blood cell count (anemia) and low white blood cell count. This may make patients more likely to develop an infection.
- In a clinical study, severe (Grade 3 or 4) platelet deficiency (39% vs. 25%), low red blood cell count (34% vs. 16%), low white blood cell count (34% vs. 13%), and fever along with a low white blood cell count (4% vs. 0 patients) occurred more commonly in patients who were taking Unituxin than in patients who were not taking Unituxin.

Electrolyte Abnormalities

- In a clinical study, electrolyte abnormalities occurring in at least 25% of patients who received Unituxin included low levels of sodium, low levels of potassium, and low levels of calcium in the bloodstream. Your healthcare professional will monitor these levels. Tell your healthcare professional about any seizures; a feeling that the heart is beating too hard or too fast, skipping a beat, or fluttering; or muscle cramping.

Atypical Hemolytic Uremic Syndrome

- Patients taking Unituxin may experience kidney problems, electrolyte abnormalities, low red blood cell count, or high blood pressure. Patients who experience these side effects may need to permanently stop treatment with Unituxin. Tell your healthcare professional about any fatigue, dizziness, fainting, extreme skin paleness, swelling, less urine output than normal, or blood in the urine.

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Tell your healthcare professional if you are pregnant before taking Unituxin.

- Unituxin may cause harm to an unborn child. Women who are taking Unituxin should use effective birth control measures during treatment and for 2 months after the last dose of Unituxin.

COMMON SERIOUS ADVERSE REACTIONS

The following is a list of the most common serious adverse reactions seen in 5% or more of patients taking Unituxin:

- Infections
- Infusion reactions
- Low levels of potassium in the blood
- Low blood pressure
- Pain
- Fever
- Capillary leak syndrome (a potentially life-threatening condition in which fluid and proteins leak out of tiny blood vessels and flow into surrounding tissue, leading to dangerously low blood pressure)

COMMON ADVERSE REACTIONS

The following is a list of the most common adverse reactions seen in 25% or more of patients taking Unituxin:

- Pain
- Fever
- Slow blood clotting
- Reduced ability to fight infections (low levels of white blood cells of various kinds)
- Infusion reactions
- Low blood pressure
- Low levels of sodium in the blood
- Increased levels of the enzyme alanine aminotransferase in the blood
- Low red blood cell count
- Vomiting
- Diarrhea
- Low levels of potassium in the blood
- Capillary leak syndrome
- Hives
- Low levels of albumin in the blood
- Increased levels of the enzyme aspartate aminotransferase
- Low levels of calcium in the blood

Important Safety Information for Unituxin (continued)

The following side effects have also been observed in patients taking Unituxin after approval: prolonged urinary retention (inability to completely empty the bladder), transverse myelitis, and reversible posterior leukoencephalopathy (swelling in the back part of the brain).

Tell your healthcare professional about any side effect seen during treatment with Unituxin. These are not all the possible side effects of Unituxin. For more information, talk to your healthcare professional.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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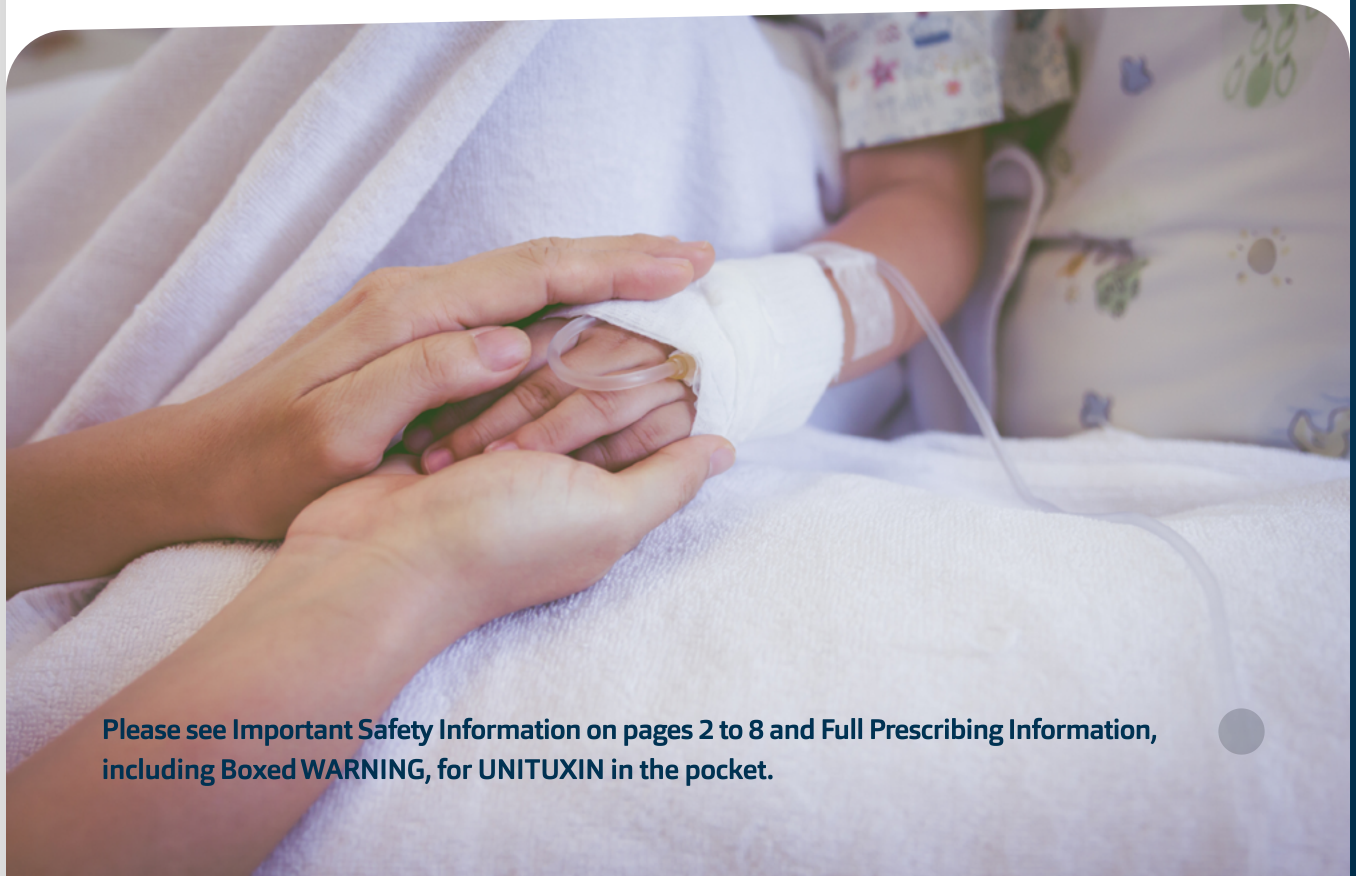


Introduction

United Therapeutics Oncology is your partner during your child's treatment for high-risk neuroblastoma. Through materials like this book, we hope to give you key information and resources that can help answer any questions you may have and prepare you for the treatment journey.

