Package leaflet: Information for the user

Mitomycin medac 40 mg powder and solvent for intravesical solution

mitomycin

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.
- If you get any side effects, talk to 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 medac is and what it is used for

Mitomycin medac is a medicine for the treatment of cancer, i.e. a medicine which prevents or considerably delays the division of active cells by influencing their metabolism in various ways (cytostatic). The therapeutic use of cytostatics in cancer therapy is based on the fact that one way in which cancer cells differ from normal cells in the body is that the rate of cell division is increased due to a lack of control of their growth.

Therapeutic indications
Mitomycin medac is introduced into the urinary bladder (intravesical application) to prevent recurrence of superficial urinary bladder cancer after the tissue affected by the cancer has been removed through the urethra (transurethral resection).

2. What you need to know before you use Mitomycin medac

Mitomycin may only be administered if strictly indicated, and by doctors experienced in this type of therapy.

Do not use Mitomycin medac
- if you are allergic to mitomycin or any of the other ingredients of this medicine (listed in section 6),
- while breast-feeding: you must not breast-feed during treatment with mitomycin,
- if you have a perforation of the bladder wall,
- if you suffer from an inflammation of the urinary bladder (cystitis).

Warnings and precautions
Talk to your doctor or pharmacist before using Mitomycin medac.

<u>Particular caution is required when using Mitomycin medac</u>
- if you are in poor general health,
- if you are suffering from impaired lung, kidney or liver function,
- if you are undergoing radiation therapy,

- if you are being treated with other cytostatics (substances which inhibit cell growth/cell division),
- if you 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 become worse (especially in the elderly and during long-term treatment with mitomycin); infection may get worse due to low blood count and may lead to fatal conditions,
- if you are of child-bearing age as mitomycin may affect your ability to have children in the future.

If you experience abdominal pain or pain in the pelvic region that occurs straight after or weeks or months after the application of Mitomycin medac in the bladder inform your doctor immediately. It can be necessary that your doctor performs an abdominal sonography to clarify the cause of your pain.

Mitomycin is a substance that can cause significant hereditary changes in genetic material, and can potentially cause cancer in humans.

Avoid contact with the skin and mucous membranes.
Please read the general hygiene instructions after an intravesical instillation into the bladder:
It is recommended to sit down for urinating to avoid spillage of the urine and to wash hands and genital area after urinating. This applies especially to the first urination following mitomycin administration.

Children and adolescents
The use of Mitomycin medac in children and adolescents is not recommended.

Other medicines and Mitomycin medac
No interactions with other medicines are known if mitomycin is given in the bladder (intravesical administration).

Possible interaction during injection or infusion in a blood vessel (intravenous administration)

If other forms of treatment (in particular other anti-cancer medicines, radiation) which also have a harmful effect on the bone marrow are used at the same time, it is possible that the harmful effect of mitomycin on the bone marrow will be intensified.

Combination with vinca alkaloids or bleomycin (medicines belonging to the group of cytostatics) can intensify the harmful effect on the lungs.

An increased risk of a particular form of kidney disease (haemolytic-uraemic syndrome) has been reported in patients receiving a concomitant administration of intravenous mitomycin and 5-fluorouracil or tamoxifen.

There are reports from animal experiments that the effect of mitomycin gets lost, if administered together with vitamin B_6.

You should not get vaccinated with live vaccines during mitomycin treatment because this may put you at an increased risk to get infected by the live vaccine.

The harmful effect on the heart of Adriamycin (doxorubicin, a medicine belonging to the group of cytostatics) can be intensified by mitomycin.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

Mitomycin can cause inherited genetic damage and can adversely affect the development of an embryo.
You must not become pregnant during treatment with mitomycin: If you become pregnant, genetic counselling must be provided.
You should not use mitomycin during pregnancy.
Your doctor has to evaluate the benefit against the risk of harmful effects on your child, if mitomycin treatment during pregnancy is necessary.

Breast-feeding

Mitomycin probably passes into breast milk. Breast-feeding must be discontinued during treatment with Mitomycin medac.

Fertility/Contraception in males and females

As a sexually mature patient you must take contraceptive measures or practise sexual abstinence during chemotherapy and for 6 months afterwards.

Mitomycin can cause inherited genetic damage. As a man treated with mitomycin you are therefore advised not to father a child during treatment and for 6 months afterwards and to seek advice on sperm conservation before starting treatment due to the possibility of irreversible infertility caused by mitomycin therapy.

