# PATIENT INFORMATION LEAFLET

**SCHEDULING STATUS**

S4

**LEMTRADA® concentrate for solution for infusion**

**Alemtuzumab**

Sugar free.

**Read all of this leaflet carefully before you start using LEMTRADA.**

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- LEMTRADA has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

**What is in this leaflet**



## 1. What LEMTRADA is and what it is used for

LEMTRADA contains the active substance alemtuzumab, which is used to treat relapsing forms of multiple sclerosis (MS) in adults. LEMTRADA does not cure MS but it can decrease the number of MS relapses. It can also help to slow down or reverse some of the signs and symptoms of MS.
LEMTRADA is used if your MS is highly active despite that you have been treated with at least one other medicine for MS or if your MS is rapidly evolving.

## 2. What you need to know before you receive LEMTRADA

**Do not receive LEMTRADA:**

- If you are allergic to alemtuzumab or any of the other ingredients of LEMTRADA (see section 6).
- If you are infected with the human immunodeficiency virus (HIV).
- If you are suffering from a serious infection.
- If you have any of the following conditions:
  - uncontrolled high blood pressure
  - history of tears in blood vessels supplying the brain
  - history of stroke
  - history of heart attack or chest pain
  - history of bleeding disorder.

**Warnings and precautions:**

Talk to your doctor before LEMTRADA is given. After having a course of treatment with LEMTRADA you may be at greater risk of developing other autoimmune conditions or experiencing serious infections. It is important you understand these risks and how to monitor for them. You will be given a Patient Alert Card and a Patient Guide with further information. It is important that you keep the Patient Alert Card with you during treatment and for 4 years after your last infusion with LEMTRADA, because side effects may occur many years after treatment. When you have medical treatment, even if it is not for your MS, show the Patient Alert Card to the doctor.

Your doctor will perform blood tests before you start treatment with LEMTRADA. These tests are done to see whether you may take LEMTRADA. Your doctor will also want to make sure that you do not have certain medical conditions or disorders before you start your treatment with LEMTRADA.

***Autoimmune conditions***

Treatment with LEMTRADA may increase the risk for autoimmune conditions. These are conditions in which your immune system mistakenly attacks your body. Information about some specific conditions that have been seen in MS patients who have been treated with LEMTRADA is provided below.

The autoimmune conditions can occur many years after treatment with LEMTRADA. Therefore, regular blood and urine tests are needed until 4 years after your last infusion. Testing is needed even if you are feeling well and your MS symptoms are under control. There are certain signs and symptoms that you should look out for yourself. In addition, these conditions may occur beyond 4 years, therefore, you must continue to look for signs and symptoms, even after you no longer need to do monthly blood and urine tests. Details about the signs and symptoms, testing, and actions you need to take are described in sections 2 and 4 – *Autoimmune conditions*.

- ***Acquired haemophilia A***
  Uncommonly, patients developed a bleeding disorder caused by antibodies that work against factor VIII (a protein needed for normal clotting of blood), called acquired haemophilia A. This condition must be diagnosed and treated immediately. Symptoms of acquired haemophilia A are described in section 4.

- ***Immune thrombocytopenic purpura (ITP)***
  Commonly, patients have developed a bleeding disorder caused by a low level of blood platelets, called immune thrombocytopenic purpura (ITP). This must be diagnosed and treated early, as otherwise the effects can be serious or even fatal. Signs and symptoms of ITP are described in section 4.

- ***Kidney disease (such as anti-GBM disease)***
  Rarely, patients have experienced autoimmune-related problems with their kidneys, such as anti-glomerular basement membrane disease (anti-GBM disease). Signs and symptoms of kidney disease are described in section 4. If untreated it can cause kidney failure requiring dialysis or transplantation and may lead to death.

- ***Thyroid disorders***

  Very commonly, patients have experienced an autoimmune disorder of the thyroid gland affecting its ability to make or control hormones that are important for your metabolism.

  LEMTRADA may cause different types of thyroid disorders, including:

  - Overactive thyroid gland (hyperthyroidism) when the thyroid produces too much hormone.
  - Underactive thyroid gland (hypothyroidism) when the thyroid does not produce enough hormone.