This book is intended for informational purposes only and is not intended as treatment advice. It is not meant to replace conversations with your child's healthcare team. You should reach out to them with any questions you have regarding your child's treatment. Your child's healthcare team is your main source of information about your child's care and treatment.

Table of contents

CHAPTER 1

Overview of high-risk neuroblastoma treatment

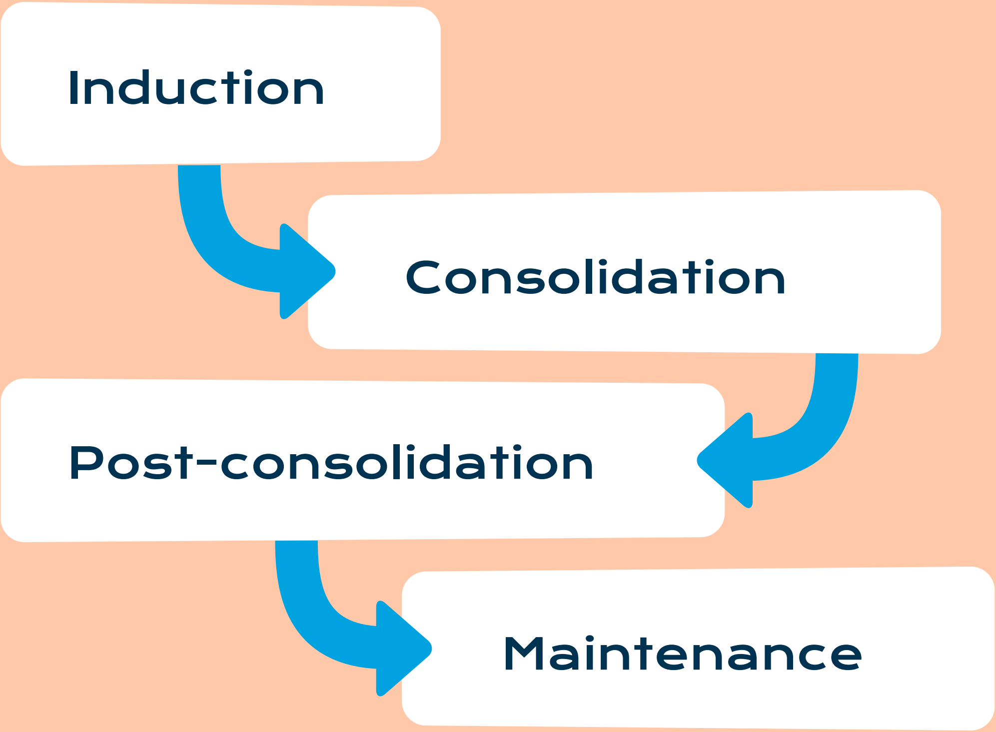
> “Once a treatment plan is established, families start to be able to **adapt to a new life** because they have an understanding about what has to take place—because now you have a plan to be able to **go forward**.”
>
> **—Dr Lori Wiener, PhD**
>
> *Head of the Psychosocial Support and Research Program at the National Cancer Institute*

Understanding the phases of neuroblastoma treatment

Neuroblastoma treatment has changed a lot over the years—and it continues to improve as doctors learn more. Today, treatment usually involves a combination of therapies that work together to give children the best chance of getting better.

Because high-risk neuroblastoma is a complex cancer, doctors use several types of treatment over many months. These treatments are grouped into phases.

Treatment phases



If you have questions about treatment options and available clinical trials, ask your child's doctor right away.

Neuroblastoma treatment options

Depending on your child's disease, they may get some or all of the treatments listed below. The care team will make the treatment plan based on your child's individual needs.

Chemotherapy (chemo)	Strong medicine to stop cancer cells from growing. It can also affect some healthy cells, which may cause side effects
Antibody therapy	Helps the body's immune system find and remove cancer cells
Surgery	Also known as "local control" or "resection," surgery removes the tumor (as much as possible)
High-dose chemo + stem-cell transplant	Very strong chemo is used to kill any remaining cancer cells. This also affects healthy cells in the bone marrow Before treatment, your child's own stem cells are collected. After the chemo, the stem cells are given back to help their body recover. This is called a stem-cell transplant
Radiation	Targets cancer cells by using high-energy rays or particles
Other targeted therapies	• DFMO (difluoromethylornithine) is an FDA-approved therapy that may help prevent relapse by blocking signals that cancer cells need to grow • Investigational—*ALK* inhibitors* • Investigational—MIBG (metaiodobenzylguanidine)*

