

PATIENT INFORMATION LEAFLET

Mitomycin-C Kyowa® 10 mg

Powder for Solution for Injection

(Mitomycin-C)

Read all of this leaflet carefully before you start using 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 pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4

What is in this leaflet:

1. What Mitomycin-C Kyowa is and what it is used for
2. What you need to know before you use Mitomycin-C Kyowa
3. How to use Mitomycin-C Kyowa
4. Possible side effects
5. How to store Mitomycin-C Kyowa
6. Contents of the pack and other information

1. WHAT MITOMYCIN-C KYOWA IS AND WHAT IT IS USED FOR

Mitomycin-C Kyowa can be used to treat different types of cancers in many different parts of the body as described below:

- In bladder cancer Mitomycin-C Kyowa can be administered by injection or, alternatively by instillation directly into the bladder after surgery to reduce the chances of a recurrence of the condition.
- In certain types of cancer of the stomach, pancreas, oesophagus, lower bowel, biliary tract and lung Mitomycin-C Kyowa can be used in combination with other drug treatments.
- In a type of cancer of the anus, Mitomycin-C Kyowa can be used in combination with other drug treatments or with radiotherapy.
- In a certain type of breast cancer, Mitomycin-C Kyowa can be used as a single agent or in combination with other drug treatments.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE MITOMYCIN-C KYOWA

Do not use Mitomycin-C Kyowa if you:

- are allergic (hypersensitive) to mitomycin or any of the other ingredients of Mitomycin-C Kyowa (listed in section 6)
- have certain types of blood disorders, e.g. if your bone marrow is not making enough blood cells (your doctor will check for this using blood tests), suffer from problems with blood clotting or bleeding, liver or kidney disorders, or have any active infections. Please tell your doctor if you have any of these problems and he will discuss with you whether this medicine is appropriate for you.

Take special care with Mitomycin-C Kyowa if you:

- have liver or kidney problems; side effects of mitomycin may be more noticeable.
- are capable of child-bearing as mitomycin may affect your ability to have children in the future
- have bone marrow depression (your bone marrow is not able to make the blood cells you need); it may be made worse (especially in the elderly)
- have an infection (including chickenpox) it may be aggravated and may lead to fatal conditions.

Special attention will be paid if this product is administered to the elderly or to children due to the possible side effects in these groups.

Treatment with Mitomycin-C Kyowa will be administered to you under the supervision of a medical doctor who is experienced in cancer chemotherapy. This person will therefore take all the necessary precautions for the safe administration of this product to you.

Other medicines and Mitomycin-C Kyowa

Tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, or been given other treatments (e.g. radiotherapy).

Mitomycin-C Kyowa may interact with certain other types of drugs:

- When given together with certain other cancer treatment there have been some reports of problems relating to bone marrow and the occurrence of cancer involving various types of blood cells.
- When given together with doxorubicin the potential for doxorubicin to cause heart damage may be made worse.
- When taken together with vinca alkaloid agents (such as vincristine) that are used in cancer treatment, shortness of breath, coughing, wheezing and tightness in the chest may occur.

Pregnancy and breast-feeding

Mitomycin-C Kyowa should not be given if you are pregnant, may be pregnant, or to mothers who are breast-feeding because animal studies have shown a possible risk of abnormalities in the developing foetus.

Ask your doctor for advice before taking any medicine.

Driving and using machines

Some people have reported that they feel tired or weak after the treatment. Do not drive or use any tools or machines if you are affected.

Mitomycin-C Kyowa contains sodium chloride

This medicinal product contains 4.1 mmol (or 95 mg) sodium per 10 mg vial. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE MITOMYCIN-C KYOWA

The precise dosage and frequency of administration of Mitomycin-C Kyowa will depend on your age, weight, medical condition and whether Mitomycin-C Kyowa is being given in combination with other drug treatment. The dosage may be decreased if side-effects are a problem. Mitomycin-C Kyowa is usually administered by injection or as an infusion (with a drip). However in the treatment or the prevention of the recurrence of bladder cancer, a solution of Mitomycin-C Kyowa will be instilled directly into the bladder through a catheter.

When given by injection the recommended dose is in the range of 4-10 mg given at 1-6 weekly intervals. A course ranging from 40-80 mg is often required for a satisfactory result when used alone or in combination with other treatments. The period of treatment could last from just a few weeks up to a number of months, depending on the condition being treated.

In the treatment of bladder cancer, the usual dose is 20-40 mg administered into the bladder, weekly or three times a week for a total of 20 doses. The dosage may be decreased if side effects are a problem.

