



Understanding AZEDRA[®] therapy

Your guide to the first and only
approved treatment for advanced
pheochromocytoma and paraganglioma

Approved Use:

AZEDRA[®] (iobenguane I 131) is a prescription medicine used to treat adult and pediatric patients 12 years and older with cancers known as pheochromocytoma and paraganglioma that are positive for the norepinephrine transporter (as determined by an iobenguane scan), and who require systemic anticancer therapy.

Important Safety Information

AZEDRA can cause serious side effects. If you experience these side effects, your health care provider may need to adjust or stop your treatment. You should always follow your health care provider's instructions. Serious side effects may include:

Radiation exposure: Treatment with AZEDRA will expose you to radiation which can contribute to your overall long-term radiation exposure. Overall radiation exposure is associated with an increased risk for cancer.

Radiation risk is greater in children than in adults. You should stay well hydrated before, during, and after your treatment and urinate frequently. Your doctor will advise you on how to lessen exposure to people who may come into contact with you after AZEDRA treatment.

Please see Important Safety Information on pages 34–37. Please see Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.



AZEDRA[®]
iobenguane I 131 injection for
intravenous use

Table of contents

04 /	Understanding pheochromocytoma and paraganglioma	16 /	Results of the AZEDRA clinical trial
06 /	Unique disease, unique goals	18 /	Understanding side effects of AZEDRA
08 /	AZEDRA is the first approved therapy for pheo and para	20 /	AZEDRA therapy
10 /	Understanding AZEDRA therapy	22 /	What to expect after AZEDRA therapy
12 /	AZEDRA targets and treats pheo and para	24 /	Talking to your doctor about AZEDRA
14 /	Understanding how AZEDRA was studied	26 /	Support services for patients and caregivers
		28 /	Frequently asked questions
		32 /	Glossary of commonly used terms
		34 /	Indications and usage, and important safety information
		38 /	References



About this guide



Pheochromocytoma (pheo) and paraganglioma (para) are rare tumors. Too often, this means that information about pheo, para, and available treatments is just as rare.

If you or someone you know is living with pheo or para, this guide can help by providing information about these tumors and about AZEDRA, the first and only therapy FDA-approved to treat certain forms of the disease.

This guide is designed to help you:

- ▶ Understand what to think about when considering treatment options for advanced pheo or para
- ▶ Learn how AZEDRA works and why AZEDRA may be the right choice for you
- ▶ Learn about other resources with additional information about pheo, para, and AZEDRA
- ▶ Get the answers you need from conversations with your doctor

Use this guide as a starting point to gain a better understanding of pheo and para and your options to control it.

Be sure to read the Important Safety Information included in this guide.

Please see Important Safety Information on pages 34–37.

Please see accompanying Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.

Understanding pheochromocytoma and paraganglioma

Pheochromocytoma (pheo) tumors and paraganglioma (para) tumors come from specific types of hormone-producing neuroendocrine cells.

The neuroendocrine system is made up of many different **neuroendocrine cells** and tissues throughout the body which together regulate different bodily processes. Most pheo and para tumors can be removed with surgery. However, some people have unresectable, locally advanced, or metastatic disease, which this guide refers to as “advanced pheo and para”:

- ▶ **Unresectable** means that a tumor or set of tumors cannot be removed with surgery
- ▶ **Locally advanced** means that the disease has spread into nearby tissue
- ▶ **Metastatic** means that the disease has spread to other parts of the body

If you or someone you know is living with advanced pheo or para, it is important to understand the nature of the disease—and what treatments may help.

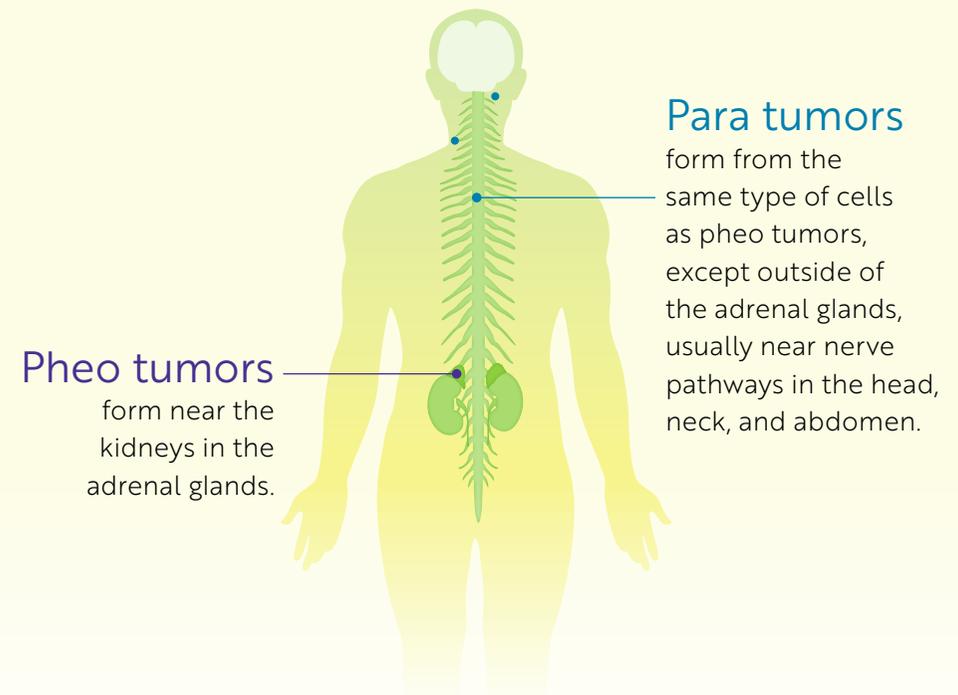
Throughout this guide you can find definitions for **purple highlighted words** in the sidebar and in the glossary on pages 32–33.