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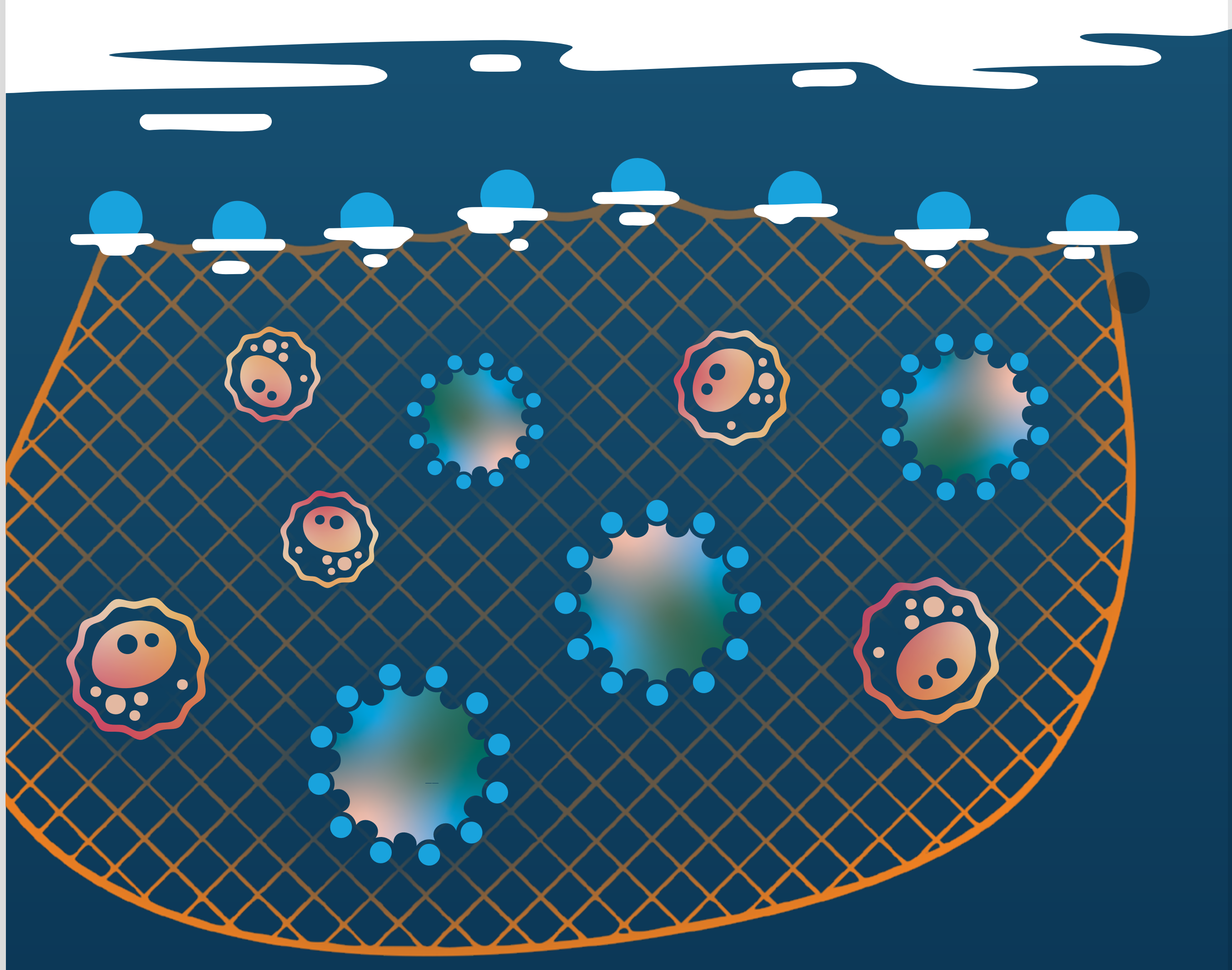
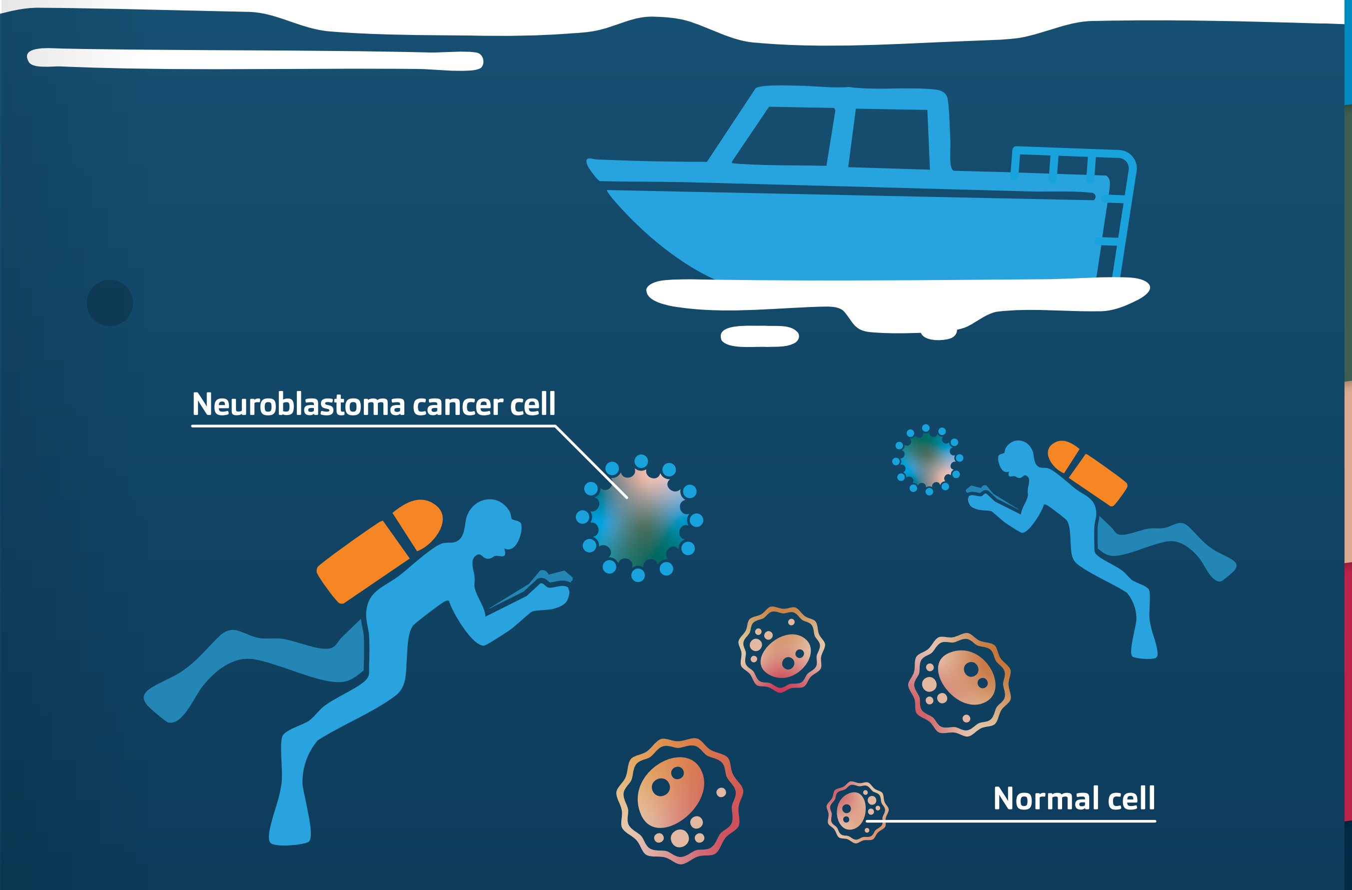
*The safety and efficacy of these investigational products have not been established, and these products have not received FDA approval.

How is antibody therapy different from chemotherapy?

Chemotherapy and antibody therapy are often mistaken for one another. Chemotherapy is like a net for cleaning up trash floating in a lake. It can catch the trash (cancer cells), but also friendly fish (normal cells). Since chemotherapy cannot tell them apart, normal cells, like hair cells, can be damaged.

Antibody therapy is different from chemotherapy. **Antibodies can find and flag cancer cells and let the body's immune system know to attack them.** Antibodies are like a team of divers. The divers will find and flag trash (cancer cells) for the ship (immune system) to pick up.





Most normal cells will recover from chemotherapy over time, but cancer cells usually will not, so chemotherapy is still a helpful option

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CHAPTER 2

How dinutuximab treatment works

Dinutuximab is an antibody that targets cancer cells

Dinutuximab is a monoclonal antibody therapy, meaning it uses the immune system to help it fight cancer cells. Use the “three F’s” to help you remember that dinutuximab **Finds**, **Flags**, and **Fights** cancer. It also can cause side effects that your child may feel.

1) Find the cancer

Neuroblastoma cancer cells can hide from the body’s defense system (the immune system). These cancer cells have a protein called GD2 on their surface. The dinutuximab antibody finds neuroblastoma cancer cells by sticking to the GD2 protein.