If during treatment you develop a dry cough, breathlessness, rapid breathing or anything else which suggests your lungs might be affected, you may require to be monitored by X-rays of your chest that could continue up to 4 weeks after the end of treatment.

If you are given more Mitomycin-C Kyowa than you should

If you have been accidentally given a higher dose you may experience symptoms such as fever, nausea, vomiting and blood disorders. Your doctor may give you supportive treatment for any symptoms that may occur.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Mitomycin-C Kyowa can cause side effects, although not everybody gets them.

If you notice any of the following severe reactions **tell your doctor immediately**:

- severe breathlessness
- fever, chills, shortness of breath or a cough
- severe allergic reaction – you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint.
- intravenous injection site reactions - you may experience severe pain, redness of the skin, blisters or ulcers around the site of the injection.

If you experience any of the following **tell your doctor as soon as possible:**

- loss of appetite and weight loss
- tiredness, weakness and headache
- feeling or being sick
- sore mouth or mouth ulcers
- diarrhoea, abdominal pain or discomfort, constipation, or jaundice
- hair loss
- significant changes in the frequency of urination, passing blood in the urine or pain when urinating
- rapid weight gain or swelling of the legs
- any infections
- bleeding (including in the vomit or faeces) or bruising
- severe damage and potentially rupture of the wall of the bladder resulting in severe lower abdominal pain, difficulty or inability to pass urine, and possibly blood in the urine.
- severe damage to the penis resulting in pain in the penis, abnormal colour of the penis and potential difficulty in passing urine.

Treatment with "Mitomycin-C" Kyowa can result in blood disorders and bone marrow depression such as

- reduction in white and red blood cells and platelets (pancytopenia)
- reduction in red blood cells (anaemia)
- reduction in white blood cells (leucopenia),
- reduction in a type of white blood cell known as neutrophils (neutropenia),
- reduction in blood cells involved in clotting, known as platelets (thrombocytopenia), bleeding tendency, and disorders of the blood coagulation system (thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome)

You may have symptoms such as weakness, tiredness, shortness of breath, bleeding or bruising or develop infections. If you develop any of these, please tell your doctor as soon as possible.

Various forms of blood cancer or serious bone marrow abnormalities have been reported including:

- acute leukaemia,
- acute myeloid leukaemia and
- myelodysplastic syndrome

These disorders may be associated with anaemia, bleeding, infections, feeling sick, having fevers, chills, night sweats and other flu-like symptoms, or feeling fatigued. Your blood will be monitored during the course of treatment for signs of undesirable effects on the blood, and the treatment amended accordingly.

Nausea, vomiting, are sometimes experienced immediately after treatment, but these are usually mild and of short duration.

Other possible side effects include:

- difficulty in breathing or cough
- weight loss
- constipation
- pain in the abdomen
- fever
- chills
- loss of hair
- bleeding
- rashes
- mouth ulcers or inflammation
- swelling, and inflammation of the lining of the mouth
- general weakness and tiredness have been reported on rare occasions, so if you are affected you should not drive or operate machinery
- loss of appetite and diarrhoea have also been reported
- increase in blood pressure in the blood vessels of the lungs (pulmonary hypertension), e.g. leading to shortness of breath, dizziness and fainting
- obstructive disease of the pulmonary veins or pulmonary veno-occlusive disease (PVOD). Symptoms may include shortness of breath, fainting and coughing up blood.
- numbness, swelling and painful redness on palms of the hands and soles of feet (palmar-plantar erythrodysaesthesia (PPE)/hand-foot syndrome)

Kidney problems may occur including kidney failure, symptoms of which include general weakness and tiredness, and an inability to pass urine. Sudden weight gain and swelling of the legs may be a sign of kidney problems.

Liver problems may occur including jaundice (yellowing of the skin and the whites of your eyes).

Inflammation of the gall bladder, inflammation of the bile ducts, bile collecting within the abdomen, and cell damage to the bile duct may also occur and this may happen after Mitomycin-C is given directly into one of the arteries leading to the liver.

Your doctor will monitor your kidney and liver regularly using blood tests.

Lung problems such as pneumonia and the formation of abnormal dense (fibrous) lung tissue (accompanied by fever, coughing, breathlessness, abnormal findings on chest X-ray and increases in a type of white blood cell known as eosinophils) can occur.