A **neuroendocrine cell** is a type of cell that uses hormones or chemicals to relay messages from the brain to different muscles and organs in the body.

What to call the disease

Because pheochromocytoma and paraganglioma tumors are so similar, they are often referred to as a single disease. You may see pheo and para referred to as “pheo/para,” “PHEO/PGL,” or “PPGL” depending on where you look, but they all mean the same thing.

Where pheo and para tumors form in the body



The importance of ongoing follow-up

Unlike some tumors, there is no way to know if a pheo or para tumor is malignant, or cancerous, until it spreads to other parts of the body. Because of this, every pheo or para tumor is considered to have malignant potential. Even if a tumor is removed or seems benign, it is important that you and your doctor continue to monitor for malignant disease.

Unique disease, unique goals

Pheo and para tumors are different from other cancers or neuroendocrine tumors.

Epinephrine and norepinephrine (adrenaline and noradrenaline) are two types of hormones created by neuroendocrine cells. Known as catecholamines, these hormones are triggered during times of stress as part of the “fight or flight” response and prepare the body for increased activity by doing things like raising heart rate and blood pressure.

Susceptibility genes are genes which, when mutated, may increase your risk for certain diseases like pheo or para. Genes provide instructions for making proteins, one of the building blocks of cells. Mutations change the instructions, which can cause a protein to malfunction or to be missing entirely. If the missing or damaged protein plays an important role in the body, this can lead to disease.

Unlike most other tumors, pheo and para tumors are able to produce large amounts of hormones, usually **epinephrine and norepinephrine** (also called adrenaline and noradrenaline). These hormones can result in a wide variety of symptoms, including:

- ▶ High blood pressure (hypertension)
- ▶ Headache
- ▶ Rapid heartbeat
- ▶ Sweating

These symptoms can be very serious for some people. Managing symptoms is therefore an important part of treating pheo and para.

Although pheo and para are rare, there are specialized medical teams that have extensive experience with this type of disease. There is also a growing amount of research into treatment options and into the genetics and causes of pheo and para.

Genes associated with pheo and para

There is ongoing research into the genetics of pheo and para. So far, over twenty different **susceptibility genes** have been identified, which are associated with more than 40% of pheo and para cases.

Ask your doctor if your pheo or para tumor is associated with a mutation in a known susceptibility gene that could guide treatment planning. You may also want to talk to a genetic counselor about the implications any mutation might have for your family members.

Dual goals for treating advanced pheo and para

If a tumor has not spread to other parts of the body, it can usually be removed with surgery. However, for advanced pheo and para there are two goals of therapy:

Symptom reduction

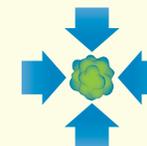


Reduce the burden of symptoms

Pheo and para symptoms can be acute, severe, and even life-threatening if untreated.



Tumor control



Control the growth of tumors

Tumor growth is the leading cause of death for people with advanced pheo and para.

AZEDRA is the first approved therapy for pheo and para

AZEDRA is the first and only therapy approved by the FDA for the treatment of unresectable, locally advanced, or metastatic pheo or para tumors that are targeted by AZEDRA.

AZEDRA has been clinically proven to reduce the need for hypertension medication and control the growth of tumors, addressing the dual treatment goals of advanced pheo and para.



FDA-approved

AZEDRA is the first and only approved treatment for patients with advanced pheo and para, and can advance the standard of care for this rare disease.



Breakthrough therapy

Based on clinical evidence suggesting substantial improvement over available therapies, AZEDRA was designated as a Breakthrough Therapy by the FDA.

**FAST
TRACK**

Fast track status

To speed up development of a therapy that fills an unmet need in a serious condition, AZEDRA was granted Fast Track Status by the FDA.

What is AZEDRA?

AZEDRA® (iobenguane I 131) is a prescription medicine used to treat adult and pediatric patients 12 years and older with cancers known as pheochromocytoma and paraganglioma that are positive for the norepinephrine transporter (as determined by an iobenguane scan), and who require systemic anticancer therapy.

Selected important safety information

AZEDRA can cause serious side effects. If you experience these side effects, your health care provider may need to adjust or stop your treatment. You should always follow your health care provider's instructions. Serious side effects may include:

Radiation exposure: Treatment with AZEDRA will expose you to radiation which can contribute to your overall long-term radiation exposure. Overall radiation exposure is associated with an increased risk for cancer. Radiation risk is greater in children than in adults. You should stay well hydrated before, during, and after your treatment and urinate frequently. Your doctor will advise you on how to lessen exposure to people who may come into contact with you after AZEDRA treatment.

Please see Important Safety Information on pages 34–37.

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Understanding AZEDRA therapy

AZEDRA is a targeted **systemic radiation therapy**:

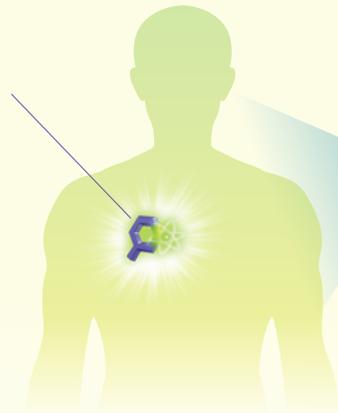
- ▶ AZEDRA is **targeted** because it only affects certain cells inside the body (such as pheo and para tumor cells) that have a specific target, called the **norepinephrine transporter**.
- ▶ AZEDRA is **systemic** because it is carried inside the body to reach tumors wherever they are. It treats the whole body system, not just one body part.
- ▶ AZEDRA is a **radiation therapy** because it uses radiation to treat tumors.