2) Flag the cancer

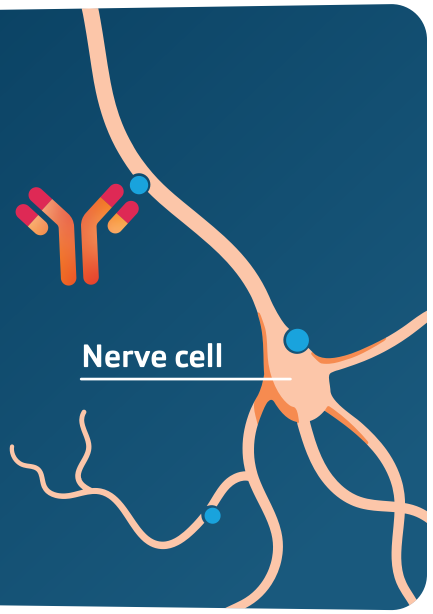
Once dinutuximab sticks to the cancer cells, it flags them so the body’s immune system can find them. This helps the body know where to respond.

3) Fight the cancer

Once the body’s immune system finds the cancer cells, it works to kill them.

Dinutuximab helps get rid of neuroblastoma cells, but it can cause side effects. Some other cells in the body also have GD2, including normal nerve cells. Dinutuximab may stick to these nerve cells, which can cause pain. This is why all patients get pain medicine before and during the infusion.

If severe pain is experienced, your healthcare professional may reduce the speed at which dinutuximab is given. Dinutuximab may be stopped if pain is not adequately controlled through medical intervention.



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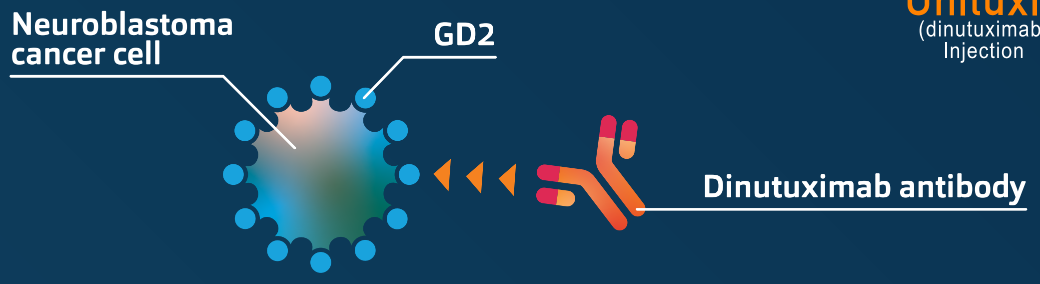
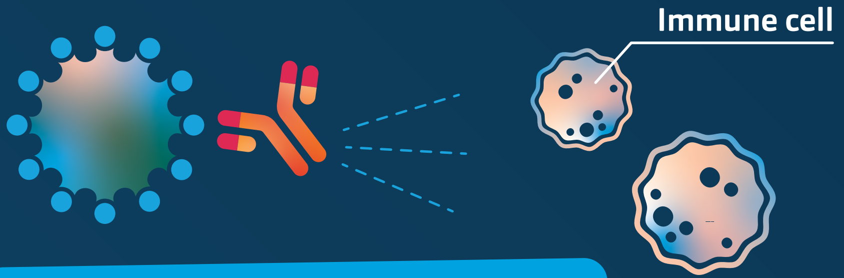
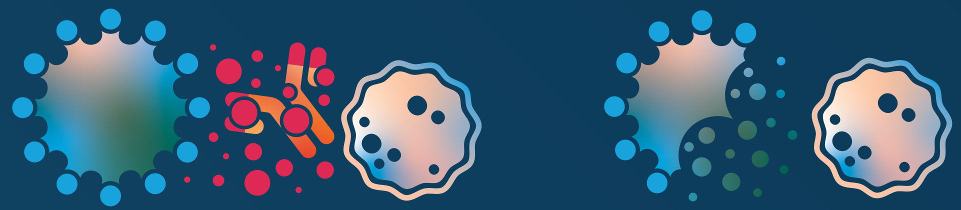


1 Find *Dinutuximab finds and sticks to GD2*



2 Flag *Dinutuximab flags the immune cells to the cancer cell*



3 Fight *Immune cells release proteins that target the cancer cells* ▶ *Then the cancer cell is killed*

View more information, including videos, on how dinutuximab antibody therapy works.

CHAPTER 3

The science and research behind dinutuximab

> “The **collaborative nature** of pediatric oncology is one of my favorite things about what I do…In the pediatric oncology world…we have to all **work together**.”
>
> **—Dr Tanya Carens Watt**
>
> *Pediatric Oncologist*

Why is dinutuximab a trusted treatment option?

It's important to know that your child's treatment has a known safety profile, works well, and has been well studied. Doctors have tested dinutuximab for many years and recommend it for high-risk neuroblastoma.* This chapter will explain why dinutuximab is a trusted treatment option.

Dinutuximab is **tested and trusted** for benefit and safety. This is shown by:

- **Recommendations by national guidelines**
- **Demonstrated benefit**
- **A well-established safety profile**

For more information on side effects and safety with dinutuximab, please see chapter 5, **Side effects and late effects**.

*Dinutuximab was approved in March 2015 by the Food and Drug Administration (FDA) for treating pediatric high-risk neuroblastoma in patients who achieve at least a partial response to prior first-line therapy.

You might hear or see "**dinutuximab**" and "**UNITUXIN**" used together. They are the same treatment

Serious infusion reactions: In a clinical study, 35 (26%) patients taking Unituxin experienced severe (Grade 3 or 4) infusion reactions. Serious infusion reactions included swelling of the face and upper airway, difficult or abnormal breathing, bronchospasm, rash and hives, and low blood pressure.

Dinutuximab is recommended by experts

FDA approved for 10 years

Dinutuximab was approved in March 2015 by the FDA for treating pediatric high-risk neuroblastoma in patients who achieve at least a partial response to prior first-line therapy. This approval is based on strong research that shows improved survival rates and an acceptable safety profile. While all treatments have some risks, dinutuximab is backed by scientific evidence and real-world use.

National Comprehensive Cancer Network® (NCCN) recommended

- The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroblastoma are developed and updated by a multidisciplinary panel of clinicians and oncology researchers with expertise in neuroblastoma. The NCCN Guidelines document evidence-based, consensus-driven management to ensure that all patients receive preventive, diagnostic, treatment, and supportive services that are most likely to lead to optimal outcomes
- The NCCN Guidelines recommend a dinutuximab-based regimen as a treatment option for patients with high-risk neuroblastoma

Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Neuroblastoma V.1.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed May 20th, 2025. To view the most recent and complete version of the guideline, go online to **NCCN.org**.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Learn more about how we tested dinutuximab.

