Platelet Rich Plasma

Issue

The Chartered Society of Physiotherapy (CSP) approached the MHRA in relation to the specific use of the autologous blood product of Platelet Rich Plasma (PRP) when this product is used in the clinical healthcare setting of managing tendinopathy and/or other musculoskeletal disorders by its members.

CSP members have been following NICE guidelines aimed at "Clinicians" wishing to administer PRP injections for knee osteoarthritis or wishing to undertake autologous blood injection for tendinopathy where clinical governance leads in their NHS trusts are informed,. The guidelines (see Annex) also require patients are aware of the safety and efficacy evidence and there is a process in place to review patient outcomes. Whilst autologous blood injection is not PRP, both papers recognise the evidence on efficacy is limited in quality or remains inadequate:

https://www.nice.org.uk/guidance/ipg637
https://www.nice.org.uk/guidance/ipg438

MHRA advice in relation to PRP has previously been directed at doctors and, while this stands, it does not follow that the same situation applies to other health care professionals such as physiotherapists and podiatrists. This statement sets out the MHRA's position in relation to the use of PRP in clinical settings with reference to applicable legal framework.

Background

PRP therapy is a complex area and PRP products will be regulated in different ways depending on the characteristics of the product and the exact purpose for which they are being supplied or administered to the patient or client. Some PRP products may be classified as (biological) medicinal products, including advanced therapy medicinal products (ATMPs), and these PRP products would be regulated under human medicines legislation. In some cases, unlicensed medicinal products, including PRP, may qualify for manufacturing and supply under the MHRA "specials" scheme.

MHRA Position

Blood products

MHRA has given consideration as to whether PRP should be regulated as a blood component under the Blood Safety and Quality Regulations 2005 (BSQR). MHRA is of the view that the BSQR have relevance in respect of standards of quality and safety for the collection of blood, irrespective of intended use or equivalent standards, but PRP is not administered intravenously and is being administered for the treatment of adverse medical conditions linked with other parts of the body. This is counter to the purpose of the BSQR which is to regulate blood and blood components used for transfusion purposes [see Annex].

When PRP is being used for medical purposes, or where a more complex manufacturing process is undertaken (such as pooling for allogeneic use, addition of other substances), MHRA regards PRP to be a blood product. In such circumstances the sourcing of the starting material will be subject to all relevant aspects of the BSQR, and the manufacture, storage and distribution will be subject to human medicines legislation.

Medicinal products

MHRA acknowledges that the use of autologous PRP does not always fall within the definition of a medicinal product. However, it is the MHRA's position that, if PRP is used with the claims described in the NICE guidelines referred to above it will meet the definition of a medicinal product set out in Regulation 2 of the Human Medicines Regulations 2012 (HMRs). Accordingly, PRP will be subject to the provisions of the HMRs [see Annex].

In coming to this view, MHRA notes that EU human medicines legislation, which UK medicines legislation transposes, envisages instances where the regulatory status is not clear and, in such instances, that status as a medicine should take precedence[1].

Consequently, PRP products used in these circumstances will be subject to authorisation and licensing to market and manufacture respectively unless an exemption exists. Exemptions from the need for a marketing authorisation and manufacturer's licence exist under the HMRs in certain circumstances for doctors and dentists. There is also an exemption from the need for a marketing authorisation under the UK specials regime which allows a doctor, dentist, nurse, independent prescriber, pharmacist independent prescriber or supplementary prescriber to sell and supply an unlicensed medicine. Both of these are in the HMRs (Regulation 3 and 167 respectively).

Under Regulation 3(5) of the HMR, a doctor may manufacture or assemble a medicinal product without a marketing authorisation or manufacturer's licence provided the medicinal product is supplied to a patient during the treatment of that patient or to a patient of another doctor who is a member of the same medical practice. In addition, the medicinal product cannot be manufactured or, as the case may be, assembled on a large scale, or by an industrial process. However, there is no equivalent exemption for a physiotherapist or a podiatrist.

'Supplementary prescriber' is defined in Regulation 8 of the HMRs and includes physiotherapists and podiatrists. Whilst supplementary prescribers may fulfil the special needs of a patient that they are directly responsible for by requesting a special medicinal product to their specification under Regulation 167 of the HMRs, the special medicinal product, which in this case will be a blood product (i.e. PRP), must be manufactured by the holder of a manufacturer's specials licence. Blood, or blood components, used by a licensed manufacturer as a starting material or raw material in the manufacture of a medicinal product must meet the standards of quality and safety set out in the BSQR, or equivalent standards.