You can learn more about how AZEDRA works on page 12.

Understanding radiation therapy

Radiation therapy uses high-energy radiation to destroy cancer cells and stop or reverse the growth of tumors. Radiation can be delivered two ways:

From inside
Targeted to specific cells, like AZEDRA
(systemic radiation therapy)



From outside
(external-beam radiation therapy)

Because AZEDRA is a systemic radiation therapy, radiation can be delivered directly to the tumor cells. From there, the radiation from AZEDRA can only travel about two and a half millimeters—less than the thickness of two pennies.



Selected important safety information

Bone marrow problems and other cancers:

Treatment with AZEDRA may cause your blood cell counts to drop (**myelosuppression**). Serious cases of myelosuppression have been observed during AZEDRA treatment. You may experience blood-related side effects such as low numbers of cells that are responsible for blood clotting (thrombocytopenia), low numbers of a type of white blood cells (neutropenia), and low red blood cells (anemia). Among the 88 patients who received a therapeutic dose of AZEDRA, 33% experienced Grade 4 thrombocytopenia, 16% experienced Grade 4 neutropenia, and 7% experienced Grade 4 anemia. Five percent of patients experienced febrile neutropenia (neutropenia with fever). People with low blood counts can develop serious infections. Your health care provider will routinely check your blood counts and tell you if they are too low. Tell your doctor if you experience any symptoms of low blood counts or infection, such as fever, chills, dizziness, shortness of breath, or increased bleeding or bruising. Your health care provider may need to adjust or stop your treatment accordingly. Other conditions that you may develop as a direct result of treatment with AZEDRA are blood and bone marrow cancers known as secondary myelodysplastic syndrome (MDS) and leukemia. MDS or acute leukemias were reported in 6.8% of the 88 patients who received a therapeutic dose of AZEDRA. The time to development of MDS or acute leukemia ranged from 12 months to 7 years. Two of the 88 patients developed other types of cancer.

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Systemic radiation therapy

is a type of radiation therapy that can find and destroy tumor cells from inside the body.

Norepinephrine transporter

is a protein on the surface of some cells, including pheo and para tumor cells, that transports norepinephrine and some similar molecules into the cell.

External-beam radiation therapy

is the most common type of radiation therapy used to treat cancer. A machine is used to aim high-energy rays (or beams) from outside the body into the tumor.

Myelosuppression

is a condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and/or platelets.



AZEDRA targets and treats pheo and para

AZEDRA is a targeted systemic radiation therapy made of two key parts

1. Targeting component

The targeting component is responsible for locating specific cells in the body.

The targeting component in AZEDRA is **MIBG**, a molecule similar to norepinephrine, which binds to the norepinephrine transporter. This transporter is found on the surface of most pheo and para tumor cells, as well as other cells in the body. Tumors that actively absorb MIBG are referred to as "**MIBG avid**."



2. Treatment component

The treatment component delivers radiation to destroy cancer cells.

The treatment component of AZEDRA is an atom called **iodine 131 (I-131)**, which has been used in the treatment of thyroid and other cancers for over six decades.

MIBG is a molecule that is actively absorbed by cells that have norepinephrine transporter, including most pheo and para tumor cells.

MIBG avid is used to describe tumors that actively absorb MIBG. Most pheo and para tumors are MIBG avid, which means treatments like AZEDRA that use MIBG can target these tumors.

Iodine 131 (I-131) is a radioactive form of iodine that can be used inside the body to destroy cancer cells with radiation.

Selected important safety information

Thyroid problems: Treatment with AZEDRA may increase your long-term risk of developing an underactive thyroid (hypothyroidism) or thyroid cancer. Hypothyroidism was reported in 3.4% of the 88 patients who received a therapeutic dose of AZEDRA. Take all thyroid-blocking agents as prescribed by your doctor to reduce the risk of these problems. You may need life-long monitoring for signs and symptoms of hypothyroidism.

Please see Important Safety Information on pages 34–37.

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iobenguane | 131 injection for intravenous use

Understanding how AZEDRA was studied

The clinical trial that studied AZEDRA was the largest one of its kind for advanced pheo and para and included a wide variety of people with this disease.

Participants in the clinical trial included:

- ▶ Men and women
- ▶ Ages 16–76 (enrollment was open to people 12 or older)
- ▶ Patients who had received previous treatments, including
 - Surgery
 - Chemotherapy
 - Other radiation therapies

In the trial, 26% of patients received one dose of AZEDRA, and 74% of patients received the full treatment regimen of two doses.

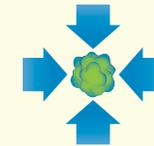


What the AZEDRA clinical trial measured

Researchers designed the AZEDRA clinical trial to measure two outcomes that reflect the dual treatment goals for treating advanced pheo and para:



Reduce the need for hypertension medication



Control the growth of tumors

Many people living with pheo or para must take daily medication to control hypertension caused by tumor-released hormones, which is one of the most common symptoms of this disease. The AZEDRA clinical trial measured reduction in use of hypertension medication over time.

Tumor growth is the leading cause of death for people with advanced pheo and para. The AZEDRA clinical trial measured the number of tumors that stopped growing and how much they shrank after AZEDRA treatment.

