Advanced Accelerator Applications

A Novartis Company

Your treatment with LUTATHERA®

Lutetium (^{177}Lu) oxodotreotide

LUTATHERA® Treatment Procedure Guide for patients

Risk Management Material

www.adacap.com

This material has been developed and funded by Advanced Accelerator Applications, for patients who have been prescribed LUTATHERA®.

If you get any side effects, you should report them to your doctor. This includes any possible side effects not listed in this guide. You can also report side effects directly to the national monitoring system. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard**. Side effects can also be reported to the manufacturer by emailing **uk.patientsafety@novartis.com**.

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ABOUT THIS GUIDE

This guide is only for patients who have made the decision with their neuroendocrine tumour (NET) team to receive Lutathera®, also known as lutetium (^{177}Lu) oxodotreotide. It may help answer some of the questions you have about Lutathera®. It is not intended to replace the advice given to you by your neuroendocrine tumour (NET) team. You should always speak with a member of your team about any questions you may have.

This guide has been developed specifically for people receiving Lutathera® treatment in the United Kingdom. The information within may not apply to people receiving Lutathera® in other countries or people on other radiation treatments. This guide has been developed by Advanced Accelerator Applications with the Medicines and Healthcare products Regulatory Agency (MHRA).

WHAT **IS LUTATHERA® AND WHAT IS IT USED FOR?**

What is Lutathera®?

Lutathera® is a treatment for a type of cancer called a neuroendocrine tumour.[1] It is a medicine that uses radiation to destroy tumour cells.[1] Treatments like Lutathera® are also sometimes known as **P**eptide **R**eceptor **R**adionuclide **T**herapy (or PRRT for short).[2]

What is Lutathera® used for?

Lutathera® is used in the treatment of neuroendocrine tumours that start in the gut or pancreas.[1] Lutathera® is used for tumours that cannot be removed by surgery or that have spread to other parts of the body.[1] Patients can receive Lutathera® if their tumours do not respond or stop responding to another therapy.[1] For Lutathera® to work, the tumours must have a certain type of receptor on their surface.[1] These receptors act like hooks where Lutathera® can attach to the tumours.[1] Your neuroendocrine tumour (NET) team will have checked that Lutathera® is suitable for your tumours before discussing it with you as a treatment option.

What does Lutathera® contain?

The active component of Lutathera® is called lutetium (^{177}Lu) oxodotreotide.[1] Lutathera® is made up of three parts:[2]

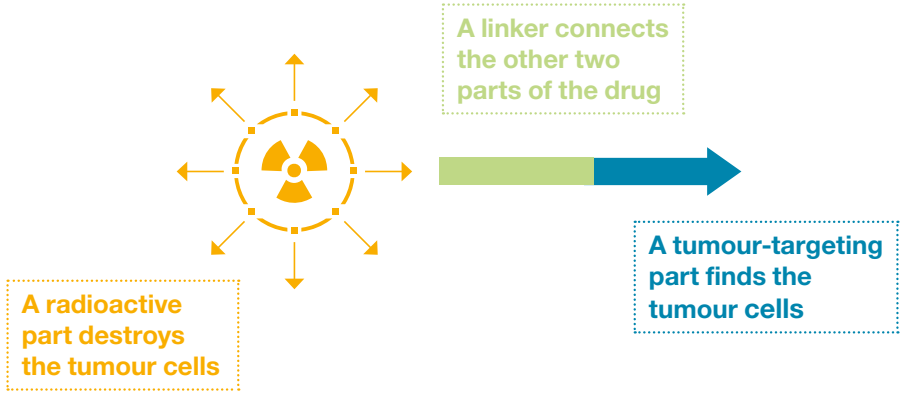

Figure 1. Parts of Lutathera®

Lutathera® comes as a solution at a concentration of 370 megabecquerels per millilitre. (The megabecquerel is a unit for measuring the amount of radioactivity.)