MHRA agrees that physiotherapists and podiatrists can administer PRP and the clinic or hospital in which they work could use their own doctor to manufacture and administer the PRP under regulation 3(5) of HMR. Alternatively, the clinic could apply for and obtain a manufacturer's special licence or go to an existing holder of such a licence. The supplementary prescribing physiotherapists or podiatrists can then provide their specification and have the special medicinal product supplied.

PRP Medical Devices

There are products on the market intended for use in the production or preparation of PRP; where the final resulting product (PRP) is intended for medical purposes, these preparation kits are regulated as medical devices and subject to the UK Medical Device Regulations 2002. Such kits must be marketed in line with the legal manufacturer's intended purpose and uses, which in turn must be supported with appropriate evidence in their technical documentation. Depending on the components included with the preparation kits (e.g. inclusion of anti-

[1] Article 2(2) of Directive 2001/83
In cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a 'medicinal product' and within the definition of a product covered by other Community legislation the provisions of this Directive shall apply

coagulant solutions), they may be subject to conformity assessment and require UKCA / CE certification from an Approved / Notified Body. The output PRP itself is not a medical device, as it does not meet the definition provided in the Medical Devices Regulations 2002 [see Annex]. Claims regarding the efficacy of the end PRP output from the kit should not therefore be made.

Dr Chris Jones.
Head of Regulatory Governance
MHRA
18 October 2023

Annex

Blood Safety and Quality Regulations

1 Citation, commencement and interpretation

(1) These Regulations may be cited as the Blood Safety and Quality Regulations 2005.

(2) Except for regulation 25(1), which shall come into force on 8th November 2005, these Regulations shall come into force on 8th February 2005. (3) In these Regulations—

"autologous transfusion" means a transfusion in which the donor and the recipient are the same person and in which pre-deposited blood or blood components are used;

["biomedical research institution" means any body which carries out biomedical research;]

"**blood**" means whole human blood collected from a donor and processed either for transfusion or for further manufacturing;

"**blood component**" means a therapeutic constituent of human blood (red cells, white cells, platelets and plasma) that can be prepared by various methods;

"blood component release" means a process which enables a blood component to be released from a quarantine status by the use of systems and procedures to ensure that the finished product meets its release specification;

["blood establishment" means any person who carries out any of the activities specified in regulation 3(2) which require an authorisation by virtue of that regulation;]

"**blood product**" means any therapeutic product derived from human blood or plasma;

2 Designation of the competent authority for Northern Ireland and scope of the Regulations

[(1) The Secretary of State is designated the competent authority in relation to Northern Ireland for the purposes of the Directive.]

(2) Subject to the following paragraphs, the requirements of these Regulations apply to the collection and testing of blood and blood components, whatever their intended purpose, and to their processing, storage, and distribution when they are intended to be used for transfusion.

Human Medicines Regulations (HMR)

Regulation 2 Medicinal products

2.—(1) In these Regulations "medicinal product" means—

(a)any substance or combination of substances presented as having properties of preventing or treating disease in human beings; or

(b)any substance or combination of substances that may be used by or administered to human beings with a view to—

(i)restoring, correcting or modifying a physiological function by exerting a pharmacological, immunological or metabolic action, or

(ii)making a medical diagnosis.

(2) These Regulations do not apply to—

(a)whole human blood; or

(b)any human blood component, other than plasma prepared by a method involving an industrial process.

Regulation 37(9):

(9) The licence holder must ensure that blood, or blood components, imported into the United Kingdom and used as a starting material or raw material in the manufacture of a medicinal product meet—

(a) the standards of quality and safety specified in Commission Directive 2004/33/EC of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components; or

(b) equivalent standards.

Regulation 167 Supply to fulfil special patient needs

(1) The prohibitions in regulation 46 (requirement for authorisation) do not apply in relation to a medicinal product (a “special medicinal product”) if—

(a) the medicinal product is supplied in response to an unsolicited order;

(b) the medicinal product is manufactured and assembled in accordance with the specification of a person who is a doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or supplementary prescriber;

(c) the medicinal product is for use by a patient for whose treatment that person is directly responsible in order to fulfil the special needs of that patient; and

(d) the following conditions are met.

(2) Condition A is that the medicinal product is supplied—

(a) to a doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or supplementary prescriber; or

(b) for use under the supervision of a pharmacist in a registered pharmacy, a hospital or a health centre.