Driving and using machines
Even when used in accordance with instructions this medicine may cause nausea and vomiting and thereby reduce your reaction times to such an extent that the ability to drive a motor vehicle or use machines is impaired. This applies in particular if you consume alcohol at the same time.

3. How to use Mitomycin medac

Mitomycin medac is administered by trained healthcare personnel only.
This medicine is intended to be used for introduction into the urinary bladder (intravesical instillation) after being dissolved.

Your doctor will prescribe a dose that is right for you.

Mitomycin medac is introduced into an empty bladder at low pressure by means of a catheter. Your healthcare professional will empty your bladder before the treatment with a catheter. **Do not** go to the toilet directly prior to your healthcare professional visit. The medicine should remain in the bladder for a period of 1 - 2 hours. To allow this, you should not drink too much liquid before, during and after the treatment. While the solution remains in your bladder, it should have sufficient contact with the entire mucosal surface, moving around supports the treatment. After 2 hours you should empty your bladder in a sitting position to avoid spillage.

If you use more Mitomycin medac 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.

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

4. Possible side effects

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

Possible side effects following instillation in the bladder (intravesical use)

Please inform your doctor immediately if you notice any of the following reactions (which have been observed very rarely following instillation in the bladder), because mitomycin therapy will have to be stopped:
- severe allergic reaction, with symptoms such as faintness, skin rash or hives, itching, swelling of lips, face and airway with difficulty in breathing, loss of consciousness,
- severe lung disease presenting as shortness of breath, dry cough and crackling sounds when breathing-in (interstitial pneumonia),
- severe renal dysfunction: kidney disease where you pass little or no urine.

Common: may affect up to 1 in 10 people
- bladder inflammation (cystitis) which may be accompanied by blood in the bladder/urine
- painful urination (dysuria)
- frequent urination at night (nocturia)
- excessive frequent urination (pollakiuria)
- blood in the urine (haematuria)
- local irritation of the bladder wall
- localised skin rash (local exanthema)
- allergic skin rash
- skin rash caused by contact with mitomycin (contact dermatitis)
- numbness, swelling and painful redness of palms and soles (palmar-plantar erythema)

Rare: may affect up to 1 in 1,000 people
- rash over the whole body (generalised exanthema)

Very rare: may affect up to 1 in 10,000 people
- bladder inflammation with damage of the bladder tissue (necrotising cystitis)
- allergic (eosinophilic) bladder inflammation (cystitis)
- narrowing (stenoses) of the urinary tract
- reduced bladder capacity
- calcium deposits in the bladder wall (bladder wall calcification)
- partial conversion of bladder wall tissue into connective tissue (bladder wall fibrosis)
- decreased number of white blood cells (leukopenia) increasing the risk of infections
- decreased number of platelets (thrombopenia) causing bruises and bleeding
- systemic allergic reactions
- lung disorder presenting as shortness of breath, dry cough and crackling sounds when breathing-in (interstitial lung disease)
- increased levels of liver enzymes (transaminases increased)
- hair loss (alopecia)
- feeling sick (nausea) and being sick (vomiting)
- diarrhoea
- kidney disease (renal dysfunction) where you pass little or no urine
- fever

Not known: frequency cannot be estimated from the available data
If mitomycin reaches other regions than the bladder by accident:
- bladder damage
- pocket of pus in the abdomen (abscess)
- death of (fat) tissue (necrocis) of the surrounding area
- vesical fistula

Possible side effects following injection or infusion into a blood vessel (intravenous administration)

Very common: may affect more than 1 in 10 people
- inhibition of blood cell production in the bone marrow (bone marrow suppression)
- decreased number of white blood cells (leukopenia) increasing the risk of infections
- decreased number of platelets (thrombopenia) causing bruises and bleeding
- feeling sick (nausea) and being sick (vomiting)

Common: may affect up to 1 in 10 people
- lung disorder presenting as shortness of breath, dry cough and crackling sounds when breathing-in (interstitial pneumonia)
- difficulties breathing (dyspnoea), cough, shortness of breath
- skin rash (exanthema)
- allergic skin rash
- skin rash caused by contact with mitomycin (contact dermatitis)
- numbness, swelling and painful redness of palms and soles (palmar-plantar erythema)
- kidney disorders (renal dysfunction, nephrotoxicity, glomerulopathy, increased levels of creatinine in the blood) where you pass little or no urine