HOW **DOES LUTATHERA® WORK?**

The picture below shows how Lutathera® uses radiation to destroy neuroendocrine tumour cells and slow the growth of the tumours.[1]

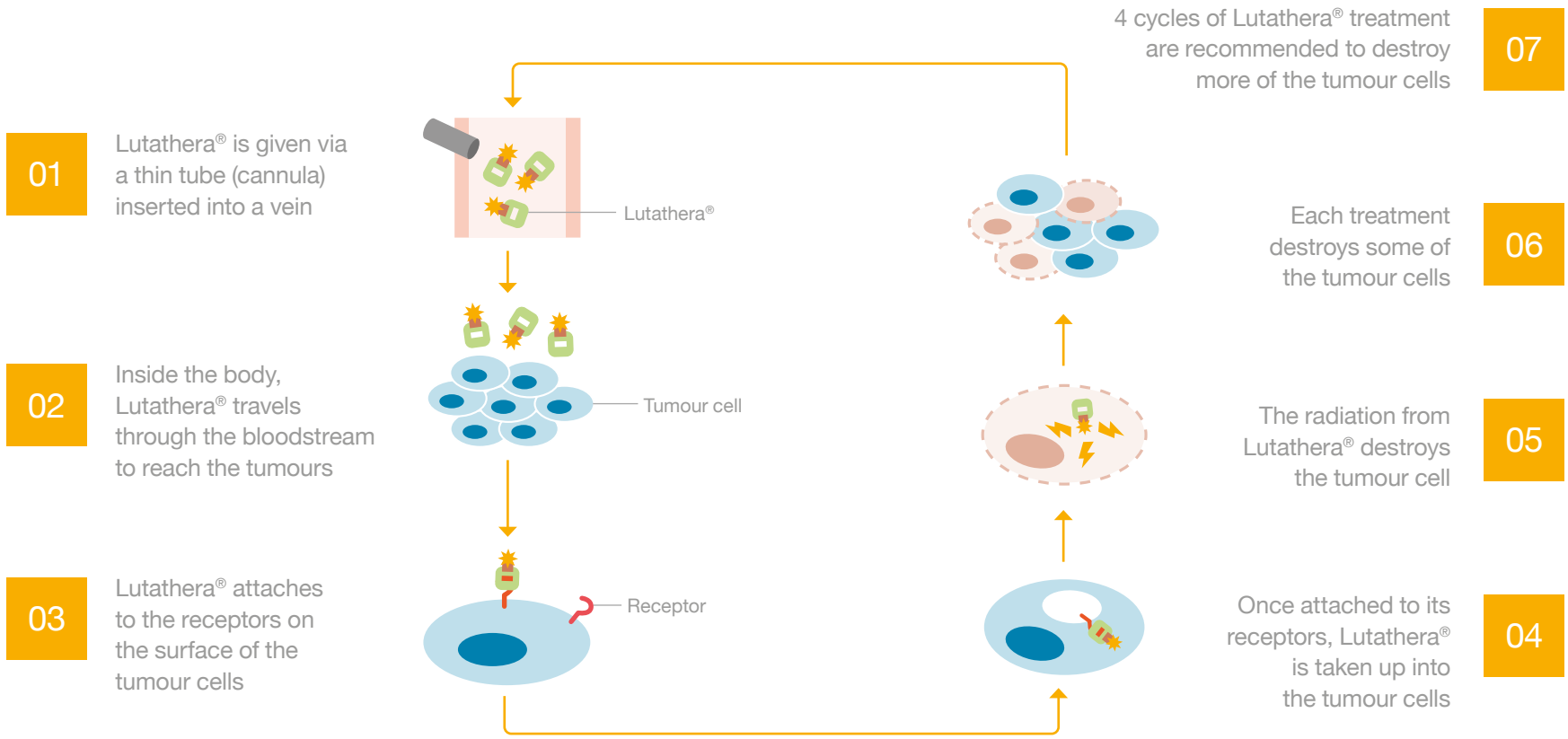

Figure 2. How Lutathera® treats neuroendocrine tumours[1,3]

CONSIDERATIONS **BEFORE YOUR LUTATHERA® TREATMENT**

To help your neuroendocrine tumour (NET) team plan your Lutathera® treatment, you should discuss everything about your disease and general health.

This should include:

- **Any symptoms you currently have.**
- **Any allergies you have.** Lutathera® is not suitable for people with certain allergies.[1]
- **All medicines you are currently taking.** Somatostatin analogues can reduce the effectiveness of Lutathera® treatment. If you are receiving this type of medication, you may be asked to stop for a short time during your Lutathera® treatment. Or, if you are receiving a somatostatin analogue as a long-acting injection, Lutathera® treatment may be timed just before your next injection.[1]
- **If you know you are pregnant or think you could be.** Lutathera® should not be used during pregnancy.[1]
- **If you are breastfeeding.** Breastfeeding should be avoided during Lutathera® treatment.[1]
- **Travel planned for the next 3 months.** After each Lutathera® treatment, you may need to take certain precautions when travelling. You can find more information about this on page 12.
- **Family responsibilities immediately after treatment.** After each Lutathera® treatment, you need to limit contact with family members at home. You can find more information about this on page 12.[1]
- **General health.** Your neuroendocrine tumour (NET) team will do tests to check your blood counts, liver and kidney function. Depending on the results they may hold off treatment until your body is ready.