Selected important safety information

Fertility problems: Treatment with AZEDRA may cause infertility due to radiation absorbed by your testes or ovaries over the treatment period that is within the range of exposure where temporary or permanent infertility may be expected.

Please see Important Safety Information on pages 34–37.

Please see accompanying Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.

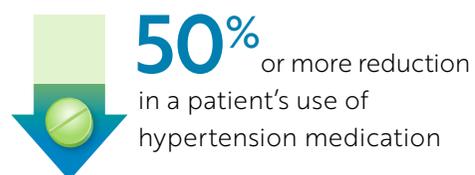

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Results of the AZEDRA clinical trial

AZEDRA was proven to reduce the need for hypertension medication

The AZEDRA clinical trial measured **significant medication reduction**, which means the reduction was **substantial and sustained**.

Substantial reduction



Sustained reduction



25% of patients who received at least one dose of AZEDRA had **significant and sustained medication reduction** (17 out of 68 patients)

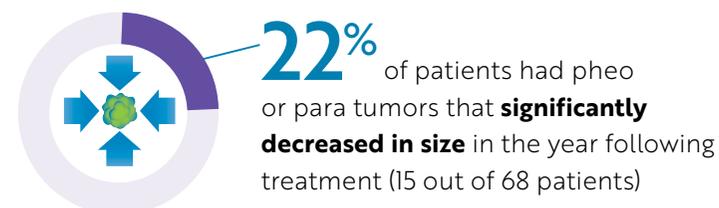


For patients with significant medication reduction, the reduction lasted anywhere from 8 months to 5 years, and most of these patients experienced sustained medication reduction **for more than one year**.

Selected important safety information

Elevations in blood pressure: During or 24 hours following AZEDRA treatment, you may experience increases of blood pressure (hypertension) as a result of hormones released from your cancer. Eleven percent of the 88 patients who received a therapeutic dose of AZEDRA experienced a worsening of pre-existing hypertension. All changes in blood pressure occurred within the first 24 hours after treatment. Monitor blood pressure frequently during the first 24 hours after each therapeutic dose of AZEDRA. Tell your doctor if you experience any cardiac-related symptoms.

AZEDRA reduced the size of tumors



For patients with a significant decrease in tumor size, over half (53%) experienced durable tumor reduction for



Selected important safety information

Kidney problems: Treatment with AZEDRA will expose your kidneys to radiation and may impair their ability to work as normal. In some cases, patients have experienced kidney failure after treatment with AZEDRA. Of the 88 patients who received a therapeutic dose of AZEDRA, 7% developed kidney failure or acute kidney injury, and 22% experienced a decrease in kidney function measured at 6 or 12 months. Your health care provider will monitor your kidneys after treatment using blood tests, particularly if you already have kidney impairment before treatment.

Respiratory problems: Treatment with AZEDRA may cause noninfectious lung inflammation (pneumonitis). Tell your doctor if you experience shortness of breath, difficulty breathing, or cough.

Please see Important Safety Information on pages 34–37.

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Understanding side effects of AZEDRA

The side effects of AZEDRA are based on the experiences of patients in the clinical trial. The most common side effects (experienced by more than 10% of patients) were:

-
- Myelosuppression**
- ▶ Lymphopenia—A decrease in the number of lymphocytes, a class of white blood cell that helps fight infections
 - ▶ Neutropenia—A decrease in the number of neutrophils, another class of white blood cell that helps fight infections
 - ▶ Thrombocytopenia—A decrease in the number of platelets, which are cellular structures involved in blood clotting
 - ▶ Anemia—A decrease in the levels of hemoglobin, an iron-bearing protein found in red blood cells

-
- Cardiovascular**
- ▶ Increased international normalized ratio—A measure of how quickly blood coagulates or solidifies, when increased blood may clot more slowly
 - ▶ Hypertension—Increase in blood pressure to 140/90 or higher

-
- Gastrointestinal**
- ▶ Nausea
 - ▶ Vomiting

-
- General**
- ▶ Dizziness
 - ▶ Fatigue

Be sure to tell your doctor about any symptoms you experience, even if they are not listed here.

Your treatment team may ask you to take certain steps to help avoid some of these side effects, including:



Taking medications to help reduce nausea and to block radiation from affecting healthy organs before treatment



Drinking lots of water before and after treatment

Selected important safety information

The most common and most serious side effects of AZEDRA include decreased blood cell counts, nausea, vomiting and fatigue. These are not all the possible side effects of AZEDRA. For more information, ask your health care provider.

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AZEDRA therapy

Therapy with AZEDRA takes place in a hospital and involves two main steps.

Step 1 / Dosimetry, to confirm the correct dose

The dosimetry step involves an injection of a small amount of AZEDRA. After the injection, doctors will schedule three body scans over the next 5 days. These scans allow doctors to confirm the correct dose of AZEDRA for you.

Small dose
of AZEDRA



3 body scans



Step 2 / Therapy, to treat tumors

The therapy step involves an **infusion** of the treatment dose of AZEDRA, lasting about 30 minutes, followed by a few days in the hospital. You will receive another treatment dose about three months after the first one. AZEDRA will continue to treat pheo and para tumors even after you leave the hospital. When you leave the hospital, you will receive additional instructions about reducing radiation exposure to others. The radiation will eventually go away completely. Until then, you may need to minimize contact with other people.

First treatment
dose of AZEDRA



Second treatment
dose of AZEDRA



Preparing for treatment with AZEDRA

Before treatment, you will need to take a non-radioactive form of iodine to prevent any radioactive iodine from going to your thyroid. Failure to block your thyroid from radiation exposure prior to treatment with AZEDRA may increase your long-term risk of developing an underactive thyroid or thyroid tumors. Take all thyroid-blocking agents as prescribed by your doctor. You may need life-long monitoring for signs and symptoms of an underactive thyroid.