High blood pressure or flushing has been reported and some patients have reported reduced blood flow to the fingers, toes and tip of the nose which may also be painful.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system:

HPRA Pharmacovigilance,
Earlsfort Terrace,
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
Email: medsafety@hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE MITOMYCIN-C KYOWA

Keep out of the reach and sight of children.

Do not use Mitomycin-C Kyowa after the expiry date which is stated on the carton and on the vial label. The expiry date refers to the last day of that month.

Do not store above 25°C. Do not refrigerate or freeze.

For single use only. Discard any unused contents.

After reconstitution, the solution should be used immediately.

Do not use Mitomycin-C Kyowa if you notice signs of deterioration.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND FURTHER INFORMATION

What Mitomycin-C Kyowa contains

- The active substance is mitomycin-C. Each vial of 10 mg Mitomycin-C Kyowa contains 10 mg of mitomycin-C.
- The other ingredient is sodium chloride

What Mitomycin-C Kyowa looks like and contents of the pack

Mitomycin-C Kyowa is a powder for solution for injection. It is a blue/purple powder. It is packaged in colourless glass vials with a rubber stopper and aluminium seal. The vials are packaged into cardboard cartons and are available in packs containing 1 or 5 vials each. Not all pack sizes may be marketed.

Marketing Authorisation Holder
Kyowa Kirin Holdings B.V.
Bloemlaan 2
2132NP Hoofddorp
The Netherlands

Manufacturer
Aesica Queenborough Limited
North Road
Queenborough
Kent
ME11 5EL
United Kingdom

This medicinal product is authorised in the Member States of the EEA under the following names:

Mitomycin-C Kyowa.

This leaflet was last revised in June 2019.

The following information is intended for healthcare professionals only:

POSODOLOGY

Intravenously, the dose should be given as slowly as possible and with great care in order to avoid extravasation.

The usual dose is in the range of 4-10 mg (0.06-0.15 mg/kg) given at 1-6 weekly intervals depending on whether other drugs are given in combination and on bone marrow recovery.

In a number of combination schedules, the dose is 10 mg/m² of body surface area, the course being repeated at intervals. A course ranging from 40-80 mg (0.58-1.2 mg/kg) is often required for a satisfactory response when used alone or in combination.

Because of cumulative myelosuppression, patients should be fully re-evaluated after each course and the dose reduced if the patient has experienced any toxic effects. Doses greater than 0.6 mg/kg have not been shown to be more effective and are more toxic than lower doses.

Treatment of superficial bladder tumours: In the treatment of superficial bladder tumours the usual dose is 20-40 mg dissolved in 20-40 ml of diluent, instilled into the bladder through a urethral catheter, weekly or three times a week for a total of 20 doses.

The dose should be retained by the patient for a minimum of one hour. During this one hour period the patient should be rotated every 15 minutes to ensure that the Mitomycin-C Kyowa comes into contact with all areas of the bladder urothelium.

When the bladder is emptied in the voiding process, care must be taken to ensure that no contamination occurs locally in the groin and genitalia areas.

In the prevention of recurrent superficial bladder tumours, various doses have been used. These include 20 mg in 20 ml of diluent every two weeks and 40 mg in 40 ml of diluent monthly or three monthly. The dose is instilled into the bladder through a urethral catheter.

In both cases, the dose should be adjusted in accordance with the age and condition of the patient.

PREPARATION AND HANDLING OF THE DRUG PRODUCT

The contents of the vial should be reconstituted with Water for Injections or saline, at least 10 ml for the 10 mg vial.

Since the potency of Mitomycin C may be reduced when a low pH solution (lower than pH 7.0) is used for reconstitution, it is recommended to use the solution immediately after reconstitution. In addition, it is recommended to avoid mixing with other low pH injectable solutions.

For single use only. Discard any unused contents.

Mitomycin-C Kyowa should not be allowed to come into contact with the skin. If it does, it should be washed thoroughly with soap and plenty of water. Hand creams and emollients should not be used as they may assist the penetration of the drug into the epidermal tissue.

In the event of contact with the eye, it should be rinsed several times with saline solution. It should then be observed for several days for evidence of corneal damage. If necessary, appropriate treatment should be instituted.

If spillage occurs, wear an approved respirator and chemically compatible gloves. Vacuum or sweep up the spillage, avoid dust. Place the spillage in an appropriate container for waste disposal. Wash contaminated clothing before re-use.

For disposal, waste should be treated with alkali or strong acid, and then neutralised with acid or alkali.

Mitomycin-C Kyowa should be prepared and administered by trained personnel in line with local cytotoxic guidelines.

Cytotoxics should not be handled by pregnant personnel.