  Signs and symptoms of thyroid disorders are described in section 4.

  If you develop a thyroid disorder, in most cases you will need to be treated for the rest of your life with medicines to control your thyroid disorder, and in some cases your thyroid gland may have to be removed.

  It is very important that you are properly treated for a thyroid disorder, especially if you become pregnant after using LEMTRADA. Having an untreated thyroid disorder could harm your unborn baby or harm your baby after birth.

- ***Liver inflammation***

  Some patients have developed liver inflammation after receiving LEMTRADA. Liver inflammation can be diagnosed from the blood tests that you will be having regularly after LEMTRADA treatment. If you develop one or more of the following symptoms report this to your doctor: nausea, vomiting, abdominal pain, fatigue, loss of appetite, yellow skin or eyes, dark urine, or bleeding or bruising more easily than normal.

- ***Thrombotic thrombocytopenic purpura (TTP)***

  A blood clotting disorder called thrombotic thrombocytopenic purpura (TTP), can occur with LEMTRADA. Blood clots form in blood vessels and can happen in the entire body. Get medical help right away if you have any of the following symptoms: skin or mouth bruising that may appear as red pinpoint dots, with or without unexplained extreme tiredness, fever, confusion, speech changes, yellowing of the skin or eyes (jaundice), low amount of urine, dark coloured urine. It is advised to seek medical attention urgently as TTP can be fatal (see section 4).

- ***Adult-onset Still's disease (AOSD)***

  AOSD is a rare condition that has the potential to cause multi-organ inflammation, with several symptoms such as fever > 39 °C lasting more than 1 week, pain, stiffness with or without swelling in multiple joints and/or a skin rash. If you experience a combination of these symptoms contact your health care provider immediately.

- ***Autoimmune encephalitis***

  This condition may include symptoms such as behaviour and psychiatric changes, movement disorders, short term memory loss or seizures as well as other symptoms resembling an MS relapse.

- ***Other autoimmune conditions***
  Uncommonly, patients have experienced autoimmune conditions involving red blood cells or white blood cells. These can be diagnosed from the blood tests that you will be having regularly after LEMTRADA treatment. If you develop one of these conditions your doctor will tell you and take appropriate measures to treat it.

***Infusion reactions***
Most patients treated with LEMTRADA will experience side effects at the time of the infusion or within 24 hours after the infusion. To try to reduce infusion reactions, your doctor will give you other medicine(s) (see section 4 - Infusion reactions).

***Other serious reactions occurring shortly after LEMTRADA infusion***
Some patients have had serious or life-threatening reactions after LEMTRADA infusion, including bleeding in the lung, heart attack, stroke or tears in blood vessels supplying the brain. Reactions may occur following any of the doses during the treatment course. In most cases reactions occurred within 1 - 3 days of the infusion. Your doctor will monitor vital signs, including blood pressure, before and during the infusion. Get help right away if you have any of the following symptoms of bleeding in the lung (trouble breathing, coughing up blood), chest pain, facial drooping, sudden severe headache, weakness on one side of the body, difficulty with speech or neck pain.

***Haemophagocytic lymphohistiocytosis***
Treatment with LEMTRADA may increase the risk of excessive activation of white blood cells associated with inflammation (haemophagocytic lymphohistiocytosis), which can be fatal if not diagnosed and treated early. If you experience multiple symptoms such as fever, swollen glands, bruising, or skin rash, contact your doctor immediately.

***Infections***
Patients treated with LEMTRADA are at a higher risk of getting a serious infection (see section 4 - Infections). In general, the infections can be treated with standard medicines.

To reduce the chance of getting an infection, your doctor will check if other medicines you are taking might be affecting your immune system. **Therefore, it is important to tell your doctor about all medicines you are taking**.

Also, tell your doctor if you are suffering from a serious infection before the start of your LEMTRADA treatment as your doctor should delay the treatment until the infection is resolved.

Patients treated with LEMTRADA are at a higher risk of developing herpes infection (e.g. a **cold sore**). In general, once a patient has had a herpes infection, they have an increased risk of developing another one. It is also possible to develop a herpes infection for the first time. It is recommended that your doctor prescribes a medicine to reduce the chance of developing a herpes infection, which should be taken on the days that you receive LEMTRADA treatment, and for one month following the treatment.

