**Package leaflet: Information for the user**

Mitocin 20 mg, powder for solution for injection/infusion or intravesical use
Active substance: 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.
- This medicine has been prescribed for you, only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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 Mitocin is and what it is used for

Mitomycin 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. The therapeutic application of medicinal products for the treatment of cancer 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 is used in cancer therapy for the relief of symptoms (palliative cancer therapy).

*Intravenous application*
When administered intravenously it is used in monochemotherapy, i.e. treatment with only one active substance, or in combined cytostatic chemotherapy, i.e. treatment with several active substances. Mitomycin is effective in the case of the following tumours:
- advanced metastatic stomach cancer (stomach carcinoma)
- advanced and/or metastatic breast cancer (breast carcinoma)
- cancer of the respiratory tract (non-small cell bronchial carcinoma)
- advanced cancer of the pancreas (pancreatic carcinoma)

*Intravesical application*
Application in the urinary bladder (intravesical application) for the prevention of a relapse in the case of superficial urinary bladder cancer after the ablation of tissue through the urethra (transurethral resection).

## 2. What you need to know before you use Mitocin

**Do not use Mitocin in the case of systemic or intravesical use**
- if you are hypersensitive (allergic) to mitomycin or any of the other ingredients of this medicine (listed in section 6).
- during breastfeeding
- in the case of **systemic** administration if you suffer from a major reduction in the number of all types of blood cells (including red and white blood cells as well as platelets [pancytopenia]), or an isolated reduction of white blood cells (leucopenia) or blood platelets (thrombocytopenia), a tendency to bleeding (haemorrhagic diathesis) or acute infections (disease caused by pathogens).
- in the case of **intravesical** administration (application in the urinary bladder) if you have perforation of the bladder wall

**Warnings and precautions**
Talk to your doctor or pharmacist before using Mitocin
- if you are suffering from impaired lung, kidney or liver function.
- if your general state of health is not good
- if you are undergoing radiation therapy
- if you are being treated with other cytostatics (substances which inhibit cell growth/cell division)
- if you have inflammation of the urinary bladder (in case of intravesical administration)
- 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 be worse (especially in elderly and during long term treatment with mitomycin); infection may be aggravated due to bone marrow depression and may lead to fatal conditions
- if you are capable to have a baby as mitomycin may affect your ability to have children in the future.

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.

**Children and adolescents**
The use of mitomycin in children and adolescents is not recommended.

**Other medicines and Mitocin**
Tell your doctor or pharmacist if you are taking/using, have recently taken/used or might take/use any other medicines.

Through the additional use of other types of therapy (in particular other anti-cancer medicines, radiation) which also have harmful effects on you, it is possible that the adverse effects of mitomycin will be reinforced.

There are reports from animal experiments that the effect of mitomycin lost, if administered together with Vitamin $B_{6.}$

You should not get vaccinated, especially with live vaccines during mitomycin treatment.

Please note that the above also applies to medications used in the recent past.

**Pregnancy, breastfeeding and fertility**

Mitomycin should not be used 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.

Women of child-bearing age should avoid becoming pregnant. Contraceptive measures must be taken by both male and female patients during and for at least six months after cessation of therapy. Still, if you become pregnant during this period you must immediately inform your doctor.

Breast-feeding must be discontinued before you start to use mitomycin.

**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 operate machinery is impaired. This applies in particular in conjunction with alcohol.

## 3. How to use Mitocin

Mitomycin should only be administered by healthcare professionals experienced in this kind of therapy.
Mitomycin is intended to be used for injection or infusion into a blood vessel (intravenous use) or for introduction into the urinary bladder (intravesical instillation) after being dissolved.

**Your doctor will prescribe a dose and treatment regimen that is right for you.**

Before you receive mitomycin as injection or infusion into a vein a blood test, check of lung, kidney and liver function is recommended to exclude any diseases, which could worsen during mitomycin therapy.

The needle must remain in the vein while mitomycin is being given. If the needle comes out or becomes loose, or the medicinal product is going into the tissue outside the vein (you may feel discomfort or pain) - tell the doctor or nurse immediately.