In addition, certain medications may affect the ability of MIBG to target the disease, and these medications may need to be modified or stopped by your doctor. Tell your doctor about all the medications you take. Be sure to follow any instructions your medical team provides about what to do before treatment begins.

Your time in the hospital

Because AZEDRA is radioactive, treatment takes place in a special room to minimize radiation exposure to others.

- ▶ Patients will have to remain in the room for a few days
- ▶ Visitors will be instructed when and how much time they can spend inside the room

Stay well hydrated by drinking at least 2 liters of water a day before receiving AZEDRA and for one week after treatment in order to minimize radiation exposure to your bladder. Your doctor will advise you on how to minimize radiation exposure to people you may come into contact with after AZEDRA treatment.

Please see Important Safety Information on pages 34–37.

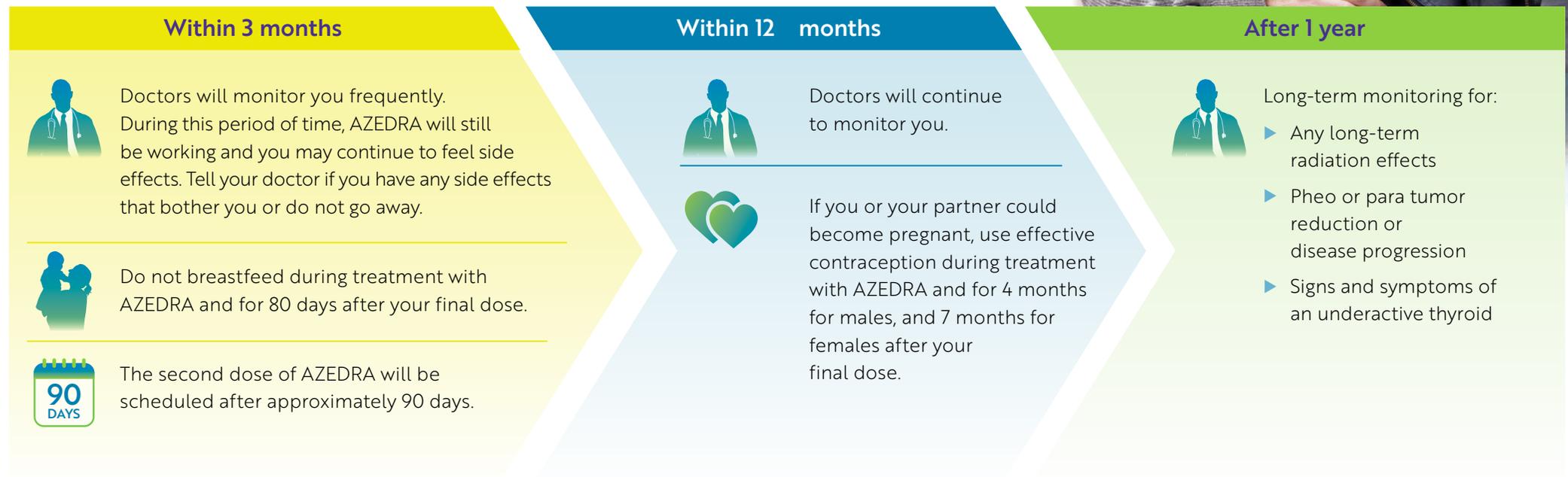
Please see accompanying Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.

An **infusion** is a method of slowly injecting fluids, including drugs, into the bloodstream. It is also sometimes called intravenous infusion or IV.



What to expect after AZEDRA therapy

After each administration of AZEDRA, your treatment team will determine when you are ready to be released from the hospital and will provide advice about contact with others and how to avoid unsafe radiation exposure to others.



Selected important safety information

Pregnancy warning: Before treatment with AZEDRA, tell your doctor if you are pregnant or plan to become pregnant. Exposure to radiation from treatment with AZEDRA can harm your unborn baby. Use an effective method of birth control during treatment with AZEDRA and for 7 months (for females) and 4 months (for males) after your final dose. Do not breastfeed during treatment with AZEDRA and for 80 days after your final dose.

Fertility problems: Treatment with AZEDRA may cause infertility due to radiation absorbed by your testes or ovaries over the treatment period that is within the range of exposure where temporary or permanent infertility may be expected.

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Talking to your doctor about AZEDRA

It is important to have clear discussions with your doctor as you plan your treatment.

Here are some tips to keep in mind when discussing options with your doctor:

- ▶ Speak up about what is important to you—understanding your priorities will help your doctor advise the most suitable treatment option for your disease
- ▶ Take plenty of notes and do not hesitate to ask clarifying questions
- ▶ If you do not understand something your doctor says, ask for a simpler explanation

Preparing for an appointment with your doctor

As you prepare for your appointment with your doctor, you may want to:

- ▶ Write down questions you have in advance so you do not forget to ask
- ▶ Bring a notebook or audio recorder so you can record your doctor's answers
- ▶ Ask a family member or friend to come with you for support, and to ask any questions you may not think of



Questions to ask your doctor

Your doctor can be a great resource for any questions you have about pheo, para, and AZEDRA. Here are some questions you may want to ask:

General information related to you

- ▶ What treatment do you recommend for my pheo or para and why?
- ▶ Do I qualify for AZEDRA treatment?
- ▶ What are the characteristics of a suitable AZEDRA candidate?