In the event of injection or leakage of mitomycin into the surrounding tissue (extravasation)
- inflammation of connective tissue (cellulitis)
- death of tissue (tissue necrosis)

Uncommon: may affect up to 1 in 100 people
- inflammation of the mucous membranes (mucositis)
- inflammation of the mucous membranes in the mouth (stomatitis)
- diarrhoea
- hair loss (alopecia)
- fever
- loss of appetite

Rare: may affect up to 1 in 1,000 people
- life-threatening infection
- blood poisoning (sepsis)
- decrease in number of red blood cells due to an abnormal breakdown of these cells (haemolytic anaemia)
- bruises (purpura) and red and purple dots (petechiae) on the skin (thrombotic thrombocytopenic purpura)
- heart failure (cardiac insufficiency) after previous therapy with anti-cancer medicines (anthracyclines)
- raised blood pressure in the lungs, e.g. leading to shortness of breath, dizziness and fainting (pulmonary hypertension)
- disease involving obstruction of the veins in the lungs (pulmonary veno-occlusive disease, PVOD)
- liver disease (liver dysfunction)
- increased levels of liver enzymes (transaminases)
- yellowing of the skin and whites of the eyes (icterus)
- disease involving obstruction of the veins in the liver (veno-occlusive liver disease, VOD)
- rash over the whole body (generalised exanthema)
- a particular form of kidney failure (haemolytic uraemic syndrome, HUS) characterised by destruction of red blood cells that outpaces your bone marrow’s production (haemolytic anaemia), acute kidney failure, and a low platelet count
- a type of haemolytic anaemia caused by factors in the small blood vessels (microangiopathic haemolytic anaemia, MAHA)

Not known: frequency cannot be estimated from the available data
- infection
- reduced blood cell count (anaemia)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Mitomycin medac

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 label and carton after "EXP". The expiry date refers to the last day of that month.

Do not store above 25 °C.
Keep the vial in the outer carton in order to protect from light.

After reconstitution this medicine should be used immediately.

Protect the reconstituted solution from light.

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 protect the environment.

6. Contents of the pack and other information

What Mitomycin medac contains

- The active substance is mitomycin.
  1 vial powder for solution for intravesical use contains 40 mg mitomycin. After reconstitution with 40 ml solvent 1 ml solution for intravesical use contains 1 mg mitomycin.

- The other ingredients are:
  Powder for solution for intravesical use: Urea
  Solvent for intravesical solution: Sodium chloride and water for injections.

What Mitomycin medac looks like and contents of the pack

Mitomycin medac is a grey to grey-blue powder.
The solvent is a clear and colourless solution.

Mitomycin medac powder and solvent for intravesical solution (instillation set) is available in packs with 1, 4 or 5 clear glass vials (50 ml) with a coated rubber stopper and aluminium seal. Instillation sets for intravesical instillation also include 1, 4 or 5 PVC bags with a volume of 40 ml containing sodium chloride 9 mg/ml (0.9%) solution for injection. The sets are available with or without catheters and connectors (conical to Luer-Lock).

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

medac Gesellschaft für klinische Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany
Tel.: +49 4103 8006-0
Fax: +49 4103 8006-100

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

Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, Iceland, Ireland, Latvia, Lithuania, Netherlands, Norway, Poland, Slovak Republic, Sweden:
Mitomycin medac

Germany:
mito-extra

Italy, Portugal:
Mitomicina medac

Slovenia
Mitomicin medac

United Kingdom:
Mitomycin medac

This leaflet was last revised in 01/2024.

The following information is intended for healthcare professionals only:

Posology

There are many intravesical mitomycin regimens, varying in the dose of mitomycin used, the frequency of instillation and the duration of therapy.

Unless otherwise specified, the dose of mitomycin is 40 mg instilled into the bladder once weekly. Regimens with instillations every 2 weeks, every month or 3 monthly can also be used.

The specialist should decide on the optimum regimen, frequency and duration of therapy on an individual patient basis.

