

SPB| SYSTEM FOR AUTOLOGOUS PRP| PLATELET RICH PLASMA

DESCRIPTION

It is a medical device for the preparation of Platelet Rich Plasma (PRP) from the collected patient's blood, which includes:

- Carton) N. 1: These are pre-labeled ACD tubes with colored caps containing ~ 0,8/1 ml of anticoagulant (ACD); each labeled tube, for example 9/12 ml capacity, has a pre-calibrated vacuum for ~ 9/12 ml of blood sample.
- In the carton there are one or two test tubes, in each of which there is a separator gel based on an inert polymer and an anticoagulant (named for simplicity of understanding, type 1 test tube, necessary for the separation between serum enriched with platelets (injectable liquid enriched with growth factors) and the concentration of red blood cells (clot) which is determined after centrifugation.
- Carton No. 2: These are 1 or 2 pre-labeled tubes with colored caps containing ~ 2 ml of activator containing calcium ion solution; each tube has a pre-calibrated vacuum for ~ 9/12 ml of concentrated platelet liquid.

ACCESSORY SET

it is advisable to obtain the following accessory components: these are disposable accessories for the use of test tubes, or a set with disposable accessories for the collection of venous blood (to be carried out before anesthesia where provided) and transfer of blood components, consisting of a sampling system with a butterfly needle and shirt, a sterile syringe 5ml, needles 30Gx13mm infiltration, needles infiltration 32Gx4mm (trichology), needles from infiltration 26Gx40mm (orthopedics) needles 21G aspiration needles, a tourniquet, a plaster, a swab, 1ml and 5ml syringes with Luer - lock -connection, a Luer lock - adapter. The PRP obtained after the centrifugation of the blood is ready for use, or, thanks to the high concentration of the final product, it is suitable for the preparation of the platelet gel using the calcium-based activator.

INSTRUCTION FOR USE

The medical device is designed to allow the preparation of blood components for use (platelet gel) in an easy, safe and fast way. The rationale for using the medical device for wound healing and tissue repair is to administer locally high concentrations of growth factors and tissue repair as found in platelet concentrate.

The medical device must be used by specially trained medical staff under medical responsibility.

Plasma and / or platelet gel are used in the fields of application for tissue repair with indications of use relating to:

- DENTISTRY AND IMPLANTOLOGY-MAXILLO-FACIAL SURGERY;
- DERMATOLOGY AND TRICHOLOGY;
- GENERAL MEDICINE, GERIATRICS AND GYNECOLOGY MEDICINE AND AESTHETIC SURGERY;
- ORTHOPEDIC MEDICINE AND SURGERY AND SPORTS MEDINA.

The product should not be used in pregnant or breastfeeding women or on people under the age of eighteen.

The most important indications for the use of the medical device include the treatment of acute wounds chronic ulcers involving skin, subcutaneous or mucocutaneous tissue, and bone injuries, subcutaneous filling, strengthening of the hair bulb.

The method based on this preparation is called "BUFFY COAT" with a glass test tube, which differs from the "EMPTY TEST" test (simple test tube for taking blood under vacuum), which does not obtain a concentrate but a serum; it is not able to separate the blood with high precision and to obtain a high concentration of PRP and does not allow to extract only the intermediate layer (PRP).

In addition, the plastic of the tubes contains micronized silicone which can also generate platelet activation. All this translates into a platelet-free serum after the centrifugation process which cannot be used for PRP. In addition to centrifugation, the PRP can 'also be obtained with a cell separation for obtaining PRP by cellular precipitation of different specific gravities (VERTICAL GRAVITY SETTLING), place the test tube vertically on a test tube holder and wait for the cell separation by natural gravitational action from 2-3 hours. The medical device in question is not produced with plastic that contains micronized silicone. It has an optimal composition for a maximum biological effect. Platelet Rich Plasma (PRP), also referred to as Autologous Platelet Gel, a growth factor rich plasma (PRGF) or platelet concentrate (PC), is essentially an increase in the concentration of autologous platelets suspended in a small amount of plasma after centrifugation of the patient's blood. The tubes are available in the following capacities for containing collected blood: 4-6-9-12-15-20-24 ml.

