PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Tepkinly 4 mg/0.8 ml

Concentrate for solution for injection

The active ingredient and its quantity:
Epcoritamab 5 mg/ml.
Each 0.8 ml vial contains 4 mg of epcoritamab.
For the list of inactive ingredients, please see section 6 "Further Information" and section 2 "Important information about some of the ingredients of the medicine" in this leaflet.
Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

In addition to the leaflet, Tepkinly has a 'Patient Safety Information Card'. This card contains important safety information that you must know and adhere to before and during the treatment with Tepkinly. Read the 'Patient Safety Information Card' and the patient leaflet before starting to use the preparation. Keep the card for further reading, if necessary.

1. WHAT IS THE MEDICINE INTENDED FOR?

Tepkinly is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy.

Therapeutic group:
Antineoplastic agents.

How Tepkinly works
Epcoritamab is specifically designed to help your immune system to attack cancer (lymphoma) cells. Epcoritamab acts by attaching to your body's immune cells and cancer cells, bringing them together, so that your immune system can destroy the cancer cells.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- you are allergic to epcoritamab or any of the other ingredients of the medicine (listed in section 6).
  If you are not sure, talk to your doctor or nurse before you are given Tepkinly.

Special warnings regarding use of the medicine
Before treatment with Tepkinly, tell the doctor if you:
- have current or past problems with your nervous system – such as seizures.
- have an infection.
- are due to have a vaccine or you know you may need to have one in the near future.

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before you are given Tepkinly.
Tell your doctor straight away if you get symptoms of any of the side effects listed below, during or after treatment with Tepkinly. You may need additional medical treatment.
- **Cytokine release syndrome (CRS)** – a life-threatening condition causing fever, vomiting, difficulty breathing/shortness of breath, chills, rapid heartbeat, headache and dizziness or light-headedness, associated with medicines that stimulate T cells.
  – Before each injection under the skin, you may be given medicines which help reduce possible effects of cytokine release syndrome.
- **Immune effector cell-associated neurotoxicity syndrome (ICANS)** – symptoms may include problems with use of language (including speech, understanding, writing and reading), drowsiness, confusion/disorientation, muscle weakness, seizures, swelling of part of the brain, and memory loss.
- **Tumour lysis syndrome (TLS)** – some people may get unusual levels of some salts in the blood – caused by the fast breakdown of cancer cells during treatment. This is called tumour lysis syndrome. Please see section 4 "Side Effects" in this leaflet for the list of symptoms.
  ◦ Your doctor or nurse will do blood tests to check for this condition. Before each injection under the skin, you should be well-hydrated and may be given other medicines that can help reduce high levels of uric acid and help reduce possible effects of 'tumour lysis syndrome'.
- **Tumour flare** – as your cancer is destroyed, it may react and appear to get worse – this is called 'tumour flare reaction'. Please see section 4 "Side Effects" in this leaflet for the list of symptoms.
- **Infections** – you may get signs of infection, such as fever of 38°C or above, chills, cough, or pain upon urination, which can vary depending on where in the body the infection is. Please see section 4 "Side Effects" in this leaflet for the list of symptoms.

Children and adolescents
Tepkinly is not intended for children and adolescents under 18 years, as there is no information about the effectiveness and safety of use of the preparation in this age group.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Pregnancy, breastfeeding and fertility

Pregnancy
If you are pregnant, think you may be pregnant or are planning to have a baby, ask the doctor or pharmacist for advice before taking this medicine. Do not use Tepkinly during pregnancy, as it may affect your unborn baby. Your doctor may ask you to take a pregnancy test before starting treatment.

Contraception
If you are a woman who is able to have children, you must use effective contraception to avoid becoming pregnant while taking Tepkinly and for at least 4 months after your last dose of Tepkinly. If you become pregnant during this time, you must talk to your doctor straight away.
Talk to your doctor or nurse about suitable methods of contraception.

Breastfeeding
You must not breastfeed during treatment with Tepkinly and for at least 4 months after the last dose. It is not known whether Tepkinly passes into breast milk and whether it could affect your baby.

Fertility
The effect of Tepkinly on male and female fertility is unknown.

Driving and using machines
Due to the possible symptoms of ICANS, you should be careful while driving, cycling or using heavy or potentially dangerous machines. If you currently have such symptoms, avoid these activities and contact your doctor, nurse or pharmacist. See section 4 for more information about side effects.

Important information about some of the ingredients of the medicine

Tepkinly contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say it is essentially 'sodium-free'.