Balancing survival benefits with side effects

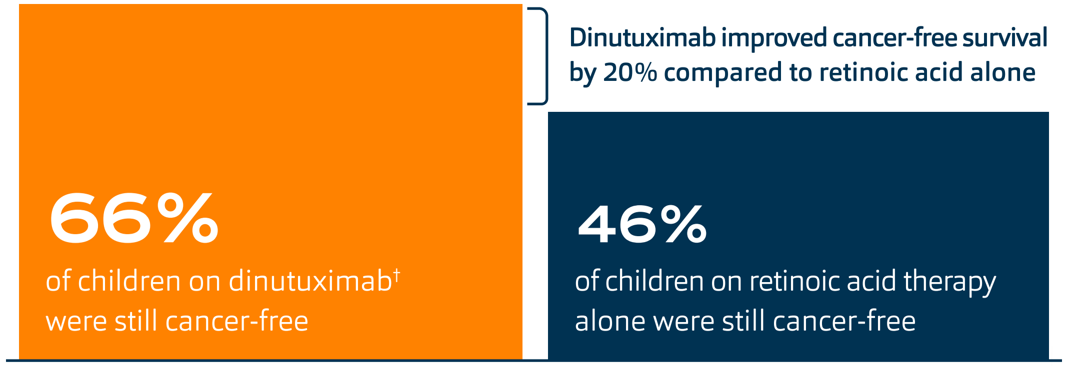
While dinutuximab improves survival, it can cause side effects that may be manageable with the right medical support. Your child's care team is trained to keep them as safe and comfortable as possible. Parents and caregivers also play a key role in looking out for side effects—ask your care team how you can help.

For more information on side effects, please see chapter 5, **Side effects and late effects**.

Key data from the ANBL0032 study

In the ANBL0032 study,* dinutuximab was proven to be a safe treatment that helped more kids stay cancer-free for longer. This study was randomized and controlled, which provides the most reliable results. It included **226 children** who had been through the first two treatment phases (induction and consolidation). **Half of those children (113)** received 5 cycles of dinutuximab (plus 5 cycles of alternating cytokines and 6 cycles of retinoic acid), while the rest received the standard treatment at the time of the study, 6 cycles of retinoic acid alone.

2 year event-free survival rates: staying cancer-free for longer



Dinutuximab improved cancer-free survival by 20% compared to retinoic acid alone

66%
of children on dinutuximab[†] were still cancer-free

46%
of children on retinoic acid therapy alone were still cancer-free

Event-free survival (EFS) is how long a child stays cancer-free without their cancer getting worse or causing serious problems. EFS helps doctors see that the cancer is under control.

The most common adverse drug reactions (≥25%) are pain, pyrexia, thrombocytopenia, lymphopenia, infusion reactions, hypotension, hyponatremia, increased alanine aminotransferase, anemia, vomiting, diarrhea, hypokalemia, capillary leak syndrome, neutropenia, urticaria, hypoalbuminemia, increased aspartate aminotransferase, and hypocalcemia.

*The ANBL0032 study was conducted by the Children's Oncology Group from October 2001 to January 2009 at 166 hospitals. The study enrolled 1449 patients, and 226 of those patients were randomized to receive the dinutuximab antibody therapy regimen or treatment with retinoic acid alone. Randomization occurred after patients completed induction chemotherapy, stem-cell transplant, and radiation therapy. This study was published in an article under the title, "Anti-GD2 antibody with GM-CSF, interleukin-2, and isotretinoin for neuroblastoma" in *The New England Journal of Medicine* in 2010.

[†] In combination with cytokines (GM-CSF, IL-2) and retinoic acid.

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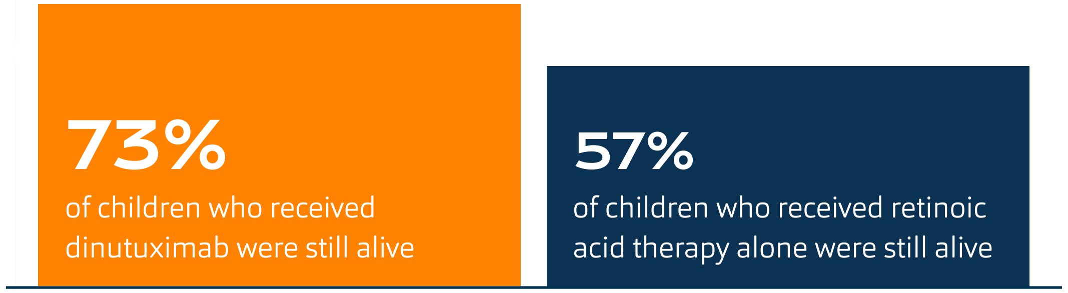
5-year survival: more children living longer

Children who got dinutuximab (in the ANBL0032 study) were more likely to stay cancer-free for a longer time. Because of this, children who first got retinoic acid alone were later switched to the dinutuximab treatment plan to give them a better chance of staying cancer-free.

At 5 years after treatment:

6 out of 10

children who initially received dinutuximab* were still cancer-free



These findings provide strong evidence that dinutuximab plays a critical role in helping children stay in remission and live longer.

Overall survival (OS) is how long a child lives after diagnosis or starting treatment, **no matter what happens with their cancer**. Improved OS shows a treatment helped children live longer, even if their cancer came back or they needed more treatment.

The most common serious adverse reactions (reported in ≥5% of patients) are infections, infusion reactions, hypokalemia, hypotension, pain, fever, and capillary leak syndrome.

*In combination with cytokines (GM-CSF, IL-2) and retinoic acid.

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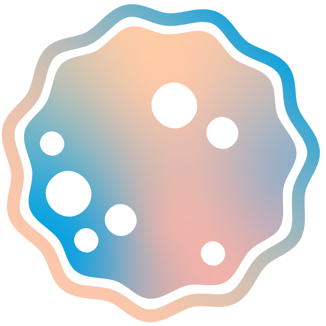
Learn more about how we tested dinutuximab.

CARE with dinutuximab: Over 3500 patients treated

When it comes to dinutuximab, CARE is key. Use the CARE chart to help your family feel more comfortable about your child's treatment.

C	Children with high-risk neuroblastoma treated with dinutuximab have improved outcomes
A	Approved by the FDA for 10 years and recommended by experts based on nearly 25 years of research and use in real practice
R	Research shows dinutuximab helped improve long-term outcomes
E	Experienced healthcare teams are familiar with dinutuximab and can support your child during the treatment process



CHAPTER 4

What to expect before, during, and after treatment with dinutuximab

> “One thing that I would do to prime Leah when we would go to the hospital is, **turn the music up** and **just start dancing** in the hospital to prepare her for what she was about to go into. I call it **putting on her game face**.”

—Devon Still

Former NFL player and father of Leah, a high-risk neuroblastoma survivor

Scan the code to learn about Devon and Leah’s story.

