Medicines & Healthcare products Regulatory Agency

# Belzer UW Cold Storage Solution and Belzer MPS UW Machine Perfusion Solution manufactured by Carnamedica (UKRP: Bridge to Life): Contamination of fluid (update to DSI/2023/002), DSI/2023/005

The MHRA is providing an update on defects identified with Belzer solutions, manufactured by Carnamedica (UK Responsible Person Bridge to Life).

## Device Details

Device Name: Belzer UW Cold Storage Solution and Belzer MPS UW Machine Perfusion Solution
Affected lot numbers/serial numbers: All
Manufactured by Carnamedica, UK Responsible Person Bridge to Life

## Summary

This Devices Safety Information **replaces advice in DSI/2023/002, which should no longer be followed**. This page details an updated list of LOTs associated with defect reports, additional problems identified with the solution, and new actions for healthcare professionals. The MHRA continues to work with Carnamedica and Bridge to Life and may provide further updates as new information is identified.

Belzer UW Cold Storage Solution (CSS) is intended for flushing and cold storage of kidney, liver and pancreas organs at the time of their removal from the organ donor in preparation for storage, transportation and eventual transplantation into a donor recipient.

Belzer UW Machine Perfusion Solution (MPS) is intended for the in-vitro flushing and continuous hypothermic machine perfusion preservation of explanted kidneys.

## For information and action by

- Transplant Unit Directors / Co-ordinators
- Healthcare professionals involved in organ retrieval, transfer and transplantation
- Healthcare professionals and laboratory staff involved in the receipt, use and storage of tissue derived from organs for transplantation – for example, accessory vessels
- Healthcare professionals and laboratory staff involved in cell isolation work as a function of islet and hepatocyte laboratories.

Instructions for Medical Device Safety Officer/Medication Safety Officer: Please circulate/forward to relevant departments.

## Bridge to Life Field Safety Notice

Bridge to Life issued a Field Safety Notice, dated 26 January 2023, following defect reports of leaks, discolouration and particulate matter in Cold Storage Solution. Bridge to Life

implemented a voluntary suspension of supply of specific LOTs of Cold Storage Solution and Machine Perfusion Solution.

We issued DSI/2023/002, dated 31 January 2023. This provided additional detail about the potential risk associated with using the affected product. It also shared advice from NHSBT about alternative product, and advised that following publication of the FSN, defect reports had been received involving additional LOTs.

Bridge to Life has now issued an updated Field Safety Notice dated 1 March 2023, broadening the scope of the corrective action.

The list of problems identified to date is:

- microbiological contamination
- particulate matter within the solution
- leakage of fluid
- growth of black mould on the exterior of the connectors

The updated list of LOTs supplied to the UK in which defects have been identified is as follows:

**Cold Storage Solution 1 L, BUWC1000**
010722
022422
022822
031122
061022
081222
090122
101822
111522
111822
112122

**Cold Storage Solution 2 L, BUWC2000**
123021
022522
030122
061022
082322

The MHRA would like to highlight that investigation is ongoing into the root cause of the problems identified. As such, unlisted LOT numbers are not guaranteed to be unaffected by these issues. LOT numbers involved in confirmed reports have been provided to support stakeholders in providing increased vigilance to patients who have received organs where affected lots were used.

Note: In addition to the LOTs listed above, Cold Storage Solution 1 L, BUWC1000 LOT 082922 has been linked to a report of leakage and microbial contamination with 2 additional

strains of microbial organism, Staphylococcus aureus and Coagulase negative Staphylococcus. However, investigation is ongoing and the microbial contamination may not be the result of a defective product. This LOT is not therefore included in the list of affected LOTs. Of note, the fluid in the defective bag was not visibly discoloured.

The updated list of LOT numbers currently under the voluntary suspension of supply to the UK implemented by Bridge to Life pending completion of their investigation and implementation of corrective actions is:

**Cold Storage Solution 1 L, BUWC1000**
061022
101822
111722
111422
111822
112122
112222

**Cold Storage Solution 2 L, BUWC2000**
022522
061022

Note: Where LOTs are in the list of LOTs associated with defects but not in the list of suspended LOTs this is because no stock remains.

Note: LOTs in the list of suspended LOTs but not the list of LOTs associated with defects have not been supplied into the UK.

The MHRA continues to work with Carnamedica and Bridge to Life to ensure that the root causes are identified, and corrective actions are implemented.

