Medicines & Healthcare products Regulatory Agency

Board Meeting

Pre-submitted questions from observers

16 September 2019

The following pre-submitted questions from two observers will be answered and discussed at the Board:

SECTION A Questions about the yellow card:

1. How can you educate and encourage patients to look at the yellow card data before they make a decision to take a drug that has been prescribed for them so that they can be more informed?

2. Is it good practice for doctors to be aware of yellow card data regarding particularly controversial medicines like cipro and Isotretinoin? What can be done to ensure these measures so that the yellow card is utilised in a way that directly informs patients in terms of reported data?

3. Because drug induced suicides and serious injuries are so unacceptable and painful to all involved – what can be done to ensure that everyone involved with these particular patients are made aware of them so that lessons can be learned? As I understand it, MHRA do not directly inform prescribing doctors or the NHS Trusts about yellow card data, not even when there is a suicide involving a child - is this not a great failing on the whole of the NHS?

We the public expect and assume that important data is shared in a way where that knowledge is used to benefit patients.

Section B Questions about the use of APCs in Clinical Trials in the UK

I am a PhD student and a practicing dentist registered with the General Dental Council. My research investigates autologous platelets concentrates (APCs) in wound healing of the dental extraction socket in dentistry. Since October 2018, I have researched the classification and use of APCs in clinical trials in the UK and I have noticed an element of lack of clarity regarding this topic.

In general, APCs **are used as autologous topical intraoperative chairside-obtained material to increase the concentration of platelets and their derived growth factors in the diseased site of the same patient, akin to autologous bone or skin grafts.**

APCs are obtained from a sample of the patient's venous blood (4 – 6 x 9 ml tubes of blood). The whole blood sample is then processed chairside through various protocols which *may or may not involve* the following:

1. The addition of anticoagulant which is sometimes pre-loaded in the tubes for blood collection;
2. Centrifugation once or twice at different forces and time durations;
3. Fractioning of the plasma via pipetting from the blood tubes to separate it from the erythrocytes;
4. In some APCs, the addition of calcium chloride or thrombin to reverse the action of the anticoagulant is used (such as in the case of platelet-rich plasma *PRP*, and plasma rich in growth factors *PRGF*);
5. Maintaining the temperature of the plasma around 37 degrees centigrade until application to the surgical site.

In the interest of raising public awareness, I would be most grateful for your advice on the regulatory classification of the various autologous platelets concentrates (APCs) (and more specifically APCs known as Plasma Rich in Growth Factors (PRGF)) for intraoperative autologous application currently in use within medicine and dentistry in the UK, and **specifically whether they are considered/classified as**

1. **Medicinal products that require a manufacturing licence and a manufacturing authorisation?**
   and
2. **Which step is considered as a manufacturing process in the preparation of APCs.**

The reason for our question above is due to a recent Scope (24 June 2019) with the Clinical Trials Helpline regarding the classification of one of these types of APCs known as Plasma Rich in Growth Factors (PRGF). Following an enquiry made to HRA in relation to clinical trials in a U.K. university PRGF was classified previously by MHRA as a non-medicinal product and not a blood product, However, the MHRA is now considering the same PRGF as a manufactured medicinal product requiring a manufacturing license, without providing a clear explanation for the change in the classification.

Based on the records of the registered clinical trials in the UK, it seems the APCs are widely recognised in the UK as non-medicinal products that do not require manufacturing licence. However, if the position of the MHRA on the classification of APCs has changed (or specifically for the PRGF), it may have an impact on the medical and dental profession, and related industry at large. For example, will there be a need/requirement for a manufacturing license for every healthcare provider (or private practice) using PRGF or other APCs.

I am keen to understand the regulatory framework for the classification of APCs since they are recognised by the global scientific community as a safe clinical intervention for patients.
I thank you in advance for taking the time to answer my questions above, and I look forward to your regulatory guidance on the classification of plasma preparations considering their significant research impact to provide patients with a safe autologous treatment alternative in various dental and medical applications in the UK.

MHRA