Contents
Overview
How dinutuximab treatment works
The science and research
What to expect

What to expect before treatment

Knowing what to expect can help make things a little easier. Learn more about the things you can do to feel ready and confident:

Pause and review

Pack for comfort

Plan with your family

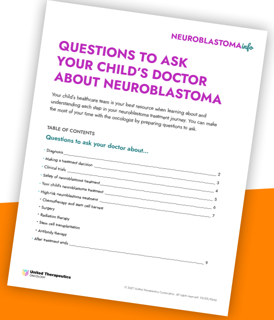
Prepare your child for treatment

Pause and review

Review important documents and write down any questions. Feel encouraged to bring up all your questions to your child's doctor.

Some examples:

- ✓ What side effects should we watch for?
- ✓ How long will the infusion take?
- ✓ How can I best support my child during this treatment?



NEUROBLASTOMA
QUESTIONS TO ASK YOUR CHILD'S DOCTOR ABOUT NEUROBLASTOMA

Our free "Questions to Ask Your Child's Doctor" worksheet has helpful questions for each step of your child's treatment. It can help you talk to the care team.

Scan to see the "Questions to Ask Your Child's Doctor" worksheet.

Side effects
Coping and support
Glossary

Pack for comfort

Pack essentials and familiar items for comfort, like toys or blankets. Items that bring comfort can help your child cope with treatment and make the hospital feel more like home.

- ✓ Pack familiar items, like your child's favorite stuffed animal, book, or toy, to help make the hospital feel more like home
- ✓ Don't forget your own essentials, such as medications, comfortable clothes, a water bottle, and a phone charger
- ✓ Bring a pillow and blanket from home for both you and your child for extra comfort
- ✓ Consider slippers or easy-to-slip-on shoes for you and your child

Plan with your family

Making a plan for your family while your child is in the hospital can help them keep calm. It's important to share tasks when possible and ask for help.

- ✓ Plan who will stay with your child in the hospital
- ✓ Talk to your child's siblings about what they can expect to help them feel prepared
- ✓ Arrange help for siblings, like childcare or meals, from friends or relatives
- ✓ Check if your child's medications need refills so you can let your child's care team know

To stay organized, consider using a calendar to keep track of appointments and notes.

Request the "Neuroblastoma Journey Calendar" here.

Prepare your child for treatment

Explaining the treatment process to your child can be hard, especially if you're unsure what's appropriate for their age. If it feels hard to explain, nurses or child life specialists at the hospital can help you find the right words.

✓ **Start by asking your child if they have any questions or worries about their treatment**

- This can help you know what to talk about and how to reassure them
- Let your child know it's okay to ask questions or share their worries while you're at the hospital

✓ **Keep your explanation simple and comforting. Older kids might want more details, so share what feels right for their age**

- Remind them they're not alone—you, their family, friends, and care team are all there to help
- Celebrate the little wins, like your child taking their medicine. Create a safe space for them to share their feelings

For more detailed coping strategies, see chapter 6.

Our free children's book explains antibody therapy—which targets neuroblastoma cancer cells—in a simple, child-friendly way. This book can help make tough topics easier for kids.

Scan the code to download *The Next Big Adventure of Little Skivolo*.

What to expect during treatment

Treatment day can feel overwhelming, but your care team knows what to do and has helped many kids before. They are there to guide you and take good care of your child.

Overview of the infusion process

STEP 1:
Checking into the hospital

STEP 2:
Pre-medication

STEP 3:
Starting the antibody infusion

STEP 1

Checking into the hospital

When you arrive at the hospital, your child will get checked in to a hospital room. The nurses will be there to help them feel safe and comfortable. They will check your child's vital signs, do a physical exam, and may draw some blood.

The care team will then walk you through your child's treatment plan. Don't hesitate to ask questions about the process.

For more details about the types of side effects your child may have, see chapter 5, **Side effects and late effects**.

STEP 2

Pre-medication

Before the infusion starts, your child will be given medicine called "pre-medications," or "**pre-meds**," to help with side effects. Some of the medicines may make your child feel sleepy, which is normal. These medicines may include:

- ✓ Fluids through an intravenous (IV) tube
- ✓ Medicine for pain, fever, or other reactions your child might have during the infusion. **The pre-meds for these side effects, as well as others, may continue to be given throughout the infusion**

STEP 3

Starting the antibody infusion

Once the pre-meds are done, the antibody infusion will start. The medicine is usually given through a central line. It will infuse slowly over 10 to 20 hours. The care team will watch your child's vital signs (blood pressure, temperature, oxygen levels, and heart rate). They are there to try to keep your child safe and comfortable every step of the way.

If side effects happen, the care team can slow or stop the antibody infusion or give medicines to help.

Many side effects improve by slowing down the infusion rate, so don't be concerned if the infusion is slowed down or stopped because of side effects

What to expect after the antibody infusion

When the infusion is finished, the care team will watch your child closely to make sure they are doing well before sending you home.

You'll get important information about anything your child might need after antibody therapy:

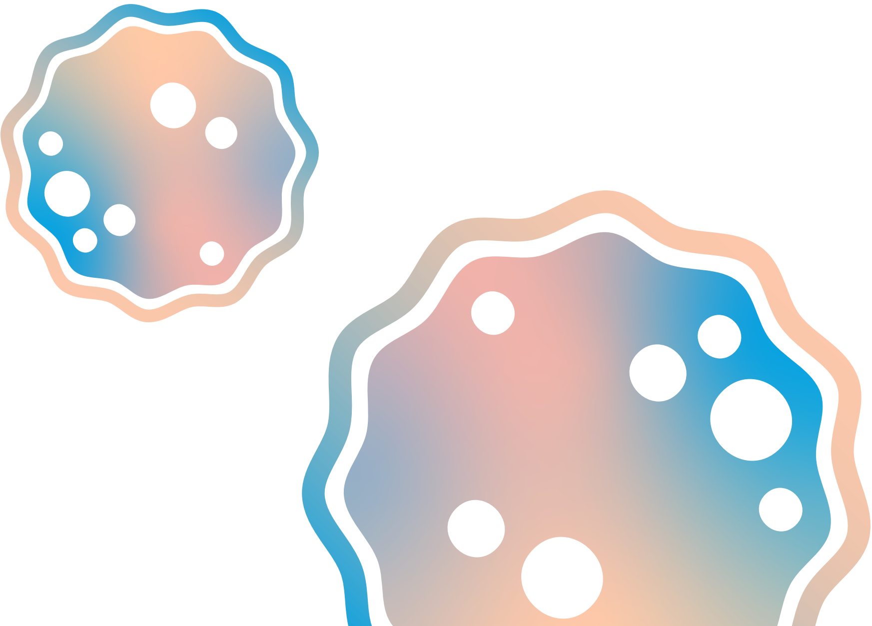
- Medicines to give at home
- Date and time of your follow-up appointment and schedule for your next antibody cycle
- A phone number to call if you have questions

Follow-up

After going home, your child will have follow-up visits at the oncology clinic. During these visits, the care team will check to see how your child is doing and talk with you about what comes next in your child's care.

