Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Talvey® 2 mg/mL
Talvey® 40 mg/mL

Solution for injection

Active ingredient
Talvey 2 mg/ml – each ml contains 2 mg talquetamab
One 1.5 ml vial contains 3 mg talquetamab.
Talvey 40 mg/ml – each ml contains 40 mg talquetamab
One 1 ml vial contains 40 mg talquetamab.

Inactive ingredients and allergens in this medicine: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

In addition to the patient information leaflet, Talvey also has a patient safety information card.

This card contains important safety information that you need to know and that you should follow before starting and during treatment with Talvey. Carefully read the patient safety information card and patient information leaflet before using this medicine. Keep the card in case you need to read it again.

1. What is this medicine intended for?

Talvey is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least 3 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti CD38 antibody and have demonstrated disease progression on the last therapy.

Therapeutic group: Other monoclonal antibodies and antibody drug conjugates, L01FX29.

Talvey is a cancer medicine that contains the active substance talquetamab. Talquetamab is an antibody, a type of protein that recognises and attaches to specific targets in your body. It has been designed to attach to the protein GPRC5D (G Protein-coupled receptor family C group 5 member D), which is found on multiple myeloma cancer cells, and to cluster of differentiation 3 (CD3), a protein on T cells (a type of white blood cell). T cells are a part of the body's natural defences and help protect the body from infection. They can also destroy cancer cells. When this medicine attaches to these cells, it brings the cancer cells and T cells together. This encourages the T cells to destroy the multiple myeloma cancer cells.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to talquetamab (the active ingredient) or to any of the other ingredients in this medicine (see section 6).

Do not take this medicine if any of the above conditions applies to you. If you are not sure, talk to your doctor or pharmacist before taking this medicine.

Special warnings about using this medicine

Talk to your doctor, nurse or pharmacist before taking Talvey.

Serious side effects

There are serious side effects that may occur after you start treatment with Talvey. You need to tell your doctor or nurse straight away if these occur, as they may require that you get immediate medical attention.

Tell your doctor or nurse right away if you experience any of the following:

- Signs of a condition known as 'cytokine release syndrome' (CRS). CRS is a serious immune reaction with symptoms such as fever, low blood pressure, chills, difficulty breathing, fatigue, headache, fast heart beat and increased level of liver enzymes in the blood.
- Effects on your nervous system. Symptoms include feeling confused, feeling disoriented, feeling sleepy, feeling less alert, slow or difficulty thinking, altered thinking or decreased consciousness, confusion, difficulty speaking and understanding speech. Some of these symptoms may be signs of a serious immune reaction called 'immune effector cell-associated neurotoxicity syndrome' (ICANS).
- Problems with the mouth, such as a loss of taste, dry mouth, difficulty swallowing and inflammation of the lining of the mouth.
- Skin problems such as rash, redness and nail problems.
- Feeling warm, fever, chills or shivering, sore throat or mouth ulcers may be signs of an infection.

Talvey and vaccines

Talk to your doctor or nurse before you are given Talvey if you have had a recent vaccination or are going to have a vaccination. Your immune system (the body's natural defences) may not respond as well to vaccination when you are taking this medicine.

You should not receive live vaccines, a specific type of vaccine, from at least 4 weeks before starting your treatment with Talvey until at least 4 weeks after you have taken your last dose.

Children and adolescents

Talvey is not intended for use in children or adolescents below 18 years of age, because this medicine has not been studied in this age group and it is not known how it will affect them.

Tests and follow-up

Before you are given Talvey, your doctor will check your blood to look at the levels of different blood cells and to test for signs of infection. Infections will be treated before you start taking this medicine.

After you are given Talvey, your doctor will monitor you for side effects. Your doctor will also regularly check your blood counts, as the number of blood cells and other blood components may decrease when you use this medicine.

Interactions with other medicines
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. If you are taking certain medicines during treatment with Talvey, your doctor will decide to monitor their concentration in the blood and/or will examine their effect.

Pregnancy, contraception, breastfeeding and fertility
Pregnancy and contraception
Talvey is not recommended for use in pregnant women or women who can become pregnant and are not using contraception. Talvey may be transmitted from the mother to the developing foetus. The effects of Talvey on the developing foetus are unknown and a risk to newborns/infants cannot be excluded.

If you are pregnant, think you may be pregnant or are planning to become pregnant, ask your doctor or nurse for advice before you are given this medicine.
If you become pregnant while being treated with this medicine, tell your doctor or nurse straight away.

If you can become pregnant, you must use effective contraception during treatment and for 3 months after stopping treatment with Talvey. Your doctor will check if you are pregnant before starting treatment.

Male patient: If your partner becomes pregnant while you are being treated with this medicine, tell your doctor straight away.