FIELDS OF APPLICATION

- Maxillofacial surgery: mandibular reconstructions, dental implants, tonal and oropharyngeal fissures;
- Plastic, reconstructive, aesthetic surgery;
- Trichology, general medicine, gynecology, geriatrics
- Orthopedics: pseudoarthrosis, osteosynthesis.

WARNINGS

Never use the product after the expiration date. Store the device in a cool, dry place away from direct sunlight. Never use the device when packaging anomalies were detected during the visual inspection. In the activation stages, be careful to prevent bacterial contamination of the blood component. Therefore, it is recommended that the medical device is used in a sterile environment or in compliance with the hygiene, cleansing and cleaning criteria generally established by good clinical practice for the point of care. The medical device should only be used by appropriately trained medical staff under medical responsibility. The device and the biological products prepared with it should be used in the range of a complete and accurate clinical-therapeutic approach, possibly following the criteria of evidence-based medicine (EBM). In no case self-medication is allowed using the device and the biological derivatives prepared with the device itself. By following these instructions for use, this medical device with a set of accessories allows to obtain a PRP with a platelet concentration 4-5 times higher than the original blood sample (1x10⁶ platelets/microliter ± 20%). Growth factors and chemotactic mediators of platelet origin are mainly released passively (i.e. without platelet activation). Therefore, platelet gel can be prepared from the blood of patients taking oral anticoagulants, heparin, calcium heparin, platelet aggregation inhibitors, cyclooxygenase inhibitors. However, since part of the release of growth factors could depend on the state of **activity** of the platelets, it is rational to wait for a delay in the release of the growth factors if the patient takes cyclooxygenase inhibitors or anti-cling platelets. There are no known interactions with systemic or topical agents.

If platelet gel is used for bone regeneration, the gel can be associated with human bones, animal bones certified for human use, other biocompatible materials certified for human use.

Use PRP with particular caution in the following cases:

- acute or chronic infections at the surgical site;
- long-term cortisone therapy; Autoimmune diseases;
- acute or chronic infections at the surgical site;

PRECAUTIONS

The devices must be used only by experienced personnel who possess requirements for handling.

- uncontrolled metabolic pathologies, such as diabetes, osteomalacia, thyroid dysfunction, severe kidney or liver pathologies;
- radiotherapy.

In the case of congenital or acquired platelet defects, patients with congenital or acquired functional platelet defects may release fewer growth factors in relation to the platelet defect.

In the case of thrombocytopenia, it is unlikely that a sufficiently rich platelet concentrate for clinical use will be obtained. The platelet gel is reabsorbed in a few days. No toxicity phenomenon is described in the gel treated tissues. Normal surveillance procedures or prophylaxis against infectious complications should be applied. Growth factors of platelet origin induce cell proliferation. The use of platelet gel is contraindicated in case of suspected lesions of malignant degeneration. To ensure tissue regeneration, the PRP must be inserted exclusively in vital tissue and in direct contact with the tissue (if necessary, by making micro-openings on the surface of the tissue).

SIDE EFFECTS

Reactions from incompatibility with PRP cannot be totally excluded, such as local allergies and the possible complications are those related to normal surgical interventions, for example swelling of the operated site, flap necrosis, hemorrhage, local inflammation, infection or pain. The method is totally safe as it uses "autologous" plates.

CONTRAINDICATIONS PREGNANCY / BREAST-FEEDING / CHILDREN

There are no adequate data regarding the use of the product in pregnant or breastfeeding women. No experimental data are available on the safety and efficacy of PRP in children who have not reached skeletal maturity. Therefore, the product should not be used in pregnant or breastfeeding women or on people under the age of eighteen

OTHER INFORMATION

The devices are disposable and cannot be resterilized at risk of infections related to different blood, not autologous.

