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Review of BBraun NRFit syringe testing protocols and results against NHS protocols

Products: BBraun NRFit Lock Syringes with GBUK Caps.

The NHS Pharmaceutical Aseptic Services Group published its requirements for the introduction of NRFit neuraxial syringes and caps for the purposes of drug storage on 13th October 2016. This is necessary as, in line with other standard plastic syringes, these are CE marked for the administration of drug products but not for storage. Hence in order to allow aseptic facilities to draw up medication in advance and store ahead of administration the additional data was requested.

This additional testing involved:

1) Syringe integrity testing (microbiological and dye intrusion testing) in accordance with Protocols for the Integrity Testing of Syringes 2nd edition April 2013' – NHS Pharmaceutical Quality Assurance Committee.
2) Extractives and leachables testing in accordance with British Pharmacopoeia Sterile Single-use Plastic Syringes monograph and testing as per Appendix XIX G, and the additional requirements for extended testing for a minimum of 7 days at 4°C & 20°C to reflect normal hospital pharmacy practice and up to a maximum of 14 days.
3) Chemical stability and drug adsorption assessment in accordance with Chemical stability testing has been carried out as per 'A Standard Protocol for Deriving and Assessment of Stability Part 1 Aseptic Preparations (Small Molecules) 3rd edition December 2015' – NHS Pharmaceutical Quality Assurance Committee. Using Fentanyl 2micrograms/ml (with Bupivacaine 0.1%) in Sodium Chloride 0.9% stored at Room Temperature 15-25°C to represent adsorption risks and Hydrocortisone sodium succinate 1mg/ml in Water For Injections stored Refrigerated at 2-8°C to assess stability risks. These compounds were selected as markers to allow extrapolation to other drugs normally stored in neuraxial syringes that are more stable and less susceptible to adsorption.

   Following agreement with BBraun I was permitted to review the various testing protocols carried out with or relevant to BBraun NRFit neuraxial syringes in accordance with the above.

1) <u>Stability studies – Fentanyl with Bupivacaine</u>

   The study was carried out in accordance with standards and the data generated indicates that Fentanyl (2mcg/ml) and Bupivacaine (1mg/ml) was stable at both 5°C and 25°C throughout the 42 days of the study period. This is in-line with expectations and shows that the syringes have no impact on drug stability and that there are no issues with adsorption of the drug onto contact surfaces

2) <u>Stability studies – Hydrocortisone sodium succinate</u>
   The study was again carried out in accordance with standards and the data generated indicates the Hydrocortisone sodium succinate (1mg/ml in WFI) was stable for approximately 12 days at 5°C or 3

days at 25°C, this is in-line with expectations from other studies and indicates that the syringes have no impact on drug stability and that there are no issues with adsorption of the drug onto contact surfaces

3) Extractables testing / BP plastic syringe testing

Testing for extractables in accordance with BP protocols and for extended periods of storage of 14 days at 5°C, 25°C and 37°C showed that extractives levels were well within the specification, indicating that extractives are not an issue of concern with these syringes

4) Integrity testing

The dye intrusion test was carried out in accordance with protocol and results were satisfactory for both 3ml and 20ml syringes. However, the microbiological integrity test using the *Brevundimonas diminuta* method did indicate issues with compatibility between the BBraun syringes and the GBUK caps. In the initial testing all 20ml syringes passed the test but a majority of the 3ml syringes failed the test. On investigation many of the caps were found to have cracked and split and hence integrity had been lost. It was thought that this may be due to overtightening the caps which are made from comparatively flexible plastic (compared to standard luer lock caps). Testing was repeated on 3ml and 5ml syringes after issuing specific instructions for capping, on this occasion all of the 3ml syringes passed the test but several 5ml syringes failed the test, investigations failed to find a root cause for the failures on this occasion.

The conclusion therefore has to be that there is an issue with compatibility between BBraun NRFit syringes and GBUK NRFit caps. It is therefore suggested that this combination is not used for storage of medicines even for the sort term until this can be addressed or until sufficient local validation studies have provided evidence to their compatibility for the period of use plus a margin of safety.

Conclusion

There is a potential compatibility issue when using BBraun NRFit syringes and GBUK NRFit caps which has resulted in failures in integrity testing for the microbiological integrity test. **Hence the use of this combination cannot be currently recommended for storage of intrathecal injections even in the short term.**

All of the other data generated by the validation work was satisfactory indicating that the syringes themselves are not impacting on drug stability and have very low extractives levels.

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