General information related to your doctor

- ▶ Do you have experience with AZEDRA?
- ▶ Have you ever referred a patient for AZEDRA treatment? If not, is there someone I can talk to who has?
- ▶ Would you consider AZEDRA if you had pheo or para?

Treatment with AZEDRA

- ▶ Who will be a part of my treatment team and what does each member do?
- ▶ How long will I need to be in the hospital and how will my discharge date be decided?
- ▶ What can I do while I am in the hospital following AZEDRA treatment?
- ▶ Who is allowed to visit, and what are the precautions they would need to take?
- ▶ What are the common side effects of AZEDRA?
- ▶ For a patient like me, what are the expected results for AZEDRA treatment?

After treatment with AZEDRA

- ▶ How should I expect to feel after I leave the hospital?
- ▶ What follow-up tests do I need after AZEDRA treatment, and how often will I need them?
- ▶ When will I come back to see you after AZEDRA treatment?

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Support services for patients and caregivers



The team behind AZEDRA is committed to providing comprehensive patient services to help ensure that the needs of patients and their loved ones are met.

Where AZEDRA is offered

AZEDRA is an inpatient treatment that will be administered in a specialized hospital with physicians licensed to order, handle, and administer radiation therapy drugs.

To see where AZEDRA treatment is offered, please visit AZEDRA.com.

Advocacy support for pheo and para

Organizations, like the Pheo Para Alliance, provide additional information about pheo and para, including the latest news on treatment options and research. In addition, the Pheo Para Alliance website shares patient stories, so you can learn about other people's experiences living with pheo and para. For more information, please visit pheopara.org.

AZEDRA Service Connection™ program

At Progenics Pharmaceuticals, part of our mission as an oncology company includes a commitment to providing a seamless experience for patients and their families.

Patient Access Specialists

- ▶ Progenics' Patient Access Specialists provide one-on-one phone assistance on matters such as co-pay and reimbursement assistance to you and your family if you are prescribed AZEDRA.
- ▶ Patient Access Specialists can also refer you to independent, third-party organizations for support*, including help finding transportation and lodging assistance.*†

Financial and Travel Support

If you have commercial insurance and have challenges affording the out-of-pocket costs, the AZEDRA Service Connection can provide assistance identifying co-pay, coinsurance, and deductible expenses. AZEDRA Service Connection can also assist with the costs of traveling to a treatment facility for AZEDRA.*†

Uninsured Patients

Patient assistance, which may include providing AZEDRA at no cost, is available to you if you are uninsured and meet program eligibility requirements.

To learn more about AZEDRA Service Connection:

Call: 1-844-AZEDRA1 (1-844-293-3721)

Email: Info@AZEDRA.com

Online: www.AZEDRA.com/support-program

Please see Important Safety Information on pages 34–37.

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* Provided through independent third-party foundations (501(c)(3), tax-exempt nonprofit organizations). AZEDRA Service Connection has no control over independent, third-party programs and provides connections as a courtesy only.

† Based on program eligibility.





Frequently asked questions

What is AZEDRA?

AZEDRA is a systemic radiation therapy made up of a targeting component (MIBG), and a treatment component (I-131). These components work together to target cells that have norepinephrine transporter, such as most pheo and para tumors, and treat them with radiation.

How is AZEDRA different from other treatments for pheo and para?

AZEDRA is the only FDA-approved treatment for advanced pheo and para based on results of the largest clinical trial of its kind for this disease.

AZEDRA was clinically proven to reduce the need for hypertension medication and control the growth of tumors, addressing the dual treatment goals of advanced pheo and para.

What is MIBG avidity and how is it assessed?

MIBG avidity describes how well a tumor absorbs I-131 MIBG. The avidity of a pheo or para tumor may be measured before a patient receives AZEDRA to determine if he or she is a candidate for treatment.

Selected important safety information

The most common and most serious side effects of AZEDRA include decreased blood cell counts, nausea, vomiting and fatigue. These are not all the possible side effects of AZEDRA. For more information, ask your health care provider.

Drugs that reduce catecholamine uptake or that deplete catecholamine stores may interact with AZEDRA and may affect how well it works. These drugs were not permitted in the clinical trials. Tell your doctor before starting any medication, including over the counter medications, herbal or dietary supplements.



How is AZEDRA given?

AZEDRA is given in a hospital by doctors who are licensed and trained in the handling and administration of radiation therapies. There are two stages to AZEDRA treatment. In the first stage, you are given a very small dose of AZEDRA. Over the next few days, you receive three body scans to check where AZEDRA is going in your body. In the second stage, you are given an infusion of a larger treatment dose of AZEDRA over approximately 30 minutes, followed by a short hospital stay. An additional treatment dose is administered approximately 90 days later.

Who administers AZEDRA?

AZEDRA may only be administered in a specialized hospital equipped to provide care and support to patients receiving radiation therapy. AZEDRA will be handled and administered by a treatment team of qualified and trained health care providers.

Please see Important Safety Information on pages 34–37.

Please see accompanying Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.



What are some of the risks of receiving AZEDRA?

The most common side effects of treatment include:

- ▶ Lymphopenia—A decrease in the number of lymphocytes, a class of white blood cell that helps fight infections
- ▶ Neutropenia—A decrease in the number of neutrophils, another class of white blood cell that helps fight infections
- ▶ Thrombocytopenia—A decrease in the number of platelets, which are cellular structures involved in blood clotting
- ▶ Anemia—A decrease in the levels of hemoglobin, an iron-bearing protein found in red blood cells
- ▶ Increased international normalized ratio—A measure of how quickly blood coagulates or solidifies, when increased blood may clot more slowly
- ▶ Hypertension—Increase in blood pressure to 140/90 or higher
- ▶ Nausea
- ▶ Vomiting
- ▶ Dizziness
- ▶ Fatigue

What radiation precautions should I take after treatment?