Any residual material must be disposed of according to local laws. Do not use after their expiration date. The product is sterile as long as the package remains closed and intact. Do not use the product if the sterile package is damaged.

DURATION

Check the expiry date on the outer carton. Do not use the material after the expiration date.

DISPOSAL

The product must be disposed of as special waste. The waste must be disposed of in accordance with national and local regulations for the disposal of medical waste.

USE PROTOCOLE

The preparation of the PRP consists in the withdrawal of autologous venous blood (that is of the patient himself) which is subsequently subjected to single or double centrifugation and concentrated (method called BUFFY COAT).

Basically, the patient's blood is collected and centrifuged at variable speeds until it separates into three layers:

- Platelet poor plasma (PPP)
- Platelet rich plasma (PRP)
- Red blood cells (RBC)

OPERATIONAL PHASE BLOOD SAMPLE AND CENTRIFUGING

The first operational phase for the preparation of the PRP is the collection of blood:

1. Collect the patient's blood using the components in envelope # 1.

2. Gently invert the tubes 3-4 times immediately after sampling to avoid the formation of microclots.

The second phase is that of centrifugation, for which reference is made to the method described in the first claim of U.S. Pat. US 4190535 of 26.2.1980 , explicitly directed to means for extracting platelets from anticoagulated blood: it is a method for separating platelets, lymphocytes and monocytes from anticoagulant blood, comprising the following steps:

(a) a substance similar to the thixotropic gel insoluble in water which is chemically inert to blood constituents and having a specific gravity between 1.065-1.077 g / cc is placed in an anticoagulated blood sample;

(b) the gel blood sample is centrifuged at a force of at least 1200 G for a period of time sufficient to cause the gelatinous substance to form a barrier between plasma, platelets, lymphocytes and monocytes and the heavier blood cells; and subsequently

(c) the plasma, platelets, lymphocytes and monocytes are removed from the top of said barrier.

Reference is also made to the European patent of Becton Dickinson no. EP0190488B1 of 4.7.1990 , which at no. 1. Claims the method for obtaining a concentration of some of the elements that make up the blood fluid by " centrifuging the blood-liquid-gel mixture at a force of at least 1200 g to cause a gel-like substance to flow sufficiently to form a barrier between lymphocytes and monocytes and granulocytes, to obtain the removal of lymphocytes and monocytes concentrated above the barrier ".

Reference is also made to the fourth patent claim

3. Carefully insert the tubes into the centrifuge so that they are correctly opposed and balanced in the centrifuge.

4. Set the centrifuge with the following parameters: •1 780 RCF (g) or 4000 RPM for 5 minutes for angle or inclined rotor centrifuges

The subsequent steps must be carried out by working in a strictly aseptic environment, preferably under a sterile hood.

*NB: Depending on the centrifuge rotor if fixed or adjustable the RCF can vary.

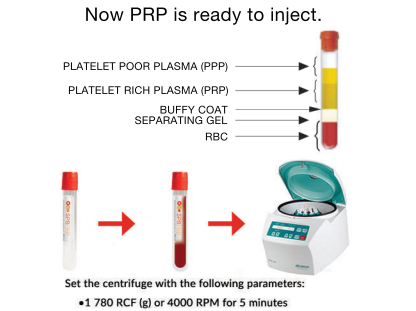
RCF = relative centrifugal force.
RPM = rotational speed (rpm).
r = centrifugal spin in mm = distance from the center of rotation to the bottom of the centrifuge.

$$RCF = \left(\frac{RPM}{1000} \right)^2 \times r \times 1,118 \Rightarrow RPM = \sqrt{\frac{RCF}{r \times 1,118}} \times 1000$$

Where "r" the radius of the centrifuge.

5. Gently remove the tubes from the centrifuge.

6. Approximately 5 / 5.5 ml of PRP at the concentration of platelets 3-5 x (3-5 times the base value of the patient's platelets) should be recovered in each tube in the case of a tube with empty capacity of 9 ml.



