Dear Colleague

Given the recent disruptions to supply of products made by Calea, I wanted to provide information on the underlying cause of the issue, how long the issue is anticipated to continue for and to seek assurance that you feel able to manage your most vulnerable patients during this time.

**Background**

The MHRA inspected Calea UK at its registered site in Runcorn on 24-26 June 2019. During the inspection, problems were identified with the design of the manufacturing process for parenteral nutrition (PN) bags that did not meet the requirements of guidance published by MHRA in 2015. Additionally, Calea’s routine monitoring, designed to detect microbial contamination in the production area and on production personnel, identified bacteria which were known human pathogens.

These pathogens could cause serious health problems (including the possibility of fatalities) if they contaminated the product during the manufacturing process.

Even though this contamination was found in the production area, it is important to stress that there is no evidence to indicate that Calea products manufactured and supplied to patients were contaminated. However, the environmental contamination, in combination with the inspection findings, presented a very serious risk to patients and required immediate action to ensure the high standards of safety for manufacturing PN. This has contributed to a reduction in Calea’s output while they make changes to their processes.
Impact timescales

Your Trust will have received a letter from Calea informing you that the supply issues will last four weeks. However, having worked closely with Calea on this matter it appears likely that the issues will last longer than initially anticipated.

The MHRA is working closely with the company to safeguard the quality and safety of these important products, with MHRA inspectors monitoring changes to the production process including carrying out regular inspection visits. This includes the implementation of a revised manufacturing process which includes additional safeguards to ensure product safety.

We realise that the disruption presents a clinical risk and have been careful to try and balance the risk of contamination and sepsis against the risk of supply disruption, which we know has already had significant impact. MHRA have been working closely with Calea to monitor the implementation of interim changes to the manufacturing process while a long term solution is being developed which will increase production while maintaining the safety of the product. This is a difficult balance, but we are of the view that the manufacturing changes are necessary to ensure safe supply now and in the long term.

Trust Processes for reviewing affected patients

As you are aware, the aseptic market is fragile and complex and there is limited capacity for bespoke compounding. The Department of Health and Social Care (DHSC) has previously communicated the importance of reviewing all of your patients to ensure that the available compounding slots are reserved for high-risk patients and that the details of these patients are clearly communicated with Calea.

It is important to us that we are assured that each patient has been risk assessed and a contingency plan put in place and to this end we would ask that you confirm this, so we have a clear national picture of where any remaining increased risk sits. I shall be grateful if returns can be submitted to england.spocskh@nhs.net ideally by COP Thursday.

Management strategies carried out

You will be aware that the DHSC convened a National Actional Group to coordinate national management strategies to ensure patients are being treated appropriately during this time. This group is comprised of DHSC, NHS England and NHS Improvement (NHSE/I), MHRA, representatives from the Devolved Administrations and national clinical experts. The group has been working on several immediate management options which have been communicated by DHSC to Chief Pharmacists and Regional Procurement Leads. This has also been formally designated as an EPRR (Emergency preparedness, resilience and response, at the highest level in view of the risk) incident within NHSE/I and being supported accordingly. As this is anticipated to be a longer term issue, several longer term management strategies are currently being explored. These include the following:
• Working with other providers to identify additional potential compounding capacity and working to expedite this where possible.
• Monitoring patient numbers affected over time and ensuring the allocation of available capacity in the most effective way to ensure the highest risk patients as identified by their nutrition teams are prioritised.
• Working with suppliers of standard multi chamber bags (MCBs) to ensure sufficient product is available in the supply chain (including access to stock from other markets globally where needed which might be more suitable for some patients).
• Working with the MHRA to expedite regulatory processes required including those required to import stock from global markets.
• Identifying facilities and nursing capacity to allow the delivery of extra infusions that may be required by patients on MCBs.
• Developing a clinical protocol for the safe preparation and administration of any extra infusions required.
• Identifying training opportunities for patients on MCBs able to independently deliver any extra infusions should they require this.
• Working with patient groups to ensure they are informed of the work the National Action Group is undertaking.
• Working to ensure all stakeholders, including clinical teams and patients are informed of all the above strategies and nationally agreed management actions to be taken locally.

All developments to these strategies will continue to be communicated to both you and your Trust.

Clinical contact for your Trust

Thank you for providing contact details to us via the SitRep. Please can you advise us of any changes to those contact details. This will help ensure that your Trust continue to receive essential communications and assume you will disseminate this information to your colleagues as appropriate.

I realise the increased workload and concern this causes, and I appreciate your ongoing support. Please be assured that it is a priority to work with all stakeholders to resolve this situation as quickly and as safely as possible and to make sure we keep you informed and updated as things develop.

Yours faithfully,

Dr Aidan Fowler
National Patient Safety Director
NHS England and NHS Improvement

For further information on the contamination issue please use the following link to the MHRA web pages. https://www.gov.uk/government/news/supply-problems-with-total-parenteral-nutrition-tpn-bags-calea-ukfresenius-kabi-site-in-runcorn-cheshire