AZEDRA contributes to your overall long-term radiation exposure. After treatment, you will need to remain in the observation room for a few days while the radiation treating your tumors is strongest. After you leave the hospital, as the radiation in your body decreases, your doctor will give you additional instructions about how to minimize any radiation exposure to those around you.

Where can I find more information?

You can find additional information on AZEDRA by visiting AZEDRA.com.

AZEDRA at a glance

First and only FDA-approved therapy for advanced pheo and para

Based on evidence from the largest clinical trial of patients with advanced pheo and para, AZEDRA is FDA-approved for the treatment of unresectable, locally advanced, or metastatic pheo and para tumors that can be targeted with MIBG.

Proven to reduce the need for hypertension medication

Twenty-five percent of patients taking AZEDRA in the clinical trial were able to reduce their use of hypertension medication by at least 50% for 6 months or longer. For these patients, their medication reduction lasted anywhere from 8 months to 5 years.

Reduced tumor size

For 22% of patients in the clinical trial, their pheo or para tumors significantly decreased in size after AZEDRA therapy.

Clinically established safety profile

The most common and most serious side effects of AZEDRA include decreased blood cell counts, nausea, vomiting and fatigue. These are not all the possible side effects of AZEDRA. For more information about the side effects of AZEDRA, ask your doctor.

Support services

The AZEDRA Service Connection™ program provides financial, caregiver, travel, and lodging support services for patients with commercial insurance.

Please see Important Safety Information on pages 34–37.

Please see accompanying Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.



Glossary of commonly used terms

Epinephrine and **norepinephrine** (adrenaline and noradrenaline). Two types of hormones created by neuroendocrine cells. Known as catecholamines, these hormones are triggered during times of stress as part of the “fight or flight” response and prepare the body for increased activity by doing things like raising heart rate and blood pressure.

External-beam radiation therapy. The most common type of radiation therapy used to treat cancer. A machine is used to aim high-energy rays (or beams) from outside the body into the tumor.

Iodine 131 (I-131). A radioactive form of iodine that can be used inside the body to destroy cancer cells using radiation.

Infusion. A method of slowly injecting fluids, including drugs, into the bloodstream. It is also sometimes called intravenous infusion or IV.

Locally advanced. Disease that has spread into nearby tissues.

Malignant tumor. A cancerous tumor.

Metastatic. Disease that has spread to other parts of the body.

MIBG. A molecule that is actively absorbed by cells that have norepinephrine transporter, including most pheo and para tumor cells.

MIBG avid. Able to actively absorb MIBG. Most pheo and para tumors are MIBG avid, which means treatments like AZEDRA that use MIBG can be used to target these tumors.

Myelosuppression. A condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and/or platelets.

Neuroendocrine cell. A type of cell that uses hormones or chemicals to relay messages from the brain to different muscles and organs in the body.

Norepinephrine transporter. A protein on the surface of some cells, including pheo and para tumor cells, that transports norepinephrine into the cell. MIBG, which is similar to norepinephrine, can also be carried by the norepinephrine transporter.

Susceptibility genes. Genes which, when mutated, may increase your risk for certain diseases like pheo or para. Genes provide instructions for making proteins, one of the building blocks of cells. Mutations change the instructions, which can cause a protein to malfunction or to be missing entirely. If the missing or damaged protein plays an important role in the body, this can lead to disease.

Systemic radiation therapy. A type of radiation therapy that can find and destroy tumor cells from inside the body.

Unresectable. A tumor or set of tumors that cannot be removed with surgery.

Please see Important Safety Information on pages 34–37.

Please see accompanying Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.


AZEDRA[®]
iobenguane | 131 injection for intravenous use

Indications and usage, and important safety information

Approved Use:

AZEDRA® (iobenguane I 131) is a prescription medicine used to treat adult and pediatric patients 12 years and older with cancers known as pheochromocytoma and paraganglioma that are positive for the norepinephrine transporter (as determined by an iobenguane scan), and who require systemic anticancer therapy.

Important Safety Information

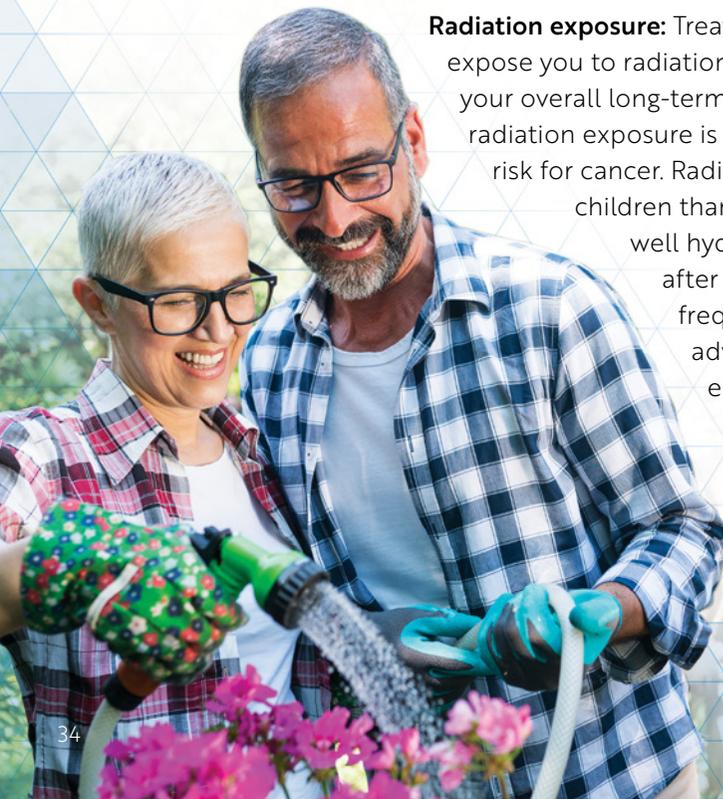
AZEDRA can cause serious side effects. If you experience these side effects, your health care provider may need to adjust or stop your treatment. You should always follow your health care provider's instructions. Serious side effects may include:

