Package leaflet: Information for the patient

Talvey 2 mg/mL solution for injection
Talvey 40 mg/mL solution for injection
talquetamab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Talvey is and what it is used for

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.

Talvey is used to treat adults with multiple myeloma, a cancer of the bone marrow.
It is used when patients have had at least three other types of treatment that have not worked or have stopped working.

2. What you need to know before you are given Talvey

You must not be given Talvey
- if you are allergic to talquetamab or any of the other ingredients of this medicine (listed in section 6).

Do not use Talvey if the above applies to you. If you are not sure, talk to your doctor or nurse before you are given Talvey.

Warnings and precautions

Talk to your doctor or nurse before you are given Talvey.

Serious side effects
There are serious side effects that may occur after you start taking 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 conciousness, confusion, difficulty speaking and understanding speech. Some of these 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.

Tests and checks
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 have Talvey your doctor will monitor you for side effects. They will also regularly check your blood counts, as the number of blood cells and other blood components may decrease when you use this medicine.

Children and adolescents
Talvey should not be used in children or young people below 18 years of age, because the medicine has not been studied in this age group and it is not known how this medicine will affect them.

Other medicines and Talvey
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines you can get without a prescription and herbal medicines.

Pregnancy, contraception and breast-feeding

Pregnancy and contraception
Talvey has the potential to 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 have a baby, 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 could 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.

If your partner becomes pregnant while you are taking 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.

Breast-feeding
It is not known if Talvey passes into breast milk. There may be a risk to breastfed newborns/infants. Ask your doctor for advice before starting this medicine. You and your doctor will decide if the benefit of breast-feeding is greater than the risk to your baby. If you and your doctor decide to stop taking this medicine, you should not breast-feed 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
Some people may feel tired, dizzy, or confused while taking Talvey. Do not drive, use tools or machines from recieving your first dose until at least 48 hours after receiving your first treatment dose of Talvey or as instructed by your doctor.

Talvey contains sodium
Talvey contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How Talvey is given

How much is given
Talvey will be given to you under supervision by a doctor experienced in treating patients with multiple myeloma. Your doctor will decide how much Talvey you are given. The dose of Talvey will depend 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, you will then receive a 'Treatment dose' once a week thereafter.
- Treatment will continue for as long as you benefit from having 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 a 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 for each 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 then receive a 'Treatment dose' of 0.8 mg per kilogram of bodyweight 2-4 days after your third dose.

- After your fourth dose, you will then receive a 'Treatment dose' once every 2 weeks thereafter.
- Treatment will continue for as long as you benefit from having 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 a 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.

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 for when you take 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 go to all your appointments to make sure your treatment works. If you miss an appointment, make another one as soon as possible.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

<u>Serious side effects</u>
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 (may affect more than 1 in 10 people):
- 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 heart beat
  - 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 (may affect more than 1 in 10 people):

- 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 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 it takes longer for blood to clot (fibrinogen decreased, INR increased 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 sense of taste (dysgeusia), dry mouth, difficulty swallowing (dysphagia), and inflammation of the lining of the mouth (stomatitis)
- skin problems, including skin rash

Common (may affect up to 1 in 10 people)
- 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 a fever

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Talvey

Talvey will be stored at the hospital or clinic by your doctor. The following information is therefore mainly intended for healthcare professionals.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial label after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (2°C to 8°C). Do not freeze.

Store in the original carton in order to protect from light.

Before using the 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.

Medicines should not be disposed of via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help protect the environment.

6. Contents of the pack and other information

What Talvey contains
- The active substance is talquetamab. Talvey comes in two different strengths:
  - 2 mg/mL – one 1.5 mL vial contains 3 mg talquetamab
  - 40 mg/mL – one 1 mL vial contains 40 mg talquetamab

- The other ingredients are EDTA disodium salt dihydrate (E385), glacial acetic acid (E260), polysorbate 20 (E432), sodium acetate trihydrate (E262), sucrose (E473), water for injection (see "Talvey contains sodium" in section 2).

What Talvey looks like and contents of the pack
Talvey is a solution for injection (injection) and is a colourless to light yellow liquid.
Talvey is supplied as a carton pack containing 1 glass vial.

Marketing Authorisation Holder
Janssen-Cilag Ltd
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

Manufacturer
Janssen Biologics B.V.
Einsteinweg 101
2333 CB Leiden
The Netherlands

Janssen Pharmaceutica NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

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This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.

The National Health Authority will review new information on this medicine at least every year and this leaflet will be updated as necessary.

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The following information is intended for healthcare professionals only:

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.

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.