

VYGORIS

Direct Healthcare Professional Communication

Date: 8 November 2021

Mitocin (mitomycin) 20mg powder for solution for injection/infusion or intravesical use: new single-use filtration device must be used to avoid patient exposure to subvisible particles and reduce risk of injection reactions

Dear Healthcare Professionals,

Vygoris Limited in agreement with the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary:

- Some vials of Mitocin 20mg may contain subvisible particles above current specifications after reconstitution ($>10\mu\text{m}$: NMT 6000 /vial)
- This issue was identified during stability studies, no adverse reactions have currently been received by the manufacturer regarding this issue
- Potential risks associated with subvisible particles injection include thrombosis, occlusion, phlebitis, embolism, inflammation, antigenic and immunologic reactions, granuloma, fibrosis and death
- From 1 November 2021 and until the quality investigation concludes, a single-use filtration device called the **Millex[®] HV (0.45 μm /PVDF) - Syringe Filter** (see Figure 1 on next page) will be included in each delivery of Mitocin 20mg
- To avoid patient exposure to potential risks, the filtration device provided must be used with Mitocin 20mg before administration and for all administration routes – full instructions are provided in **Appendix 1**
- Filtration does not alter the amount of the active ingredient mitomycin in the solution, nor does it reduce in the effectiveness of the medicine
- The current stock of Mitocin 20mg vials will not be recalled, but the filtration device should be used with existing stock and can be obtained from the wholesaler

Background of the safety concerns

Mitomycin is used in palliative tumour therapy. Mitomycin is administered **intravenously** as monochemotherapy or in combined cytostatic chemotherapy in the case of:

- Advanced metastatic gastric carcinoma
- Advanced and/or metastatic breast cancer

Furthermore, mitomycin is administered **intravenously** in combined chemotherapy in the case of:

- Non-small cell bronchial carcinoma
- Advanced pancreatic carcinoma

Intravesical administration for relapse prevention in superficial urinary bladder carcinoma after transurethral resection.

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Some vials of Mitocin 20mg may contain subvisible particles above the current specifications after reconstitution ($>10\mu\text{m}$: NMT 6000 /vial). To avoid patient exposure to the risks associated with injection of subvisible particles (described in the summary), the product should be filtered before administration.

The **Millex® HV filtration device will be included with each delivery of Mitocin 20mg powder for solution (see picture below)**. These devices are for single use only.

Figure 1: Millex® HV (0.45 μm /PVDF)



The filtration device provided must ALWAYS be used, across all routes of administration. The filtration must be performed before the administration of the reconstituted solution of Mitocin 20mg. Full filtration instructions are provided in the instructions below. Please note that this is a temporary measure until the end of the investigation regarding the subvisible particles issue. This letter will be joined to each delivery.

The current stock of Mitocin 20mg vials will not be recalled. If you have current stock of Mitocin 20mg powder for solution for injection/infusion or intravesical use, please contact our pre-wholesaler for the filtration device:

MPW – Quest 90
Quest Park, Wheatley Hall Road
Doncaster
DN2 4LT
michelle.biggs@mawdsleys.co.uk

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme.

Please report:

- All suspected ADRs that are serious or result in harm.
- Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- All suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

It is easiest and quickest to report ADRs online via the Yellow Card website –<https://yellowcard.mhra.gov.uk> or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, you can report to the Yellow Card scheme by calling **0800 731 6789** for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

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Company contact point

If you have any questions or require further information about Mitocin 20mg powder for solution for injection/infusion or intravesical use, you can contact:

PRODUCT LIFE Limited

Tel +44 (0) 1223 395 301

Email: safety@productlife-group.com

Best Regards,

Hussain Tahan

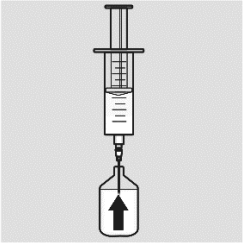
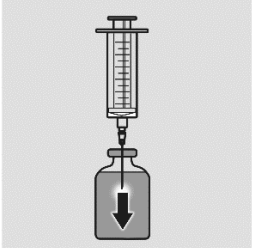
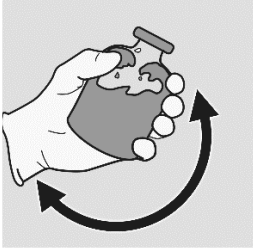
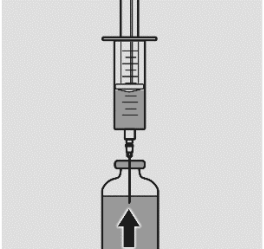
Responsible Person, Vygoris Limited



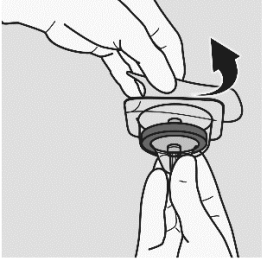
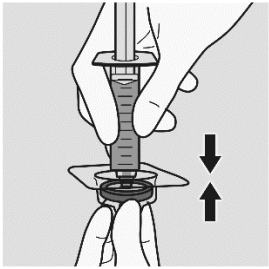
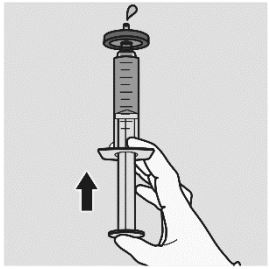
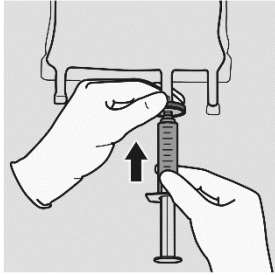
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Instructions:

- To ensure sterility do not use the package if the package is damaged
- Do not use this filter as an in-line filter for intravenous fluid administration; it is not designed for long-term continuous use.
- Do not use with syringes smaller than 10 cc because pressures in excess of the maximum pressure rating may be reached, potentially causing damage to the filter unit and/or personal injury.

<p>1)</p> 	<p>1) Fill syringe with water for injection or NaCl 0.9%.</p>
<p>2)</p> 	<p>2) Reconstitute with a volume of water for injection or NaCl 0.9% (20mL or 40 mL) the lyophilizate of Mitocin 20mg in function of desired concentration (respectively 1 mg/mL or 0.5 mg/mL according to the corresponding SmPC).</p>
<p>3)</p> 	<p>3) Agitate the vial until complete dissolution, for 2 minutes at least</p>
<p>4)</p> 	<p>4) Fill the syringe with the solution of Mitocin 20mg</p>

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5) 	5) Aseptically remove filter cover from the filter package
6) 	6) Attach syringe to filter unit and remove assembly from package. Attach needle to Luer-slip outlet if necessary.
7) 	7) Hold syringe with filter (and needle if attached) pointing up and top off by pushing a few drops through. Do not contaminate underside of filter unit with fingers.
8) 	8) For intravenous injection: Connect the filter with full Mitocin 20mg syringe to the intravenous catheter and push plunger to deliver filtered solution. or For perfusion or intravesical administration: Connect the filter with full Mitocin 20mg syringe to the luer-slip outlet of the infusion bag (if equipped) and push plunger to deliver filtered solution or attach a needle to deliver the solution in the infusion bag by the septum.