Radiation exposure: Treatment with AZEDRA will expose you to radiation which can contribute to your overall long-term radiation exposure. Overall radiation exposure is associated with an increased risk for cancer. Radiation risk is greater in children than in adults. You should stay well hydrated before, during, and after your treatment and urinate frequently. Your doctor will advise you on how to lessen exposure to people who may come into contact with you after AZEDRA treatment.

Bone marrow problems and other cancers: Treatment with AZEDRA may cause your blood cell counts to drop (myelosuppression). Serious cases of myelosuppression have been observed during AZEDRA treatment. You may experience blood-related side effects such as low numbers of cells that are responsible for blood clotting (thrombocytopenia), low numbers of a type of white blood cells (neutropenia), and low red blood cells (anemia). Among the 88 patients who received a therapeutic dose of AZEDRA, 33% experienced Grade 4 thrombocytopenia, 16% experienced Grade 4 neutropenia, and 7% experienced Grade 4 anemia. Five percent of patients experienced febrile neutropenia (neutropenia with fever). People with low blood counts can develop serious infections. Your health care provider will routinely check your blood counts and tell you if they are too low. Tell your doctor if you experience any symptoms of low blood counts or infection, such as fever, chills, dizziness, shortness of breath, or increased bleeding or bruising. Your health care provider may need to adjust or stop your treatment accordingly. Other conditions that you may develop as a direct result of treatment with AZEDRA are blood and bone marrow cancers known as secondary myelodysplastic syndrome (MDS) and leukemia. MDS or acute leukemias were reported in 6.8% of the 88 patients who received a therapeutic dose of AZEDRA. The time to development of MDS or acute leukemia ranged from 12 months to 7 years. Two of the 88 patients developed other types of cancer.

Thyroid problems: Treatment with AZEDRA may increase your long-term risk of developing an underactive thyroid (hypothyroidism) or thyroid cancer. Hypothyroidism was reported in 3.4% of the 88 patients who received a therapeutic dose of AZEDRA. Take all thyroid-blocking agents as prescribed by your doctor to reduce the risk of these problems. You may need life-long monitoring for signs and symptoms of hypothyroidism.

(Continued)




AZEDRA[®]
iobenguane I 131 injection for
intravenous use

Indications and usage, and important safety information

Important Safety Information (continued)

Elevations in blood pressure: During or 24 hours following AZEDRA treatment, you may experience increases of blood pressure (hypertension) as a result of hormones released from your cancer. Eleven percent of the 88 patients who received a therapeutic dose of AZEDRA experienced a worsening of pre-existing hypertension. All changes in blood pressure occurred within the first 24 hours after treatment. Monitor blood pressure frequently during the first 24 hours after each therapeutic dose of AZEDRA. Tell your doctor if you experience any cardiac-related symptoms.

Kidney problems: Treatment with AZEDRA will expose your kidneys to radiation and may impair their ability to work as normal. In some cases, patients have experienced kidney failure after treatment with AZEDRA. Of the 88 patients who received a therapeutic dose of AZEDRA, 7% developed kidney failure or acute kidney injury, and 22% experienced a decrease in kidney function measured at 6 or 12 months. Your health care provider will monitor your kidneys after treatment using blood tests, particularly if you already have kidney impairment before treatment.

Respiratory problems: Treatment with AZEDRA may cause noninfectious lung inflammation (pneumonitis). Tell your doctor if you experience shortness of breath, difficulty breathing, or cough.

Pregnancy warning: Before treatment with AZEDRA, tell your doctor if you are pregnant or plan to become pregnant. Exposure to radiation from treatment with AZEDRA can harm your unborn baby. Use an effective method of birth control during treatment with AZEDRA and for 7 months (for females) and 4 months (for males) after your final dose. Do not breastfeed during treatment with AZEDRA and for 80 days after your final dose.

Fertility problems:

Treatment with AZEDRA may cause infertility due to radiation absorbed by your testes or ovaries over the treatment period that is within the range of exposure where temporary or permanent infertility may be expected.

The most common and most serious side effects of AZEDRA include decreased blood cell counts, nausea, vomiting and fatigue. These are not all the possible side effects of AZEDRA. For more information, ask your health care provider.

Drugs that reduce catecholamine uptake or that deplete catecholamine stores may interact with AZEDRA and may affect how well it works. These drugs were not permitted in the clinical trials. Tell your doctor before starting any medication, including over the counter medications, herbal or dietary supplements.

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.

Please see Important Safety Information on pages 34–37.

Please see full [Prescribing Information](#) for AZEDRA.

Distributed by: Progenics Pharmaceuticals, Inc., NY 10007

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AZEDRA[®]
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Please see Important Safety Information on pages 34–37.

Please see accompanying Patient Counseling Information within the full [Prescribing Information](#) for AZEDRA.

Learn more at AZEDRA.com



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