Your child may need to have additional blood drawn, so prepare them in advance.

Remember, the care team is just a phone call away to help with any questions or concerns you may have while at home



Taking the next step together

Antibody therapy can feel like a lot, but you are not alone. Your care team is here to help you every step of the way. By knowing what to expect and planning ahead, you can make this process easier for you and your child—one step at a time!

CHAPTER 5

Side effects and late effects

"Any little bit of hope that you can hold on to is so powerful to help you get to the end of this journey... I want people to see the ups and downs that we experienced and how **we came out on the other side**."

—Devon Still

Former NFL player and father of Leah, a high-risk neuroblastoma survivor

Understanding side effects with dinutuximab

During and after treatment, your child can expect to feel side effects. The care team will try to keep your child as comfortable as possible. Knowing what to expect can help you support and reassure your child throughout the process.

Supporting your child throughout treatment is a team effort, so ask the care team about your concerns.

Common side effects

It's important to know about the side effects that could occur with dinutuximab. Here are the side effects that at least 1 out of 4 patients have experienced:

General side effects

Pain, fever, low blood pressure, and infusion reactions

Blood-related side effects

Low levels of sodium, potassium, calcium, and albumin, as well as low counts of platelets and white and red blood cells. May also include increased liver enzyme levels

Gastrointestinal side effects

Vomiting and diarrhea

Skin-related side effects

Hives or rash

Some side effects of dinutuximab may require your child's infusion to be slowed, paused, or even stopped until they have resolved. Dinutuximab infusion may have to be permanently stopped in some cases

Pain

Pain is the most common side effect of treatment with dinutuximab (reported in 85% of patients) and all other GD2 antibodies.

Dinutuximab can stick to healthy nerve cells that also have GD2, which can cause pain. To help with this, patients are given pain medicine before the infusion and during the infusion.

Pain usually goes away once the antibody infusion is finished.

How the care team can help

Before the antibody infusion	The care team will give pain medicine (such as morphine) to help. This is a safe way to treat pain and make sure your child is comfortable.
During the antibody infusion	Pain is monitored throughout the infusion. Pain medication may need to be adjusted or increased for better pain control. **If severe pain is experienced:** The antibody infusion may be slowed or stopped.

It can be very hard for a child to explain the type of pain they are feeling. **Speak up** if you notice that your child is uncomfortable.

Infusion reactions

Infusion reactions are similar to allergic reactions. Your child may show signs of mild-to-severe symptoms. Their skin may show rashes or hives. They may cough, wheeze, or have difficulty swallowing or breathing. Their face may swell up, and they may shiver or have a fever.

How the care team can help

Before the antibody infusion	The care team will give medicine(s) (such as diphenhydramine) to help prevent reactions.
During the antibody infusion	Your child will continue to get medicine to help with reactions from the antibody infusion. **If a serious reaction is experienced:** The antibody infusion may be paused, slowed down, or stopped.

Let the care team know if your child has a **rash**, is **coughing**, has **swollen lips or face**, **cannot breathe**, or if you are worried about any other symptoms.

Fever

Fever is a common side effect. Your child's skin may feel warm or hot to the touch, and they may be sweating or shivering.

How the care team can help

Before the antibody infusion	The care team will give medicine (such as acetaminophen) to help prevent a fever.
During the antibody infusion	Your child's temperature will be checked often, and they will continue to get medications to help with fever. The care team also will follow their hospital guidelines for handling fever (which may include blood cultures and/or antibiotics).

Report symptoms right away if your child appears **feverish**, is **sweating**, or is **shivering.**

Low blood pressure

Low blood pressure is also known as "hypotension." It can be a direct side effect of the dinutuximab infusion or a sign of capillary leak syndrome (see next page). Your child may feel dizzy, nauseous, or lightheaded.

How the care team can help

Before the antibody infusion	The care team will give IV fluids to help prevent low blood pressure.
During the antibody infusion	The care team will check your child's blood pressure often during the antibody infusion. If it gets too low, they may slow, pause, or stop the antibody infusion.

Tell the care team right away if your child feels **dizzy**, **lightheaded**, or **nauseous.**

Capillary leak syndrome

Capillary leak syndrome happens when tiny blood vessels (capillaries) let fluid leak into different parts of the body instead of keeping it in the bloodstream. It develops slowly but can become serious. It's important to let the care team know if you notice the signs shown below.

How the care team can help

Before the antibody infusion	The nurse may ask you how much your child usually drinks and how much they are peeing.
During the antibody infusion	The care team will closely check your child's vital signs, weight, and how much they are drinking and peeing. If capillary leak syndrome happens and is serious, the antibody infusion may be paused, slowed, or stopped.

Let the care team know if your child has any **swelling**, is **not peeing**, or if they feel **lightheaded**, **dizzy**, **or weak.**

Long-term and late effects with high-risk neuroblastoma treatment

Long-term effects were not seen with dinutuximab.

Side effects from other treatments could affect your child later in life. It's normal to worry about these side effects, but it may be helpful to know that the long-term efficacy and safety findings were published in the *Clinical Cancer Research* medical journal, and it was found that even though there are side effects during the dinutuximab infusion, they will usually resolve with time.

How are long-term and late effects different?

Long-term effects	Late effects
• Side effects from treatment that **don't go away** when treatment is complete	• Side effects that show up years later after treatment is complete

Learn more about late effects with other neuroblastoma therapies.

Managing long-term and late effects with follow-up care

Long-term effects from neuroblastoma treatments may worry you and your child. To help, your child will have long-term checkups with healthcare specialists.

These checkups are called "survivorship care." They usually start 2 or more years after treatment ends.

Supporting your child's long-term follow-up care

Use the STAR chart below to help your child shine like a STAR as they grow up and take charge of their own health.

S	Share all medical information with your child's doctor
T	Teach your child that they should speak to their doctor if they feel late effects develop
A	Ask your child's care team for long-term follow-up care suggestions. These could include seeing doctors at your child's current hospital or follow-up care programs
R	Request your child's treatment summary to help your child's future doctors give the best care they can

After treatment is complete, care teams will continue to closely watch your child's health as they grow up.