It is advised to use this medicinal product at its optimal pH (urinary pH > 6) and to maintain the concentration of mitomycin in the bladder by reducing fluid intake before, during and after instillation. The bladder must be emptied before instillation. Mitomycin is introduced into the bladder by means of a catheter and at low pressure. The length of individual instillation should be 1 – 2 hours. During this period the solution should have sufficient contact with the entire mucosal surface of the bladder. Therefore the patient should be mobilised as much as possible. After 2 hours the patient should void the instilled solution, preferably in a sitting position.

Reconstitution of the solution for intravesical use ready for use

A catheter (and a connector [conical to Luer-Lock]) should be at hand before starting reconstitution of the medicinal product.
Dissolve the content of one vial of Mitomycin medac (equivalent to 40 mg mitomycin) in 40 ml sterile sodium chloride 9 mg/ml (0.9 %) solution for injection. The contents of the vial must dissolve to form a blue-purple clear solution within 2 minutes.

Only clear solutions may be used.

The content of the vials is intended for single use/single entry only. Unused solution must be discarded.

After reconstitution the medicinal product should be used immediately.

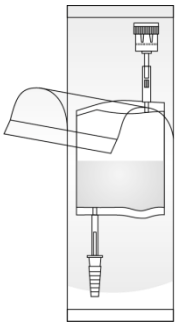
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

For further information regarding the catheter please see the corresponding instructions for use.

<u>Instructions for use for the solvent for intravesical solution (instillation set)</u>

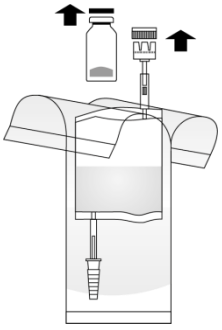
Fig. 1 – 8:

(1)



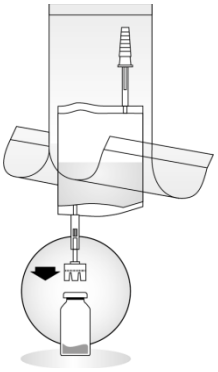
Tear open the protective cover, but do not remove completely! This will protect the tip of the instillation system from contamination up to the last minute.

(2)



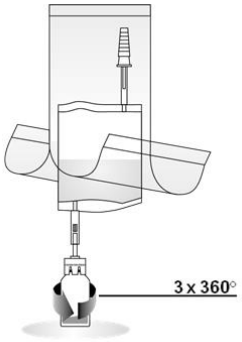
Remove the caps from the vial and instillation system. Lay out a disposal bag.

(3)



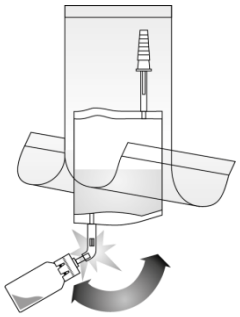
Place the vial on a firm surface (e.g. table) and press the vial connector of the instillation system firmly in a straight manner on to the vial.

(4)



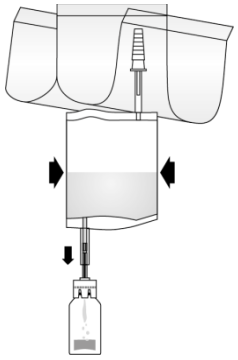
Make sure to turn the vial 3 times completely.

(5)



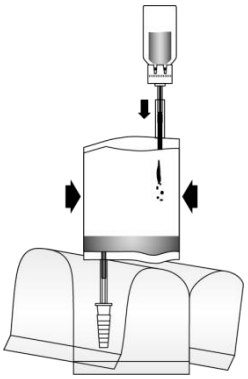
Break open the mechanism in the tube of the vial connector by repeated bending backwards and forwards. This establishes the connection. Please hold the tube – and not the vial – during this process!

(6)



Pump the liquid into the vial, but do not fill the vial completely. If flow is not possible, turn the vial again three times in the other direction to assure that the septum is completely pierced. Repeat this step until flow is possible.

(7)



Invert the entire system. Pump air from the instillation system into the vial at the top and draw the reconstituted mitomycin solution into the instillation system. Do not remove the vial.

(8)

Keep the instillation system in an upright position. Now remove the protective cover completely. Connect a catheter (and a connector [conical to Luer-Lock]) to the instillation system. Now break the

sealing mechanism in the tube section by bending backwards and forwards and instil the solution into the bladder.
At the end of instillation free the catheter by pressing air through.
Keep the instillation system squeezed and place it together with the catheter into the disposal bag.