**If you use more Mitocin 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, please 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 administration into a vein**

Severe lung disease presenting as shortness of breath, dry cough and crackles during breath-in (interstitial pneumonia) as well as severe renal dysfunction (nephrotoxicity) may occur. If you notice any of the above reactions please inform your doctor immediately because mitomycin therapy must be stopped.

**Very common** (may affect more than 1 in 10 people)
- Blood disorders: Inhibition of blood cell production in the bone marrow; decreased number of white blood cells (leucopenia) increasing the risk of infections; decreased number of platelets (thrombocytopenia) causing bruises and bleedings
- Nausea, vomiting

**Common** (may affect up to 1 in 10 people)
- Lung disorders presenting as shortness of breath, dry cough and inspiratory crackles (interstitial pneumonia)
- Dyspnoe, cough, shortness of breath
- Skin rashes and irritation of the skin
- Numbness, swelling and painful redness on palms and soles (palmar-plantar erythema)
- Kidney disorders (renal dysfunction, nephrotoxicity, glomerulopathy, increased levels of creatinine in the blood) - the kidneys may not be able to work
- Inflammation of connective tissue (cellulitis) and death of tissue (tissue necrosis) following accidental injection into the surrounding tissue (extravasation)

**Uncommon** (may affect up to 1 in 100 people)
- Inflammation of a mucous membrane (mucositis)
- Inflammation of the mucosa of the mouth (stomatitis)
- Diarrhoea
- Hair loss (alopecia)
- Fever
- Loss of appetite (anorexia)

**Rare** (may affect up to 1 in 1,000 people)
- Life-threatening infection
- Blood poisoning (sepsis)
- Decrease in number of red blood cells sometimes together with a acute renal dysfunction (haemolytic anaemia, microangiopathic-haemolytic anaemia (MAHA syndrome), Haemolytic uraemic syndrome (HUS))
- Loss of cardiac function (heart failure) after previous therapy with other anti-cancer medicines (anthracyclines)
- Increase in blood pressure in the vasculature of the lungs, e,g, leading to shortness of breath, dizziness and fainting (pulmonary hypertension)
- Obstructive disease of the pulmonary veins (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)
- Blockage of the small veins in the liver (veno-occlusive disease [VOD] of the liver) leading to fluid retention, increased liver size and raised levels of bilirubin in the blood
- Widespread skin rash

**Very rare** (may affect up to 1 in 10,000 people)
- Severe allergic reaction (symptoms may include faintness, skin rash or hives, itching, swelling of lips, face and airway with difficulty in breathing, loss of consciousness)

**Possible side effects following installation in the bladder**

**Common** (may affect up to 1 in 10 people)
- Skin rashes (exanthema, allergic skin rash, contact dermatitis)
- Numbness, swelling and painful redness on palms and soles (palmar-plantar erythema)
- Bladder inflammation (cystitis) - which may be accompanied with blood in the bladder/urine
- Painful urination, excessive frequent urination sometimes over the night (dysuria, pollakisuria, nocturia)
- Blood in urine (hematuria)
- Local irritation of the bladder wall

**Rare** (may affect up to 1 in 1,000 people)
- Widespread skin rash

**Very rare** (may affect up to 1 in 10,000 people)
- Severe inflammation of the bladder where portions of the bladder wall may undergo tissue death (allergic cystitis, necrotizing cystitis)
- Stenosis of the efferent urinary tract
- Reduction in bladder capacity
- Hardening of bladder wall (bladder wall calcification, bladder wall fibrosis)

**Reporting of side effects**
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme, Website: 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 Mitocin

Do not store above 25°C.

Keep the vial in the outer carton in order to protect from light.

Chemical and physical in-use stability of reconstituted solution has been demonstrated at room temperature and light effect with:
- 0.9% sodium chloride solution for 2 hours
- water for injections for 1 hour.

All reconstituted solutions should be used immediately.