Lutathera® is not expected to affect your ability to drive. However, if you feel your driving ability may be affected by your illness or side effects of this medication, please speak to a member of your neuroendocrine tumour (NET) team.[1]

HOW **IS** LUTATHERA® GIVEN?

It will be planned for you to receive a total of four Lutathera® treatments, each given approximately 8 weeks apart.[1] The time between treatments may be increased to up to 16 weeks if you have certain side effects.[1] For each of the four Lutathera® treatments, the recommended dose is 7,400 megabecquerels.[1] (The megabecquerel is a unit for measuring the amount of radioactivity.)

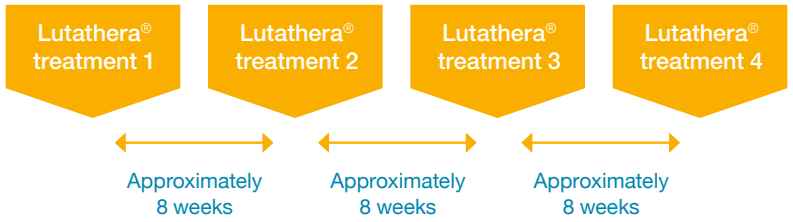

Figure 3. Treatment schedule for Lutathera®[1]

What happens at each Lutathera® treatment

You will receive your Lutathera® treatment in a special room at hospital, within a controlled area specialising in nuclear medicine and please note that you won't be able to have anyone else in the room with you during treatment.[1] The nuclear medicine team are specially trained to use medicines like Lutathera®.

Lutathera® is given by intravenous infusion.[1] This means the drug is slowly given via a thin tube (cannula) inserted into a vein in your arm. Lutathera® itself is given over approximately 30 minutes.[1] However, the time needed for tests and other medications means the whole procedure lasts 5–6 hours. The flow chart on the next page shows what to expect at each treatment visit.

The whole treatment cycle takes **5-6 hours**.

- Any paperwork will be completed with a member of your neuroendocrine tumour (NET) team on arrival.
- You will be asked to consent to the treatment.

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- A thin tube (cannula) will be inserted into a vein in one or both arms.
- You may have a blood test to check your blood counts, liver and kidney function again before your treatment.

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- You will be given an anti-sickness medication to help with any nausea or vomiting during the treatment.

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- To protect your kidneys, you are given an amino acid infusion. It starts before your Lutathera® treatment and lasts for about 4 hours in total.

- During the amino acid infusion, Lutathera® will be slowly given over about 30 minutes via a tube in the same or other arm.

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- Your neuroendocrine tumour (NET) team will have discussed with you whether you will go home on the day or stay in hospital overnight.
- You may have a scan before you leave the hospital.

Figure 4. Your treatment visit[1]

WHAT **PRECAUTIONS SHOULD I TAKE AFTER MY LUTATHERA® TREATMENT?**

Since Lutathera® is a radioactive medicine, there are some things you should do to minimise exposure to family members and the general public after you leave the hospital.[1]

After discharge

The table shows the main precautions to consider after each Lutathera® treatment. Your neuroendocrine tumour (NET) team may give you personalised durations for precautions based on your circumstances. They can also help you with any questions you may have. In addition, you may receive a wristband or card to show that you have recently received a radioactive treatment.

What to consider after every treatment with Lutathera®	
Daytime	• **For the first 7 days**, keep at least 1 metre away from other people, limiting any close contact with children and pregnant women to a maximum of 15 minutes per day.[1]
Night-time	• **For the first 7 days**, sleep in a separate bedroom from your partner.[1] • **For the first 15 days**, sleep in a separate bedroom from children and pregnant partners.[1]
Drinking	• **On the day and day after you receive Lutathera®**, drink plenty of water (one glass every hour).[1] The more you urinate, the faster the radiation leaves your body.

Using the toilet	• **For the first 7 days:**
	  • Try to pass a stool every day. Use laxatives if you need to.[1]
	  • Men should always use the toilet in a seated position and use toilet paper, even if only urinating.
	  • Flush all toilet paper down the toilet, and flush twice each time.
	  • Wash your hands carefully after every toilet visit.