In addition, infections which can result in **abnormalities of the cervix** (the neck of the womb) are possible. Therefore, it is recommended that all female patients have an annual screening performed, such as a cervical smear. Your doctor will explain to you what tests you will need.

Infections with a virus called **cytomegalovirus** have been reported in patients treated with LEMTRADA. Most cases occurred within two months of alemtuzumab dosing. Tell your doctor right away if you have symptoms of infection such as fever, or swollen glands.

Patients treated with LEMTRADA have had infections due to a virus called **Epstein-Barr virus (EBV)**, including cases with severe liver inflammation. Tell your doctor right away if you have symptoms of infection such as fever, swollen glands, or fatigue.

Patients treated with LEMTRADA are also at a higher risk of developing **listeria infection** (a bacterial infection caused by ingestion of contaminated foods). Listeria infection can cause serious illness, including meningitis, but can be treated with appropriate medicines. To reduce this risk, you should avoid eating uncooked or undercooked meats, soft cheeses and unpasteurised dairy products two weeks before treatment, during the treatment and for at least one month after LEMTRADA treatment.

**Pneumonitis** (inflammation of lung tissue) has been reported in LEMTRADA-treated patients. Most cases occurred within the first month after treatment with LEMTRADA. You should report to your doctor symptoms like shortness of breath, cough, wheezing, chest pain or tightness and coughing up blood, as these could be caused by pneumonitis.

If you live in a region where **tuberculosis** infections are common, you may be at greater risk of infection with tuberculosis. Screening for tuberculosis will be arranged by your doctor.
Your doctor will screen for active and inactive ("latent") **tuberculosis** prior to starting, between courses, as well as after LEMTRADA treatment.
If you display symptoms of tuberculosis (e.g. coughing up blood, night sweats, weight loss) or you have been in contact with someone who has tuberculosis, please contact your doctor to arrange a screening.

If you are a carrier of **hepatitis B** or **hepatitis C** infection (these affect the liver), extra caution is needed before you receive LEMTRADA treatment as it is unknown if treatment could lead to activation of the hepatitis infection which could subsequently damage your liver.

No case of a rare brain infection called **progressive multifocal leukoencephalopathy** (PML) has been reported in clinical studies of LEMTRADA in patients with multiple sclerosis. PML has been reported in patients in the post-marketing setting with other risk factors, specifically prior treatment with MS medicines associated with PML.
PML may lead to severe disability over weeks or months and may be fatal.
Symptoms may be similar to a relapse of MS and include progressive weakness or clumsiness of limbs, disturbance of vision, speech difficulties or changes in thinking, memory, and orientation leading to confusion and personality changes. It is important to inform your relatives or caregivers about your treatment, since they may notice symptoms of which you are not aware. Contact your doctor immediately if you develop any symptoms suggestive of PML.

***Inflammation of the gallbladder***
LEMTRADA may increase your chance of getting inflammation of the gallbladder. This may be a serious medical condition that can be life-threatening. You should report to your doctor if you have symptoms such as stomach pain or discomfort, fever, nausea or vomiting.

***Previously diagnosed cancer***
If you have been diagnosed with cancer in the past, please inform your doctor about it.

***Vaccines***
It is not known if LEMTRADA affects your response to a vaccine. If you have not completed the standard required vaccinations, your doctor will consider whether you should have them before your LEMTRADA treatment. Your doctor will consider vaccinating you against chickenpox if you have never had it. Any vaccination will need to be given to you at least 6 weeks before starting a LEMTRADA treatment course.

You must NOT receive certain types of vaccines (live viral vaccines) if you have recently received LEMTRADA.

**Children and adolescents:**
LEMTRADA is not intended to be used in children and adolescents under the age of 18 years, as it has not been studied in MS patients of this age group.