## Background to identified safety issue

The manufacturer (Carnamedica) has identified a number of issues with their third-party suppliers of Belzer UW Cold Storage Solution and Belzer MPS UW Machine Perfusion Solution. Concerns have been raised about the aseptic filling process, leak testing of the bags and the conditions under which filled bags are stored and transported.

To date, 5 strains of microbial organisms, Brachybacterium conglomeratum, Kocuria rhizophila, Rothia kristinae, Staphylococcus aureus and Coagulase negative Staphylococcus have been cultured from contaminated Cold Storage Solution. The potential clinical consequences of using a product with microbial contamination include peritonitis, infection, sepsis and failure of graft.

In addition, bags of Cold Storage Solution have been identified containing visible particulate matter. Carnamedica has identified that this is hydroxyethyl starch precipitated from the solution. This could potentially occlude small capillaries in transplant organs and result in regional ischaemia, regional necrosis, delayed graft function and loss of the graft.

Reports of leaking bags of Cold Storage Solution have also been received.

An additional defect, black mould on the exterior of the connectors, was identified by Bridge to Life during a stock inspection.

The MHRA has not received reports of adverse events involving Belzer UW MPS Machine Perfusion Solution. However, they are not guaranteed to be unaffected.

A review of data held by the MHRA shows no safety signals resulting from reports of infections over the last 5 years associated with Belzer UW cold storage solution or Belzer UW machine perfusion solution. The manufacturer has also not received any reports of infections related to these devices.

## Actions

### Actions for healthcare professionals

- Check and segregate stocks of Belzer UW Cold Storage Solution and Belzer UW Machine Perfusion Solution.

- NHS Blood and Transplant has advised that Custodiol HTK, manufactured by Dr. Franz Kohler Chemie GmbH, should be used as an alternative product for cold storage of organs for transplant. If using alternative reagents such as HTK, please be aware of the different storage requirements. Please ensure you follow the manufacturer's instructions for storage carefully. Be aware that the labelling on Custodiol HTK bags is similar to that of saline bags and take steps to avoid accidental use of the incorrect product.

- NHS Blood and Transplant has advised that limited stock of an additional alternative product, Servator B manufactured by S.A.L.F. and supplied by Global Transplant Solutions, is being released and should be used within cell processing laboratories as an alternative product to the Belzer UW Cold Storage Solution. Servator B has the same formulation as Belzer UW Cold Storage Solution and MHRA does not anticipate that changes to usage protocols are required; however, laboratories should check with appropriate authorities before use to ensure suitability.

- For purposes where neither Custodiol HTK or Servator B is an appropriate alternative, existing stocks of Belzer UW Cold Storage Solution and Belzer UW MPS Machine Perfusion Solution, excluding those from LOTs listed above, can be used **at risk**. Prior to use, each bag should be visually inspected for:

    - Discolouration – the fluid should be colourless and clear
    - Particulate matter – hold up to a light source for this check to be effective
    - Leakage – squeeze the bag firmly to check for leaks
    - Mould or contamination on the outside of the bags, especially around the connectors

    Bags with any of these defects should **not** be used and the defect should be reported to Bridge to Life and your national incident reporting authority. Bags with defects

should be quarantined and arrangements made to return them to the manufacturer where possible for further investigation and testing.

When using bags without a visible product defect please continue to follow any local guidelines and procedures that govern the sampling and testing of fluid for microbial contaminants.

- Patients who have received an organ preserved with Belzer UW Cold Storage Solution or Belzer UW MPS Machine Perfusion Solution should be placed under increased vigilance.
    - If a transplant recipient develops an infection with an unusual organism or with an unusual antibiotic resistance pattern after receiving an organ or cells from an organ preserved with Belzer UW Cold Storage Solution, please report these through both NHSBT clinical governance and your national incident reporting authority.
    - If a transplant recipient develops unexpected vascular complications, including regional ischaemia, regional necrosis and delayed graft function after receiving an organ, or cells from an organ preserved with Belzer UW Cold Storage Solution, please report these cases through both NHSBT clinical governance and your national incident reporting authority.

- There are specific reporting arrangements for healthcare professionals to follow in each of the devolved administrations. Healthcare professionals should report incidents:
    - in England and Wales to the Yellow Card scheme or via the Yellow Card app
    - in Scotland to Incident Reporting & Investigation Centre (IRIC) and their local incident recording system
    - in Northern Ireland to the Northern Ireland Adverse Incident Centre and their local incident recording system

**Actions for patients**

The advice in this DSI is aimed at the healthcare team responsible for providing and monitoring your organ transplant. If you have any concerns about this advice, contact the specialist team with responsibility for your care for assistance.

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