(3) Condition B is that no advertisement relating to the medicinal product is published by any person.

(4) Condition C is that—

(a) the manufacture and assembly of the medicinal product are carried out under such supervision; and

(b) such precautions are taken,

as are adequate to ensure that the medicinal product meets the specification of the doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or supplementary prescriber who requires it.

(5) Condition D is that written records of the manufacture or assembly of the medicinal product in accordance with condition C are maintained and are available to the licensing authority or to the enforcement authority on request.

(6) Condition E is that if the medicinal product is manufactured or assembled in the United Kingdom[, imported into Northern Ireland from a country other than an EEA State or Great Britain, or imported into Great Britain from a country other than an approved country for import or Northern Ireland]—

(a) it is manufactured, assembled or imported by the holder of a manufacturer's licence that relates specifically to the manufacture, assembly or importation of special medicinal products; or

(b) it is manufactured, assembled or imported as an investigational medicinal product by the holder of a manufacturing authorisation granted by the licensing authority for the purposes of regulation 36 of the Clinical Trials Regulations.

(7) Condition F is that if the product is [imported into Northern Ireland from an EEA State or imported into Great Britain from a country other than an approved country for import]—

[(a) it is manufactured or assembled in that State or country (as appropriate) by a person who is the holder of an authorisation in relation to its manufacture or assembly in accordance with—

(i) in the case of a product for sale or supply in Northern Ireland, the provisions of the 2001 Directive as implemented in that State, and

(ii) in the case of a product for sale or supply in Great Britain, in accordance with the provisions applicable in that country; or]

[(b) it is manufactured or assembled as an investigational medicinal product in that State or country (as appropriate) by the holder of an authorisation in relation to its manufacture or assembly in accordance with—

(i) in the case of a product for sale or supply in Northern Ireland, Article 13 of the Clinical Trials Directive as implemented in that State, and

(ii) in the case of a product for sale or supply in Great Britain, regulations 13 and 43 of the Clinical Trials Regulations][,

and it is imported by the holder of a wholesale dealer's licence in relation to the product in question].

(8) Condition G is that if the product is distributed by way of wholesale dealing by a person (“P”), who has not, as the case may be, manufactured, assembled or imported the product in accordance with paragraph (6)(a) or (7)(a), P must be the holder of a wholesale dealer's licence in relation to the product in question.

(9) In this regulation “publish” has the meaning given in regulation 277(1) (interpretation: Part 14 advertising).

Medical Device Regulations

Regulation 3

3. These Regulations shall not apply to—

(a) medicinal products governed by the Human Medicines Regulations 2012 (including medicinal products derived from human blood or human plasma);

(b) human blood, human blood products, plasma or blood cells of human origin;

(c) devices that incorporate, at the time of placing on the market, human blood, blood products, plasma or blood cells of human origin, except for

(i) stable derivatives devices,

(ii) active implantable medical devices and accessories to such devices, and

(iii) in vitro diagnostic medical devices and accessories to such devices,;

(d) transplants or tissues or cells of human origin or products incorporating or derived from tissues or cells of human origin [F4, except for F5..., in vitro diagnostic medical devices and accessories to such devices] [F6save where medicinal products are incorporated as ancillary to the device];

(e) transplants or tissues or cells of animal origin, unless—

(i) a device is manufactured utilising animal tissue which is rendered non-viable or non-viable products derived from animal tissue, or

(ii) a product is F8... an in vitro diagnostic medical device, or an accessory to such a device;]

(f) cosmetic products governed by [F9Regulation (EC) 1223/2009 of the European Parliament and of the Council of 30th November 2009 on cosmetic products;] or

NICE

Clinicians wishing to give platelet-rich plasma injections for knee osteoarthritis should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the procedure's safety and efficacy, as well as any uncertainties about these. Provide them with clear information to support shared decision making. In addition, the use of NICE's information for the public on platelet-rich plasma injections for knee osteoarthritis is recommended.
- Audit and review clinical outcomes of all patients having platelet-rich plasma injections for knee osteoarthritis, including details of the methods used to prepare and administer the platelet-rich plasma injections. NICE has identified relevant audit criteria and has developed NICE's interventional procedure outcomes audit tool (which is for use at local discretion).

The procedure

2.3 Platelet-rich plasma is prepared by a clinician or a technician. Blood is taken from the patient and centrifuged to obtain a concentrated suspension of platelets in plasma. Different preparation methods may affect the concentrations of platelets and the level of contamination with red and white blood