**Other medicines and LEMTRADA:**
Always tell your health care provider if you are taking any other medicine. (This includes complementary or traditional medicines.)
Please consult with your doctor, pharmacist or health care provider for advice if you need to take any other medicines.
This also includes any vaccinations that you may have recently received.
If you have used another MS treatment in the past or any medicines that may affect your ability to fight infections, your doctor may ask you to stop the other medicine in advance prior to starting treatment with LEMTRADA.

**Pregnancy and breastfeeding:**
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you receive LEMTRADA.

LEMTRADA should not be administered during pregnancy.

Women who are able to conceive should use effective contraceptive methods during each treatment course with LEMTRADA and for 4 months after each course of treatment.

If you become pregnant after treatment with LEMTRADA and experience a thyroid disorder during pregnancy, extra caution is needed. Thyroid disorders could be harmful to the baby (see section 2: Warnings and precautions – *Autoimmune conditions*).

It is recommended that you do not breastfeed during each course of treatment with LEMTRADA or for 4 months after each treatment course. Talk to your doctor if you are planning to breastfeed your baby. Your doctor will advise you what is right for you and your baby.

**Driving and using machines**
LEMTRADA does not directly affect your ability to drive or use machines. However, you may experience side effects during the treatment course which could make driving or using machines unsafe, such as dizziness. If you are affected, stop these activities immediately.

**LEMTRADA contains potassium and sodium**
LEMTRADA contains less than 1 mmol potassium (39 mg) per infusion, i.e. it is essentially potassium free.
LEMTRADA contains less than 1 mmol sodium (23 mg) per infusion, i.e. it is essentially sodium free.

## 3. How LEMTRADA will be administered

LEMTRADA will be administered to you by a person who is qualified to do so.
LEMTRADA will be administered to you as an infusion into a vein. Each infusion will take approximately 4 hours.

*First treatment course:*
You will receive one infusion per day for 5 days (course 1).

*Second treatment course:*
One year later you will receive one infusion per day for 3 days (course 2). There is no LEMTRADA treatment between the two courses.

Some patients, if they have symptoms or signs of MS disease after the initial two courses, may receive additional treatment courses consisting of one infusion per day for 3 days. These additional treatment courses may be administered twelve months or more after the prior treatments.

The maximum daily dose is one infusion.

*Duration of effects:*
Monitoring for side effects must continue for 4 years after the last infusion.

*Follow-up after treatment with LEMTRADA:*
Once you have received LEMTRADA, you will need to undergo regular tests to ensure that any potential side effects can be diagnosed and treated quickly.

**If you are given more LEMTRADA than you should receive:**
Patients who accidentally were given too much LEMTRADA in one infusion have experienced serious reactions, such as headache, rash, low blood pressure or increased heart rate. Doses higher than the recommended dose may result in more serious or longer lasting infusion reactions (see section 4) or a stronger negative effect on the immune system. The treatment consists of stopping LEMTRADA administration and treatment of the symptoms of the overdosage.

**Missed LEMTRADA doses**
It is unlikely that your dose would be missed since it is administered by a health care provider. In case of a missed dose, this should not be given on the same day as a scheduled dose.

## 4. Possible side effects

LEMTRADA can have side effects.
Not all side effects reported for LEMTRADA are included in this leaflet. **Should your general health worsen or if you experience any untoward effects while you are receiving LEMTRADA, please consult your doctor, pharmacist or other health care provider for advice.**

**If any of the following happens, stop receiving LEMTRADA and tell your doctor immediately or go to the casualty department at your nearest hospital:**

- Swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing.
- Rash or itching.
- Fainting.
- Yellowing of your skin and eyes (also called jaundice).

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to LEMTRADA. You may need urgent medical attention or hospitalisation.