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 folding box after “EXP”. 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 protect the

environment

## 6. Contents of the pack and other information

### What Mitocin contains

The active substance is mitomycin.
1 vial powder for solution for injection/infusion or intravesical use contains 20 mg mitomycin. After reconstitution with 40 ml water for injections 1 ml solution for injection/infusion contains 0.5 mg mitomycin. After reconstitution with 20 ml solvent 1 ml solution for intravesical use contains 1 mg mitomycin

The other excipients are:
Mannitol,
hydrochloric acid 36% and sodium hydroxide for pH adjustment

### What Mitocin looks like and contents of the pack

Mitomycin is a grey powder.

Mitocin, powder for solution for injection/infusion or intravesical use is available in packs containing 1 amber glass vial and packs containing 5 amber glass vials with powder for solution for injection/infusion or intravesical use

Not all pack sizes may be marketed.

### Marketing Authorisation Holder and Manufacturer

*Marketing Authorisation Holder*
Vygoris Limited
930 High Road
London N12 9RT
United Kingdom
Tel: +44 (0)12 2339 5301

*Manufacturer*

Creapharm Clinical Supplies
ZA Air-Space,
Avenue de Magudas CS 2007,
Le Haillan Cedex, 33187,
France

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

| | |
|---|---|
| **Finland** | Mitomycin Substipharm 20 mg, injektio/infuusiokuiva-aine, liuosta varten/virtsarakkoon |
| **Germany** | Mitocin 20 mg, Pulver zur Herstellung einer Injektions- bzw. Infusionslösung und Herstellung einer Lösung zur intravesikalen Anwendung |

| | |
|---|---|
| **Italy** | Mitomicina Substipharm 20 mg, Polvere per soluzione iniettabile / infusione e per soluzione endovescicale |
| **The Netherlands** | Mitomycine Substipharm 20 mg, Poeder voor oplossing voor injectie of infusie en voor intravesicaal gebruik |
| **Norway** | Mitomycin Substipharm 20 mg, pulver til intravesikaloppløsning/injeksjons-/infusjonsvæske, oppløsning |
| **Sweden** | Mitomycin Substipharm 20 mg, Pulver till injektions-/infusionsvätska, lösning eller för intravesikal användning |
| **United Kingdom** | Mitocin 20 mg, powder for solution for injection/infusion or intravesical use |

**This package leaflet was last revised in 03/2022.**

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The following information is intended for healthcare professionals only:

**General Information**

It is essential that the injection is administered intravenous. If the medicinal product is injected perivasally, extensive necrosis occurs in the area concerned. To avoid necrosis following recommendations apply:

- Always inject into large veins in the arms.
- Do not directly inject intravenously, but rather into the tube of a good and securely running infusion.
- Before removing the cannula after central venous administration, flush it through for a few minutes using the infusion in order to release any residual mitomycin.

If extravasation occurs, it is recommended that the area is immediately infiltrated with sodium bicarbonate 8.4% solution, followed by an injection of 4 mg dexamethasone. A systemic injection of 200 mg of Vitamin B6 may be of some value in promoting the regrowth of tissues that have been damaged.

Contacts with the skin and mucous membranes must be avoided.

**Method of administration**

Mitomycin is intended to be used for intravenous injection or infusion or for intravesical instillation after being dissolved.

*Preparation of the ready-to-use solution for injection or infusion*

The contents of a vial of Mitocin 20 mg are dissolved in 40 ml of water for injection purposes by swirling.

Shake until the reconstituted solution becomes clear and free of particles.

For intravenous infusion the solution of Mitocin 20 mg can be diluted in 40 ml of water for injection with isotonic sodium chloride infusion solution down to a concentration of 20 - 40 micrograms of mitomycin/ml.

*Preparation of the ready-to-use solution for intravesical administration*

The contents of 1 - 2 vials of Mitocin 20 mg are dissolved in 20 - 40 ml of water for injections or sodium chloride (0.9%) solution.

*Incompatibilities*

Incompatibilities occur with highly acidic or alkaline substances. The optimum pH value for the ready-to-use mitomycin solution is 7.0.

*Note*

- All reconstituted solutions are intended for immediate use!
- Shake until the reconstituted solution becomes clear and free of particles.
- The contents of the vials are intended for single use only.
- Unused solutions are to be discarded.
- Mitocin must not be used in mixed injections.
- Other injection solutions or infusion solutions must be administered separately.
- It is essential that the injection is administered intravenous.