If you have taken this medicine during pregnancy, your newborn baby should not be given any live vaccines until he or she is at least four weeks old.

Breastfeeding
It is not known if Talvey passes into breast milk. Do not breastfeed during treatment with Talvey. There may be a risk to breastfed newborns/infants. If you and your doctor decide to stop treatment with this medicine, you should not breastfeed for 3 months after stopping treatment.

Fertility
There are no data on the effect of talquetamab on fertility. Effects of talquetamab on male and female fertility have not been evaluated in animal studies.

Driving and using machines
The medicine has a significant effect on the ability to drive and operate machines. Some people may feel tired, dizzy, or confused while taking Talvey. Do not drive, use tools or machines from receiving your first dose until at least 48 hours after receiving your first treatment dose of Talvey, or as instructed by your doctor.

Important information about some of this medicine's ingredients
Talvey contains less than 1 mmol (23 mg) sodium per dose, that is to say essentially 'sodium-free'.

3. How to use this medicine?
Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine. Talvey will be given to you under supervision by a doctor experienced in treating patients with multiple myeloma.

The dose of Talvey depends on your body weight.

Talvey is given either once a week or once every 2 weeks, depending on the dose, as follows:

0.4 mg/kg once a week:
- For your first dose, you will receive 0.01 mg per kilogram of bodyweight.
- For your second dose, which will be given 2-4 days later, you will receive 0.06 mg per kilogram of bodyweight.
- For your third dose, you will receive a 'Treatment dose' of 0.4 mg per kilogram of bodyweight 2-4 days after your second dose.
- After your third dose onwards, you will receive a 'Treatment dose' once a week.
- Treatment will continue for as long as you benefit from receiving Talvey.

Your doctor will monitor you for side effects after each of your first three doses. They will do this for 2 days after each dose. You should stay close to the healthcare facility after each of the first three doses in case you have side effects.

If you experience side effects after any of your first two doses, your doctor may decide to wait up to 7 days before giving you your next dose.

0.8 mg/kg once every 2 weeks:
- For your first dose, you will receive 0.01 mg per kilogram of bodyweight.
- For your second dose, which will be given 2-4 days later, you will receive 0.06 mg per kilogram of bodyweight.
- For your third dose, which will be given 2-4 days later, you will receive 0.4 mg per kilogram of bodyweight
- For your fourth dose, you will receive a 'Treatment dose' of 0.8 mg per kilogram of bodyweight 2-4 days after your third dose.
- After your fourth dose onwards, you will receive a 'Treatment dose' once every 2 weeks.
- Treatment will continue for as long as you benefit from receiving Talvey.

Your doctor will monitor you for side effects after each of your first four doses. They will do this for 2 days after each dose. You should stay close to the healthcare facility after each of the first four doses in case you have side effects.

If you experience side effects after any of your first three doses, your doctor may decide to wait up to 7 days before giving you your next dose.

The decision to use either the 0.4 mg/kg once weekly or 0.8 mg/kg every two weeks should be made in consultation with your doctor.

Do not exceed the recommended dose.

How the medicine is given
Talvey will be given to you by a doctor or nurse as an injection under your skin ('subcutaneous' injection). It is given in the stomach area (abdomen) or thigh.

Medicines given during treatment with Talvey
Before the first three doses (if you are given 0.4 mg/kg bodyweight) or the first four doses (if you are given 0.8 mg/kg bodyweight) of Talvey, you will be given medicines which help to lower the chance of side effects. These may include:
- medicines to reduce an allergic reaction (antihistamines)
- medicines to reduce inflammation (corticosteroids)

- medicines to reduce fever (such as paracetamol)

You may also be given these medicines when you receive later doses of Talvey, based on any symptoms you have.

You may also be given additional medicines, based on any symptoms you experience or your medical history.

If you are given more Talvey than you should
This medicine will be given by your doctor or nurse. In the event that you are given too much (an overdose), your doctor will check you for side effects.

If you forget your appointment to have Talvey
It is very important to attend all your appointments to ensure maximal chances for your treatment to work. If you miss an appointment, schedule another one as soon as possible.
Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. <u>Side effects</u>
As with any medicine, using Talvey may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Serious side effects
Get medical help straight away if you get any of the following serious side effects, which may be severe and can be fatal.

Very common side effects - occur in more than one in ten users:
- Immune effector cell-associated neurotoxicity syndrome (ICANS), a serious immune reaction that may affect your nervous system. Some of the symptoms are:
  - feeling confused
  - being less alert or aware
  - feeling disoriented
  - feeling sleepy
  - low energy
  - slow and difficulty thinking
- Cytokine release syndrome (CRS), a serious immune reaction. CRS may cause symptoms such as:
  - fever
  - low blood pressure
  - chills
  - low level of oxygen in the blood
  - headache
  - fast heartbeat
  - increased level of liver enzymes in the blood
- low levels of neutrophils (neutropenia), a type of white blood cell that helps fight infection

- low number of blood platelets (thrombocytopenia), which help blood to clot

Tell your doctor right away if you notice any of the above listed serious side effects.