The most important side effects are the autoimmune conditions described in section 2 which include:

- **Acquired haemophilia A (a type of bleeding disorder)**, (occurs less frequently): may show as spontaneous bruising, nose bleeds, painful or swollen joints, other types of bleeding, or bleeding from a cut that may take longer than usual to stop.
- **ITP (bleeding disorders)**, (occurs frequently): may show as small scattered red, pink or purple spots on your skin; easy bruising; bleeding from a cut that is harder to stop; heavier, longer or more frequent menstrual periods than normal; bleeding between menstrual periods; bleeding from your gums or nose that is new or takes longer than usual to stop; or coughing up blood.
- **TTP (blood disorder)**, (occurs less frequently): may show as bruising under the skin, or bruising in the mouth, that may appear as red pinpoint dots, with or without unexplained extreme tiredness, fever, confusion, speech changes, yellowing of the skin or eyes (jaundice), low amount of urine, dark coloured urine.
- **Kidney disorders**, (occurs less frequently): may show as blood in the urine (your urine may be red or tea-coloured), or as swelling in your legs or feet. It can also lead to damage of your lungs, which can result in coughing up blood.

**If you notice any of these signs or symptoms for bleeding or kidney disorders, call your doctor immediately to report the symptoms. If you cannot reach your doctor, you must seek immediate medical attention.**

- **Thyroid disorders** (occurs frequently): may show as excessive sweating; unexplained weight-loss or gain; eye swelling; nervousness; fast heartbeat; feeling cold; worsening tiredness; or newly occurring constipation.
- **Red and white blood cells disorders** (occurs less frequently): diagnosed from your blood tests.
- **Sarcoidosis** (occurs less frequently): symptoms can include persistent dry cough, shortness of breath, chest pain, fever, lymph swelling, weight loss, skin rashes, blurred vision.

All of these serious side effects can start many years after you have received LEMTRADA. **If you notice any of these signs or symptoms, call your doctor right away to report them**. You will also have regular blood and urine tests to ensure that if you develop any of these conditions, they **are treated promptly**.

Summary of tests you will have for autoimmune conditions:

| **Test** | **When** | **For how long?** |
|---|---|---|
| **Blood test**<br>(to diagnose all important serious side effects listed above) | **Before treatment starts and every month after treatment** | **Until 4 years after your last LEMTRADA infusion** |
| **Urine test**<br>(additional test to diagnose kidney disorders) | **Before treatment starts and every month after treatment** | **Until 4 years after your last LEMTRADA infusion** |

After this time, if you have symptoms of blood, liver, kidney or thyroid disorders, your doctor will perform more tests. You should also continue looking for signs and symptoms of side effects beyond four years as detailed in your Patient Guide, and you should continue carrying the Patient Alert Card with you.

Another side effect is an increased risk of infections (see below for information on how often patients experience infections). In most cases, these are mild but serious infections can occur.

Tell your doctor right away if you have any of these signs of infection:

- fever and/or chills
- swollen glands.

To help reduce the risk of some infections your doctor may consider giving you a vaccination against chickenpox and/or other vaccinations that they think are necessary for you (see section 2: What you need to know before you receive LEMTRADA - *Vaccines*). Your doctor can also prescribe a medicine for cold sores (see section 2: What you need to know before you receive LEMTRADA – *Infections*).

The most frequent side effects are infusion reactions (see below for information on how often patients experience these), which can happen at the time of the infusion or within 24 hours after the infusion. In most cases these are mild, but some serious reactions are possible. Occasionally allergic reactions could occur.

To try to reduce infusion reactions, your doctor will give you medicine (corticosteroids) before each of the first 3 infusions of a LEMTRADA course. Other treatments to limit these reactions can also be given before the infusion or when you experience symptoms. In addition, you will be monitored during the infusion and for 2 hours after the infusion has been completed. In case of serious reactions, the infusion may be slowed down or even stopped.

**Tell your doctor if you notice any of the following:**

***Frequently occurring side effects may include:***

- Infusion reactions that can happen at the time of the infusion or within 24 hours after the infusion: headache, rash, fever, feeling sick, hives, itching, reddening of the face and neck, feeling tired, nausea, increased heart rate, indigestion, chills, chest discomfort, pain, dizziness, altered taste, difficulty sleeping, difficulty breathing or shortness of breath, rash over your body, low blood pressure.
- Infections: airway infections such as colds and sinus infections, urinary tract infections (cystitis), herpes infections, cough, ear infection, flu-like illness, bronchitis, pneumonia, oral thrush or vaginal thrush, shingles, chickenpox, cold sore, swollen or enlarged glands, influenza, tooth infection.
- A decrease in the number of white blood cells (e.g. lymphocytes, leukocytes, neutrophils).
- An increase in white blood cells counts such as neutrophils, eosinophils (different types of white blood cells), anaemia, decrease in percentage of red blood cells, easy or excessive bruising or bleeding, swelling of lymph nodes.
- Exaggerated immune response.
- Pain at the site of the infusion, pain in the back, the neck, or in arms or legs, muscle pain, muscle

