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 you get any of the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

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

As a single medicine or in a combination with other medicines, 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 given by injection or, alternatively introduced directly into the bladder after surgery to reduce the chances of a recurrence of the condition
- Breast cancer and cancer of the neck of the womb (the cervix).
- It shows some activity in cancers of the stomach, pancreas, lung, liver, head and neck, prostate, leukaemia (a disease of the blood) and certain other types of tumours.
- It has a possible role with other anti-cancer medicines in cancer of the lower bowel, skin cancer and sarcomas (cancers of a particular kind of body tissue called connective tissue).
- It has been successfully used in combination with surgery, before operations (in cases of cancer of the upper digestive tract) and after operations (in cases of cancer of the stomach).
- It has been shown to be effective when used in combination with radiotherapy.

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 (ask your doctor for advice).

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 been told that you have bone marrow depression (your bone marrow is not able to make the blood cells that you need); it may be made worse (especially in the elderly); infection (including chickenpox) may be aggravated due to bone marrow depression and may lead to fatal conditions.
Special attention will be paid if this product is given to the elderly or to children due to the possible side effects in these age groups.

You will be given the treatment under the supervision of a healthcare professional who is experienced in this particular branch of medicine to minimise any unwanted side effects in the injection site.

**Other medicines and Mitomycin-C Kyowa**
Please 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).

When given together with certain other cancer treatment there have been some reports of problems related to bone marrow and the occurrence of cancer involving various types of blood cells.

**Pregnancy and breast-feeding**
You should not be given Mitomycin-C Kyowa if you are pregnant, may be pregnant or if you are breast-feeding. Ask your doctor for advice before taking any medicine.

**Driving and using machines**
A few 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.

### 3. HOW TO USE MITOMYCIN-C KYOWA

Always use the medicine as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Mitomycin-C Kyowa is usually given 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 given directly into the bladder through a type of tube called a catheter.

The precise dosage, frequency of dosing and duration of treatment with 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.

For example, 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. Thus, 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 recommended dose is 20-40mg 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, this medicine can cause side effects, although not everybody gets them. If you notice any of the following severe reactions tell your doctor immediately:

- severe breathlessness
- pneumonia – 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.

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

- fever on the day of treatment
- loss of appetite and weight loss
- tiredness, weakness and headache
- feeling or being sick (this may shortly disappear during treatment)
- high blood pressure or flushing
- pain, swelling, redness or tenderness at the site of the injection
- sores mouth and mouth ulcers
- diarrhoea, abdominal discomfort or constipation
- hardening, thickening, redness, tenderness or swelling of the tips of the fingers and hair loss
- changes in urinating or pain when urinating
- ridging of nails, blisters on pressure points e.g. elbows
- easily pick up infections
- reduced blood flow to the fingers, toes and tip of the nose
- bleeding and 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
- 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 or liver problems have also been reported. Your doctor will monitor your kidney (urine test) and liver (blood test) regularly.

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 Yellow Card Scheme (www.mhra.gov.uk/yellowcard).

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 sight and reach of children.

Mitomycin-C Kyowa should be kept in its original packaging.

Do not use this medicine after the expiry date which is stated on the label after “Exp Date”. The expiry date refers to the last day of that month.
Do not throw away any medicines 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 OTHER INFORMATION

What Mitomycin-C Kyowa contains
- The active substance is 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 which is mixed before injection. It is packaged in glass vials with a rubber stopper and aluminium seal.

Marketing Authorisation Holder
Kyowa Kirin Ltd
Galabank Business Park
Galashiels
TD1 1QH
UK

Manufacturer
Aesica Queenborough Limited
North Road
Queenborough
Kent
ME11 5EL
UK

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 May 2019.

The following information is intended for healthcare professionals only:

POSOLOGY

Intravenous administration

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 for as long as required. 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. A higher dosage course may be given when used alone or as part of a particular combination schedule and total cumulative doses exceeding 2 mg/kg have been given.

Intra-arterial administration

For administration into specific tissues, Mitomycin-C Kyowa can be given by the intra-arterial route directly into the tumours.

Dose reductions
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.

**Disease progression**

If disease progression continues after two courses of treatment, the drug should be stopped since the chances of response are minimal.

**Use in patients with 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 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 Injection or saline, at least 5 ml for the 2 mg, at least 10 ml for the 10 mg and at least 20 ml for the 20 mg vial. If possible, avoid mixing with other low pH injectable solutions.

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.