> "Long-term follow-up care is extremely important for NBL patients… there's so much research going into how we detect some of these long-term side effects and how we help to manage them."
>
> **—Dr Tanya Carens Watt**
>
> *Pediatric Oncologist*

CHAPTER 6

Tips for coping and support resources

> "I think that **self-care** for the caregivers and parents is a vital piece to the **success** of their child, really through this entire process."
>
> **—Stacy Ettinger, APRN, PNP-AC/PC**
>
> *Nurse practitioner, Pediatric Oncology*

Helpful tips

Try using the following tips to help you and your child as you go through the treatment journey:

✓ **Notice your feelings**
You might feel a lot of emotions at once. It's okay! Talk to a friend or family member about how you're feeling

✓ **Look for small happy moments**
Try to find little things that bring you joy, like the smell of flowers, the sound of rain, or someone smiling

✓ **Take little breaks**
Do something nice for yourself, like taking deep breaths, going for a short walk, listening to a song, or reading a book

✓ **Ask for help**
Let family, friends, or people in your community know if you need support, like help with meals or just someone to talk to

✓ **Be kind to yourself**
It's okay to have tough days or feel tired. Give yourself some grace

Many hospitals have counselors and social workers. If you need more support, ask to meet with them.

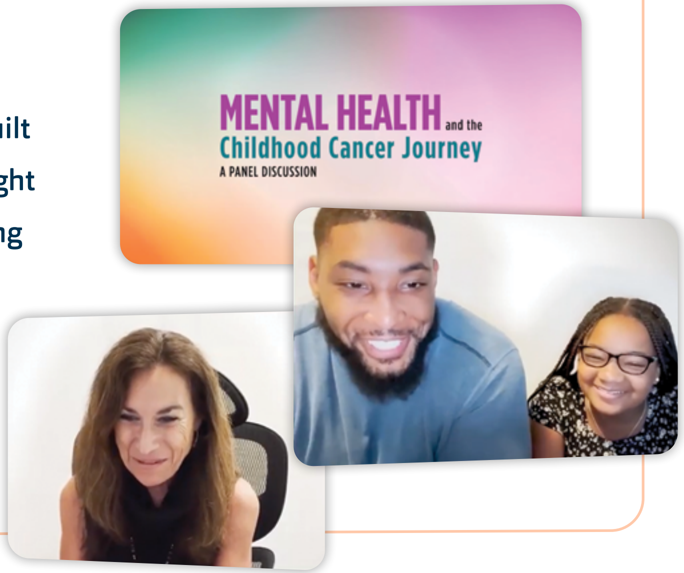
Support for you

It's normal to feel worried about your child and look for comfort by reaching out to other families who have children being treated for neuroblastoma.

It may be helpful to watch some clips from the video series "The Psychological Effects of Childhood Cancer." The series explores mental health and wellness with an expert and families dealing with neuroblastoma.

Topics include:

- Dealing With the Initial Guilt
- Finding the Strength to Fight
- Finding Joy and Celebrating Small Victories
- Life After Treatment



Watch the video series now to learn more.

Additional resources

These educational materials for caregivers and children can help make things less overwhelming. Your child's care team may also provide handouts, medical play toys, and more to help explain treatment.

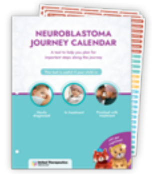
Downloadable resources

Instantly access these free materials, including the Braving Neuroblastoma Resource Guide, Fast Facts for Your Child, Coping with Childhood Cancer Guide, and four Skivolo books, which can help your child understand their treatment journey.

Explore downloadable resources at no cost to you.

Order free resources

Braving Neuroblastoma Toolkit: This toolkit can help you talk to your child about what it's like to have neuroblastoma and what to expect. It includes a Skivolo Plush, four Skivolo books, crayons, a treatment calendar with stickers, Skivolo masks, and a guide to the helpful website, **neuroblastoma-info.com**.



Neuroblastoma Journey Calendar: This treatment calendar, with stickers included, can help you keep track of important dates and highlight the milestones of your child's treatment journey.

Coping with Childhood Cancer Kit: This kit can help you and your child deal with the stress and worry of treatment. It includes the "Childhood Cancer Coping Guide," which helps you from the first diagnosis all the way through life after treatment. The kit also has a marble maze with a Velcro® back, 2 PunkinPitch® balls, and a drawstring backpack.

Scan the code to order helpful resources at no cost to you.

Neuroblastoma support and advocacy groups

There are many resources available to help you find your own support network and share your story.

Resources include:

Children's Oncology Group Family Handbook
www.childrensoncologygroup.org/cog-family-handbook

Coalition Against Childhood Cancer
www.cac2.org

Coping Skills for Kids
www.copingskillsforkids.com

Hope Portal
www.cac2.org/impact-areas/family-support/childhood-cancer-hub

Solving Kids Cancer
www.solvingkidscancer.org

The Evan Foundation
www.theevanfoundation.org

The National Cancer Institute
www.cancer.gov

United Therapeutics Corporation is not affiliated with any of these organizations. The information provided by these organizations is meant for informational purposes only. It is not meant to replace the medical advice of your child's healthcare team.

CHAPTER 7

Glossary

Commonly used terms

Anaphylaxis: An allergic reaction that your child may have during the infusion, with symptoms like your child not breathing easily, too fast, coughing, and having a tight throat or not being able to swallow.

Antibody: A Y-shaped protein that helps flag harmful cells for your immune system to attack.

Antigen: A protein marker on cells that can be targeted by antibodies like dinutuximab.

Blood pressure: A measurement that tells you how hard your child's heart is pumping to move blood through the blood vessels.

Capillary leak syndrome: A side effect caused by tiny blood vessels (capillaries) leaking blood into surrounding tissues.

Care team: The team of experts caring for your child in the hospital (doctors, nurse practitioners, nurses, etc).

Cytokines: Proteins that help activate the immune system response.

Event-free survival (EFS): Doctors measure how well a treatment works by looking at event-free survival. This means how long a child stays cancer-free without their cancer getting worse or causing serious problems. EFS helps doctors see that a treatment is keeping the cancer under control.

GD2: A protein (found at high levels on neuroblastoma cells) that antibodies can recognize. Some healthy cells (nerve cells and pain fibers) also have GD2.

GM-CSF: Doctors may prescribe GM-CSF to help your child create more white blood cells to strengthen their immune system. GM-CSF stands for granuloctye-macrophage colony-stimulating factor.

Hypotension: Low blood pressure.

IL-2: Interleukin-2, a type of protein, known as a cytokine, that is produced by white blood cells and used in cancer treatment to boost the immune system.

Infusion: Giving medicine by directly flowing it into the bloodstream through a vein (intravenously).

Infusion rate: How quickly medicine enters your body. This can be adjusted by the infusion nurse.

Infusion reaction: An allergic response to a medicine that is being given by infusion.

Isotretinoin, also called retinoic acid: A pill that can help to stop neuroblastoma cells from growing.

Monoclonal antibodies: Immune system proteins, made by scientists in a lab, that can be designed to target different cells.

Neuroblastoma: A cancer found in developing nerve cells.

Overall survival (OS): A measure of how long children live after being diagnosed or starting treatment, no matter what happens with their cancer afterward. Even if the cancer comes back and more treatment is needed, improved OS shows that a treatment helped children live longer.

United Therapeutics
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We are honored to serve this brave community and are committed to providing comprehensive care to families and caregivers touched by a neuroblastoma diagnosis.