spasms, joint pain.
- Inflammation of the mouth/gums/tongue, painful mouth or throat.
- General discomfort, weakness, vomiting, diarrhoea, abdominal pain, gastric flu (most common symptoms of diarrhoea).
- Abnormal liver test.
- Heartburn.
- Abnormalities that can be found during examinations: blood or protein in urine, decreased heart rate, irregular or abnormal heartbeat, high blood pressure, impaired kidney function, white blood cells in urine.
- Contusion.
- MS relapse.
- Trembling, loss of sensation, burning or prickling sensation.
- Overactive or underactive thyroid gland, or goitre (swelling of the thyroid gland in the neck).
- Swelling of arms and/or legs.
- Vision problems, conjunctivitis, eye disease associated with thyroid disease.
- Sensation of spinning or loss of balance.
- Feelings of anxiety, depression.
- Abnormally heavy, prolonged or irregular menstruation.
- Acne, redness of the skin, excessive sweating.
- Nose bleeds, bruises.
- Hair loss.

***Less frequently occurring side effects may include:***
- Infections: genital herpes, eye infection, inflammation of the lung tissue (pneumonitis), cytomegalovirus infection.
- Problems with blood clotting.
- Athlete's foot.
- Abnormal cervical Pap smear.
- Tuberculosis (TB).
- Inflammation of the gallbladder.
- Autoimmune disease characterised by bleeding (acquired haemophilia A).
- Excessive activation of white blood cells associated with inflammation (haemophagocytic lymphohistiocytosis).

***Other side effects where the frequency cannot be determined:***
- Listeriosis/listeria meningitis.
- Bleeding in lungs.
- Heart attack.
- Stroke.
- Tears in carotid or vertebral arteries (blood vessels supplying the brain).
- Infection due to a virus known as Epstein-Barr virus.
- Sarcoidosis (an immune disorder that can cause inflammation of one or more organs including lungs,

lymph nodes, skin or heart).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

**Reporting of side effects:**

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email) or 011 256 3700 (tel), or
- SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

By reporting side effects, you can help provide more information on the safety of LEMTRADA.

## 5. How to store LEMTRADA

**Vials**

Store at 2 °C to 8 °C, protected from light.

Do not freeze or shake.

Keep the vial in the outer carton until required for use.

**Infusion solution**

LEMTRADA diluted medicine may be stored at room temperature (15 °C to 25 °C) or refrigerated (2 °C to 8 °C) for up to 8 hours.

Protect from light.

Partially used, unused, or damaged medicine vials should be discarded appropriately.

For the reconstituted medicine, from a microbiological point of view, the medicine should be used immediately. If not used immediately in-use storage time and conditions prior to use are the responsibility of the user and would normally be 2 – 8 °C, unless reconstitution/dilution has taken place in controlled and validated conditions.

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

## 6. Contents of the pack and other information

**What LEMTRADA contains:**

The active substance is alemtuzumab.

The other ingredients are disodium edetate dihydrate, polysorbate 80, potassium chloride, potassium dihydrogen phosphate, sodium chloride, sodium phosphate dibasic and water for injection.

**What LEMTRADA looks like and contents of the pack:**

LEMTRADA is a clear, colourless to slightly yellow concentrate with pH 7,0 – 7,4, containing no antimicrobial preservatives.

LEMTRADA is supplied in a clear, 2 mL Type 1 glass vial, with a grey butyl rubber stopper and aluminium seal with a green plastic flip-off cap.

Pack size: carton with 1 vial.

**Holder of the certificate of registration**

sanofi-aventis south africa (pty) ltd
Hertford Office Park, Building I, 5th Floor
90 Bekker Road, Vorna Valley
Midrand 2196
South Africa
Tel. no.: 011 256 3700

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