Tepkinly contains sorbitol
This medicine contains 21.9 mg sorbitol in each vial, which is equivalent to 27.33 mg/ml.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.
The dosage and treatment regimen will be determined by the doctor only.
Tepkinly will be given to you by a doctor or nurse as an injection under your skin.
The usual dosage is generally:
Tepkinly will be given to you in cycles of 28 days, on a dosing schedule given to you by your doctor.
You will be given Tepkinly according to the following schedule:

Cycle	Dosing schedule
Cycles 1 to 3	Weekly
Cycles 4 to 9	Every two weeks
Cycles 10 and beyond	Every four weeks

You may be given other medicines before you are given Tepkinly. This is to help prevent reactions such as cytokine release syndrome and fever in Cycle 1 (and potentially in future cycles).
These medicines may include:
- Corticosteroids – such as prednisolone or similar medicine
- An antihistamine – such as diphenhydramine
- Paracetamol

The starting treatment doses:
The initial dose (0.16 mg) of Tepkinly will be given to you on Cycle 1 Day 1.
The second dose (0.8 mg) of Tepkinly will be given to you on Cycle 1 Day 8.
Transition to administration of a full dose:
The first full dose (48 mg) of Tepkinly will be given to you on Cycle 1 Day 15. Your doctor will monitor how your treatment is working and ask you to stay in a hospital for 24 hours after the first full dose (48 mg), because this is when reactions such as CRS, ICANS and fever are most likely to occur.
You will be given Tepkinly for as long as your doctor thinks you are benefitting from the treatment.
Your doctor may delay or completely stop your treatment with Tepkinly if you have certain side effects.

Do not exceed the recommended dose.

If you forget to use Tepkinly
If you forget or miss your medical appointment, contact your doctor immediately for instructions. For the treatment to be fully effective, it is very important not to miss a dose.
Adhere to the treatment regimen as determined by the doctor.

If you stop using Tepkinly
Do not stop treatment with Tepkinly unless you have discussed this with your doctor. This is because stopping treatment may make your condition worse.
Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them. If you have further questions regarding the use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of the medicine may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Serious side effects
Tell your doctor straight away if you notice any of the symptoms of the following serious side effects. You may only get one or some of these symptoms.
For further information, please see section 2 "Special warnings regarding use of the medicine".

Cytokine release syndrome (CRS) (**Very common side effect:** effects that occur in more than 1 in 10 users)
Symptoms can include:
- fever
- vomiting
- dizziness or light-headedness
- chills
- fast heartbeat
- difficulty breathing/shortness of breath
- headache

Immune effector cell-associated neurotoxicity syndrome (ICANS) (**Common side effect:** effects that occur in 1-10 out of 100 users)
- effects on your nervous system, the symptoms of which can occur days or weeks after you receive the injection, may initially be subtle. Some of these symptoms may be signs of a serious immune reaction called "immune effector cell-associated neurotoxicity syndrome" (ICANS).
  Symptoms can include:
  - difficulty speaking or writing
  - drowsiness
  - confusion/disorientation
  - muscle weakness
  - seizures
  - memory loss

Tumour lysis syndrome (TLS) (**Common side effect:** effects that occur in 1-10 out of 100 users)
Symptoms can include:
- fever
- chills
- vomiting
- confusion
- shortness of breath
- seizures
- irregular heartbeat
- dark or cloudy urine
- unusual tiredness
- muscle or joint pain

Other side effects
Tell your doctor or nurse straight away if you notice any of the following side effects or if they get worse:

Very common side effects: effects that occur in more than 1 in 10 users
- viral infection
- pneumonia (lung infection)
- decreased hunger
- irregular heartbeat
- pain in bones, joints, ligaments and muscles
- pain in the belly area
- headache
- nausea
- diarrhoea
- vomiting
- tiredness
- injection site reactions
- fever
- swelling

Side effects shown in blood tests:
- low levels of a type of white blood cells that fight infection (neutropenia)
- low levels of red blood cells, which can cause tiredness, pale skin, and shortness of breath (anaemia)
- low levels of blood platelets, which can lead to bleeding and bruising (thrombocytopenia)

Common side effects: effects that occur in 1-10 out of 100 users
- fever due to infection when you have low levels of white blood cells (febrile neutropenia)
- upper respiratory tract infections (infection of the airways)
- tender swollen lymph nodes, chest pain, cough or difficulty breathing, pain at the site of the tumour (tumour flare)
- fungal infections (caused by a type of germ called a fungus)
- skin infections
- life-threatening reaction the body has to an infection (sepsis)
- decrease in a type of white blood cell called a lymphocyte, which may affect the body's ability to fight infection (lymphopenia)
- a rapid breakdown of tumour cells resulting in chemical changes in the blood and damage to organs, including the kidneys, heart and liver (tumour lysis syndrome)
- extra fluid around the lungs that can make it difficult to breathe (pleural effusion)
- rash
- itching (pruritus)

Side effects shown in blood tests:
- low level of phosphates in the blood, potassium, magnesium or sodium
- increased blood level of creatinine, a breakdown product from muscle tissue
- increased blood level of liver proteins, which may show problems with the liver

If a side effect occurs, if one of the side effects worsens, or if you are suffering from a side effect not mentioned in the leaflet, consult the doctor.

Reporting of side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects due to Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, must be kept in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
Tepkinly will be stored by the doctor, nurse or pharmacist at the hospital or clinic. To correctly store Tepkinly:
- Do not use the medicine after the expiry date (exp. Date) which is stated on the vial label and carton. The expiry date refers to the last day of that month.
- Store and transport refrigerated (2°C to 8°C).
- Do not freeze.
- Keep the vial in the outer carton in order to protect from light.
- Tepkinly 4 mg/0.8 ml is a concentrated solution and must be diluted prior to use.
- If not used immediately, the prepared solution may be stored for up to 24 hours at 2°C to 8°C from the time of preparation.
- Within these 24 hours, the prepared solution can be stored for up to 12 hours at room temperature (20°C to 25°C) from the start of dose preparation to administration.
- Allow the diluted solution to warm to room temperature before using.