Waste	• **For the first 7 days**, flush down the toilet any tissues containing bodily fluids (e.g. blood, urine or faeces).[1] • If you expect to have non-flushable waste items (e.g. sanitary towels), please discuss this with your neuroendocrine tumour (NET) team.
Showering or bathing	• **For at least the first 7 days**, shower or bathe every day.
Laundry	• **For the first 7 days**, wash your underwear, pyjamas, sheets and any clothes that contain sweat, blood or urine separately from the laundry of other members of your household, using a standard washing cycle. You do not need to use bleach and do not need extra rinses.

WHAT **PRECAUTIONS SHOULD I TAKE AFTER MY LUTATHERA® TREATMENT?**

Public contact	• **For at least the first 7 days**, avoid situations that would place you close to the same members of the public for prolonged periods (e.g. going to the cinema or church).
Public transport	• **For at least the first 7 days**, avoid public transport if possible. If you must use public transport, single journeys should last no longer than 1 hour. For single journeys over an hour, discuss these with your neuroendocrine tumour (NET) team. • **From day 8 until day 14**, single public transport journeys should last no longer than 3 hours. • After this time, you can use public transport as usual.
Car travel	• **For at least the first 7 days**, sit in the rear passenger seat diagonally opposite the driver if travelling by car, ensuring no other passengers are in the vehicle.
Air travel	• **For the first 7 days**, air travel journeys should ideally last no longer than 1 hour. Please discuss with your neuroendocrine tumour (NET) team if you may need to take longer air travel journeys. • After each treatment, you may set off airport radiation detectors. Please discuss any planned air travel with your neuroendocrine tumour (NET) team.

Work	• **For at least the first 7 days**, do not go to work. • After this time, discuss with your neuroendocrine tumour (NET) team when you are able to return to work.
Pets	• There is no evidence to suggest that your pet's health will be at risk after your treatment.
Pregnancy and fatherhood	• **During Lutathera® treatment and for 7 months after completing treatment**, female patients should use effective birth control. • **During Lutathera® treatment and for 4 months after completing treatment**, male patients should use effective birth control.

Special circumstances

If you have specific care needs, your neuroendocrine tumour (NET) team will provide appropriate advice based on your circumstances. If you use devices such as colostomy bags or catheters, please discuss the precautions you need to take with a member of your neuroendocrine tumour (NET) team.

WHAT **SIDE EFFECTS ARE POSSIBLE?**

Treatment with Lutathera® may cause side effects. Your neuroendocrine tumour (NET) team will explain possible side effects in detail and answer any questions you may have about them. Some of the most common side effects are discussed briefly below. Please remember that not all patients will have these. You may have a greater risk of some side effects with more cycles of treatment. In the table below, side effects are described as:

- **'Very common'** if they affect at least one in every 10 people,
- **'Common'** if they affect at least one in every 100 but less than one in every 10 people,
- **'Uncommon'** if they affect at least one in every 1,000 but less than one in every 100 people.

Please note that the side effects listed in this guide are not a full list of the known side effects. This guide should be read in conjunction with the Lutathera Patient Information Leaflet (PIL).

Short-term side effects

These side effects may occur during therapy or within the few weeks afterwards. They can include:

Nausea and vomiting are very common.[1]

Nausea and vomiting usually only occur in the first 24–48 hours after each treatment.[1] To help prevent and control nausea and vomiting, you will be given anti-sickness medication, both in hospital and to take home with you.[1]

Falls in blood counts are very common.[1]

Treatment with Lutathera® can cause a drop in the number of blood cells, including white cells, red cells and platelets.[1] A low white cell count can make you prone to infection, whereas a low red cell count can make you feel tired and short of breath. A low platelet count can cause bruising or bleeding. Any fall in blood counts is usually only temporary.[1] However, a few patients may need to delay treatment by up to 16 weeks to give their blood counts more time to recover.[1] Your blood counts will be carefully checked before and after each treatment with Lutathera®.[1] If you notice any bruising or bleeding, please let your neuroendocrine tumour (NET) team know straight away.

Decreased appetite is very common.[1]

Decreased appetite is quite common in the first 1–2 weeks after each treatment.[1] If you have less appetite than usual, try eating small meals frequently and make sure you drink plenty of fluids. Use anti-sickness medication if needed, as this can help improve your appetite.

Fatigue is very common.[1]

Any fatigue is usually only mild.[1,4] Fatigue may last for several weeks during treatment. Some people find their energy levels are lower in later cycles of treatment.

Hair loss is common.[1]

Any hair loss is usually minimal, and any lost hair should regrow after the treatment is finished.[1,4]

WHAT **SIDE EFFECTS ARE POSSIBLE?**

Abdominal pain is common.[1]

Pain in the stomach area may be caused by the effects of the drug on the tumours. It may last for a few days after each treatment, but can usually be well controlled with over-the-counter painkillers.