DESCRIPTION OF USE AND RISK CLASS

Medical devices for the preparation of the concentrate platelet liquids are classified in Class IIa medical device according to MDD rule 3 of Annex IX of Directive 2007/47/EC.

WARNING: the presence of a small percentage of red blood cells in the preparation does not interfere with the effectiveness of the product because they are autologous.

7. Mount the plastic needle on the 5 ml syringe and gently aspirate excess platelet-poor plasma (PPP), top to bottom, aspirate slightly less than 50% of the volume and avoid touching the platelet pellet in the lower part of the test tube near the gel. Mix the remaining liquid with the platelet pellet present in the buffy coat until PRP is obtained.

8. If necessary, this PPP can be used for the preparation of fibrin membranes in association with the activator, by inserting it in an empty test tube or syringe and centrifuging it.

9. Mount the plastic needle on the 1 ml syringe and gently resuspend the platelet pellet in the plasma residue present in the test tube (a small amount of partial aggregates will remain in the PRP and will be released in a short time).

10. The PRP concentrate is ready for use. Use within 6 hours of blood collection.

The PRP activator is made up of gluconate / calcium chloride. The calcium gluconate supplied is found in a sterile liquid form at a concentration suitable to saturate the anticoagulant present in the blood components to be transformed into gel. The peculiar factor is that it is used to transform fibrinogen into fibrin.

A higher quantity of anticoagulant compared to blood plasma or pathologically low concentrations of fibrinogen could delay or prevent gelation even with optimal amounts of calcium.

The sterilized gel preparation container is not provided. If you want to make the platelet membrane, the liquid product (PPP and PRP) obtained at the end of the 2 centrifugations of tests should be mixed with 1 ml of calcium chloride contained in the "tube type 2", inside a syringe sufficient capacity.

At this point we can proceed through two alternative ways:

- transferring the PRP into a new test tube to be subjected to further centrifugation, at 4000 RPM for 7 minutes. The calcium chloride serves at this point as an activator for the clotting cascade of platelet material and following centrifugation it's possible to separate on the one side the limped platelet-free serum (or with traces) and on the other, a clot that contains all the starting platelets;
- waiting 10 minutes (without centrifugation) so that the PRP in contact with the calcium chloride gels (platelet gel).

In both cases, a clot or platelet membrane rich in growth factors is obtained. To complete the whole procedure, store the components used in suitable containers for biological waste. The platelet gel obtained after centrifugation belongs to a new generation of platelet concentrates and can be considered as an autologous healing agent.

Warning: if the platelet gel is not handled, spontaneous retraction of the fibrin network (clot) may occur; the gel surface shrinks, and the plasma is released. Therefore, immediate application after gelling is recommended. However, the released plasma is rich in platelet growth factors and can be used as it is (liquid) or reactivated with calcium glucose (fibrin gel).

Growth factors and fibrin components in the platelet gel are known as accelerators and inducers of cell proliferation and cooperate in the regenerative and reparative processes of tissue lesions.

The activator allows the activation of topical blood components (platelet concentrate) in the gel. The device and the products biohazard prep plowed with it (platelet gel) should be employed in the range of a complete and accurate clinical and therapeutic approach, possibly following the criteria of evidence-based medicine (EBM). In no case self-medication is allowed using the device and biological derivatives prepared with the device itself.

Physicians using the activator should recognize that the therapeutic qualities of the component produced with this set depend on the quality of the original blood component (platelet plasma and / or low platelet plasma). The intrinsic qualities of the original blood component depend exclusively on the center that produces, stores, qualifies and distributes the blood component.

The platelet gel produced with the activator is used for the treatment of wounds, ulcers, acute and chronic injuries of hard and soft tissues.

Revision number and date: 01 March 2020

SYMBOL	DESCRIPTION
	Read use instructions before application
	Lot number
	Product code
	Sterilized
	Monouse device
	Expiry date
	Manufacturer
	European conformity by notified body 0425
	Storage temperature

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