Other side effects
Other side effects are listed below. Tell your doctor or nurse if you get any of these side effects.

Very common side effects - occur in more than one in ten users:
- nail problems
- pain in the muscles and bones (musculoskeletal pain)
- low number of red blood cells (anaemia)
- feeling tired
- chills
- weight loss
- abnormally dry skin or mucous membranes such as the mouth and eyes (xerosis)
- low number of lymphocytes (lymphopenia), a type of white blood cell
- problem being able to produce or control movement (motor dysfunction)
- feeling dizzy
- nerve damage that may cause tingling, numbness, pain or loss of pain sensation (sensory neuropathy)
- damage or disease affecting brain function (encephalopathy)
- diarrhoea
- nausea
- constipation
- stomach pain
- vomiting
- infected nose, sinuses or throat (upper respiratory tract infection)
- itching (pruritus)
- decreased appetite
- pain
- low number of white blood cells (leukopenia)
- low levels of potassium in the blood (hypokalaemia)
- low levels of phosphate in the blood (hypophosphataemia)
- low levels of magnesium in the blood (hypomagnesaemia)
- low level of immunoglobulins, a type of antibody in the blood (hypogammaglobulinaemia), which may make infections more likely
- swelling caused by fluid build-up in the body (oedema)
- irritation or pain where the injection is given
- increased level of liver enzymes in the blood
- COVID-19 infection
- blood tests may show that it takes longer for blood to clot (fibrinogen decrease, INR increase and PTT prolongation)
- bacterial infection
- mouth pain
- fungal infection
- fever (pyrexia)
- headache
- shortness of breath (dyspnoea)
- cough

- problems with the mouth and swallowing, such as change in the sense of taste (dysgeusia), dry mouth, difficulty swallowing (dysphagia), and inflammation of the lining of the mouth (stomatitis)
- skin problems, including skin rash

Common side effects - occur in up to one in ten users:
- hair loss
- bleeding, which can be severe (haemorrhage)
- infection of the lungs (pneumonia)
- viral infection
- blood poisoning (sepsis)
- low number of a type of white blood cell (neutrophils), with fever

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or you can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your doctor.
Do not use the medicine after the expiry date (exp. date) which is stated on the package/label. The expiry date refers to the last day of that month.

Storage conditions:
Talvey will be stored at the hospital or clinic by healthcare professionals. Therefore, the following information is mainly intended for them.
Store in a refrigerator (2°C to 8°C). Do not freeze.
Store in the original package in order to protect from light.

Before using this medicine, check the solution for particles or discolouration. The solution should be colourless to light yellow. Do not use this medicine if it is cloudy, discoloured, or contains visible particles.

Do not throw away any medicine via wastewater or household waste. The healthcare professional will dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:
Sucrose, sodium acetate trihydrate, polysorbate 20, glacial acetic acid, EDTA disodium salt dihydrate, water for injection.

What the medicine looks like and contents of the pack:
Colourless to light yellow solution for injection (injection).
A carton pack containing one glass vial.

Registration holder: J-C Health Care Ltd., Kibbutz Shefayim, 6099000.

Manufacturer: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium.

Approved in September 2024.

Registration numbers of the medicine in the Ministry of Health National Drug Registry:
Talvey 2 mg/ml - 177-31-37916-00
Talvey 40 mg/ml - 177-32-37917-00

Guidelines for healthcare professionals:

The Talvey vials are supplied as ready-to-use solution for injection that do not need dilution prior to administration.

Talvey vials of different concentrations should not be combined to achieve treatment dose.

Aseptic technique should be used to prepare and administer Talvey.

Shelf life

- Unopened vial: The expiry date of the product is indicated on the packaging materials.
- Prepared syring: Chemical and physical in use stability has been demonstrated up to 24 hours at 2 to 8°C followed by up to 24 hours at temperature of 15°C to 30°C.
  From a microbiological point of view, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless preparation has taken place in controlled and validated aseptic conditions. Discard if stored for more than 24 hours refrigerated or more than 24 hours of being at ambient temperature.
  The prepared syringe should be stored protected from light.

Preparation of Talvey

- Refer to the following reference tables for the preparation of Talvey

    - Use Table 1 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.01 mg/kg dose using Talvey 2 mg/mL vial.