Diarrhoea is common.[1]

Diarrhoea is usually mild and generally does not need any specific treatment.[1,4]

Hormonal symptoms are uncommon.[1]

The tumour cells destroyed by the treatment can release hormones into your system.[1] This may lead to temporary symptoms such as flushing, wheezing and diarrhoea.[1] If you have any of these symptoms, you must let your neuroendocrine tumour (NET) team know as soon as possible. Untreated hormonal symptoms can lead to a serious condition called hormonal crisis. Your neuroendocrine tumour (NET) team will advise whether the symptoms need treatment or if you should stay in the hospital for observation.[1]

Tumour lysis syndrome is uncommon.[1]

Treatment with Lutathera® can destroy the tumour cells very quickly.[1] The contents of these cells are then released into your system.[1] Within a week of treatment, it is possible that you may have abnormal blood test results, experience an irregular heart beat, kidney problems or seizures.[1] Your blood tests will be carefully checked for this syndrome.[1] If you develop muscle cramps or weakness, confusion, or shortness of breath, it's important to let your NET team know.[1]

Long-term side effects

These side effects can occur late after treatment. Long-term side effects can include:

Problems with kidney function are common and can be long-term.[1]

Treatment with Lutathera® can impair your kidneys' ability to function and in some cases patients have experienced kidney failure. However, the risk of life-threatening kidney problems is reduced by receiving amino acids during treatment.[1] Your kidney function will also be tested before each treatment so that you can be monitored more closely if required.[1]

Long-term bone marrow problems affect 1–2% of people.[1,4]

Lutathera® treatment can cause conditions called myelodysplastic syndrome and acute leukaemia.[1] These are types of blood cancer that stop the bone marrow from producing enough blood cells. They are serious side effects and can be life-threatening. However, your neuroendocrine tumour (NET) team will routinely monitor your blood counts after treatment.

REPORTING **SIDE EFFECTS**

If you get any side effects, you should report them to your doctor. This includes any possible side effects not listed in this guide.

You can also report side effects directly to the national monitoring system. It is easiest and quickest to report adverse drug reactions online via the Yellow Card website: **www.mhra.gov.uk/yellowcard** or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary), by emailing **yellowcard@mhra.gov.uk**, by telephoning the Commission on Human Medicines (CHM) free phone line: 0800 731 6789, or by downloading and printing a form from the Yellow Card section of the MHRA website.

Side effects can also be reported to the manufacturer by emailing **uk.patientsafety@novartis.com**.

REFERENCES

1. Lutathera 370/MBq/ml solution for infusion Summary of Product Characteristics. Advanced Accelerator Applications.
2. Öberg K. Molecular Imaging Radiotherapy: Theranostics for Personalized Patient Management of Neuroendocrine Tumors (NETs). Theranostics; 2012; 2(5): 448-458.
3. Bodei L, Jaroslaw C. B., Kidd M. et al. The role of peptide receptor radionuclide therapy in advanced/metastatic thoracic neuroendocrine tumors. J Thorac Dis 2017; 9 (Suppl 15): S1511-S1523.
4. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 Trial of (177)Lu-Dotatate for Midgut Neuroendocrine Tumors. N Engl J Med. 2017; 376(2): 125-135.

NOTES

You and your neuroendocrine tumour (NET) team can use these pages to make any notes during each treatment cycle.

Lutathera® treatment 1

Date of treatment:

Notes:

Lutathera® treatment 2

Date of treatment:

Notes:

NOTES

You and your neuroendocrine tumour (NET) team can use these pages to make any notes during each treatment cycle.

Lutathera® treatment 3

Date of treatment:

Notes:

Lutathera® treatment 4

Date of treatment:

Notes:

KEY CONTACTS

You and your neuroendocrine tumour (NET) team can write here who to contact if you have any questions or concerns before, during or after Lutathera® treatment.

Other sources of support

Support organisations such as those listed below can provide you with information you may find helpful.

Neuroendocrine Cancer UK

Help and support:

Phone: 0800 434 6476

Email: nikie@nc-uk.org; catherine@nc-uk.org

General enquiries:

Phone: 01926 883487

Website: www.neuroendocrinecancer.org.uk

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Side effects can also be reported to the manufacturer by emailing **uk.patientsafety@novartis.com**.

For use by healthcare professionals with patients who have been prescribed Lutathera® to treat neuroendocrine tumours.

For more information please visit:
https://www.ema.europa.eu/en/medicines/human/EPAR/lutathera

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