Your doctor, nurse or pharmacist will throw away any unused medicine following local requirements. These measures will help protect the environment.

6. FURTHER INFORMATION

What Tepkinly contains
– In addition to the active ingredient, the medicine also contains:
D-Sorbitol, sodium acetate trihydrate, polysorbate 80, acetic acid glacial, water for injection
(See in section 2 "Tepkinly contains sodium" and "Tepkinly contains sorbitol").

What the medicine looks like and contents of the pack
Tepkinly is a concentrate for solution for injection. It is a colourless to slightly yellow solution provided in a glass vial.
Each carton contains 1 vial.
License holder and its address: AbbVie Biopharmaceuticals Ltd., 4 Hacharash St., Hod Hasharon, Israel.
Manufacturer name and its address:
AbbVie Deutschland GmbH & Co. KG, Knollstrasse, 67061 Ludwigshafen, Germany.
This leaflet was checked and approved by the Ministry of Health in March 2024

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 176-07-37755

המידע הבא מיועד לאנשי צוות רפואי בלבד:
المعلومات التالية مخصصة لأفراد الطاقم الطبي فقط:

The following information is intended for healthcare professionals only:
Epcoritamab is prepared and administered as a subcutaneous injection.
Each vial of epcoritamab is intended for single use only.
Each vial contains an overfill that allows withdrawal of the labelled amount.
Epcoritamab must be diluted and administered by a healthcare professional using aseptic technique.
Filtration of the diluted solution is not required.
Epcoritamab should be inspected visually for particulate matter and discolouration prior to administration. The concentrate should be a colourless to slightly yellow solution. Do not use if the solution is discoloured, or cloudy, or if foreign particles are present.
0.16 mg priming dose preparation instructions – **2 dilutions required**
Use an appropriately sized, syringe, vial and needle for each transfer step.
1) Prepare Tepkinly vial
   a) Retrieve one 4 mg/0.8 ml Tepkinly vial with the **light blue** cap from the refrigerator.
   b) Allow the vial to come to room temperature for no more than 1 hour.
   c) Gently swirl the Tepkinly vial.

DO NOT vortex or vigorously shake the vial.
2) Perform first dilution
   a) Label an appropriately sized empty vial as **"dilution A"**.
   b) Transfer **0.8 ml of Tepkinly** into the **dilution A** vial.
   c) Transfer **4.2 ml of sodium chloride 9 mg/ml (0.9%) sterile solution** into the **dilution A** vial. The initial diluted solution contains 0.8 mg/ml of epcoritamab.
   d) Gently swirl the **dilution A** vial for 30-45 seconds.
3) Perform second dilution
   a) Label an appropriately sized empty vial as **"dilution B"**.
   b) Transfer **2 ml of solution** from the **dilution A** vial into the **dilution B** vial. The **dilution A** vial is no longer needed and should be discarded.
   c) Transfer **8 ml of sodium chloride 9 mg/ml (0.9%) sterile solution** into the **dilution B** vial to make a final concentration of 0.16 mg/ml.
   d) Gently swirl the **dilution B** vial for 30-45 seconds.
4) Withdraw dose
   Withdraw **1 ml of the diluted epcoritamab** from the **dilution B** vial into a syringe. The **dilution B** vial is no longer needed and should be discarded.
5) Label syringe
   Label the syringe with the product name, dose strength (0.16 mg), date and the time of day.
6) Discard the vial and any unused portion of Tepkinly in accordance with local requirements.

0.8 mg intermediate dose preparation instructions – **1 dilution required**
Use an appropriately sized, syringe, vial and needle for each transfer step.
1) Prepare Tepkinly vial
   a) Retrieve one 4 mg/0.8 ml Tepkinly vial with the **light blue** cap from the refrigerator.
   b) Allow the vial to come to room temperature for no more than 1 hour.
   c) Gently swirl the Tepkinly vial.

DO NOT vortex or vigorously shake the vial.
2) Perform dilution
   a) Label an appropriately sized empty vial as **"dilution A"**.
   b) Transfer **0.8 ml of Tepkinly** into the **dilution A** vial.
   c) Transfer **4.2 ml of sodium chloride 9 mg/ml (0.9%) sterile solution** into the **dilution A** vial to make a final concentration of 0.8 mg/ml.
   d) Gently swirl the **dilution A** vial for 30-45 seconds.
3) Withdraw dose
   Withdraw **1 ml of the diluted epcoritamab** from the **dilution A** vial into a syringe. The **dilution A** vial is no longer needed and should be discarded.
4) Label syringe
   Label the syringe with the product name, dose strength (0.8 mg), date and the time of day.
5) Discard the vial and any unused portion of Tepkinly in accordance with local requirements.

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.