Table 1: 0.01 mg/kg dose: injection volumes using Talvey 2 mg/mL vial

	Body weight (kg)	Total dose[a] (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.5 mL)
0.01 mg/kg dose	35 to 39	0.38	0.19	1
	40 to 45	0.42	0.21	1
	46 to 55	0.5	0.25	1
	56 to 65	0.6	0.3	1
	66 to 75	0.7	0.35	1
	76 to 85	0.8	0.4	1
	86 to 95	0.9	0.45	1
	96 to 105	1.0	0.5	1
	106 to 115	1.1	0.55	1
	116 to 125	1.2	0.6	1
	126 to 135	1.3	0.65	1
	136 to 145	1.4	0.7	1
	146 to 155	1.5	0.75	1
	156 to 160	1.6	0.8	1

[a] The Total dose (mg) is calculated based on the rounded Volume of injection (mL)

- Use Table 2 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.06 mg/kg dose using Talvey 2 mg/mL vial.

Table 2: 0.06 mg/kg Dose: injection volumes using Talvey 2 mg/mL vial

	Body weight (kg)	Total dose[a] (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.5 mL)
0.06 mg/kg dose	35 to 39	2.2	1.1	1
	40 to 45	2.6	1.3	1
	46 to 55	3	1.5	1
	56 to 65	3.6	1.8	2
	66 to 75	4.2	2.1	2
	76 to 85	4.8	2.4	2
	86 to 95	5.4	2.7	2
	96 to 105	6	3	2
	106 to 115	6.6	3.3	3
	116 to 125	7.2	3.6	3
	126 to 135	7.8	3.9	3
	136 to 145	8.4	4.2	3
	146 to 155	9	4.5	3
	156 to 160	9.6	4.8	4

[a] The Total dose (mg) is calculated based on the rounded Volume of injection (mL)

- Use Table 3 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.4 mg/kg Dose using Talvey 40 mg/mL vial.

Table 3: 0.4 mg/kg dose: injection volumes using Talvey 40 mg/mL vial

	Body weight (kg)	Total dose[a] (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.0 mL)
0.4 mg/kg dose	35 to 39	14.8	0.37	1
	40 to 45	16	0.4	1
	46 to 55	20	0.5	1
	56 to 65	24	0.6	1
	66 to 75	28	0.7	1
	76 to 85	32	0.8	1
	86 to 95	36	0.9	1
	96 to 105	40	1	1
	106 to 115	44	1.1	2
	116 to 125	48	1.2	2
	126 to 135	52	1.3	2
	136 to 145	56	1.4	2
	146 to 155	60	1.5	2
	156 to 160	64	1.6	2

[a] The Total dose (mg) is calculated based on the rounded Volume of injection (mL)

- Use Table 4 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.8 mg/kg dose using Talvey 40 mg/mL vial.

Table 4: 0.8 mg/kg dose: injection volumes using Talvey 40 mg/mL vial

	Body weight (kg)	Total dose[a] (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.0 mL)
0.8 mg/kg dose	35 to 39	29.6	0.74	1
	40 to 45	34	0.85	1
	46 to 55	40	1	1
	56 to 65	48	1.2	2
	66 to 75	56	1.4	2
	76 to 85	64	1.6	2
	86 to 95	72	1.8	2
	96 to 105	80	2	2
	106 to 115	88	2.2	3
	116 to 125	96	2.4	3
	126 to 135	104	2.6	3
	136 to 145	112	2.8	3
	146 to 155	120	3	3
	156 to 160	128	3.2	4

[a] The Total dose (mg) is calculated based on the rounded Volume of injection (mL)

- Check that the Talvey solution for injection is colourless to light yellow. Do not use if the solution is discoloured, cloudy, or if foreign particles are present.
- Remove the appropriate strength Talvey vial from refrigerated storage (2°C to 8°C) and equilibrate to ambient temperature (15°C to 30°C) for at least 15 minutes. Do not warm Talvey vial in any other way.
- Once equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake.
- Withdraw the required injection volume of Talvey from the vial(s) into an appropriately sized syringe using a transfer needle.
    - Each injection volume should not exceed 2.0 mL. Divide doses requiring greater than 2.0 mL equally into multiple syringes.
- Talvey is compatible with stainless steel injection needles and polypropylene or polycarbonate syringe material.
- Replace the transfer needle with an appropriately sized needle for injection.

Administration of Talvey

- Talvey should be administered via subcutaneous injection.
- Talvey should be administered by a healthcare professional with adequate medical equipment and personnel to manage severe reactions, including CRS.
- Inject the required volume of Talvey into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively, Talvey may be injected into

the subcutaneous tissue at other sites (e.g., thigh). If multiple injections are required, Talvey injections should be at least 2 cm apart.

- Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard or not intact.
- Any unused medicinal product or waste material should be disposed in accordance with local requirements.