

CONTRAINDICATIONS TO PRP IN MSK DISEASES: CONSENSUS FROM THE GRIIP



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CONFLICTS OF INTEREST

Regenlab

Fidia

Nordic Pharma

Labrha

BMS

UCB



WHAT DO WE KNOW ABOUT PRP IN MUSCULOSKELETAL DISEASES IN 2025?



- Anabolic and anti-inflammatory effects on cells and tissues
- Symptomatic efficacy in several MSK diseases
- > Few adverse events



WHAT'S NOT KNOWN?



- Which is the best PRP?
- Which protocol should be used?
- Who are the good responders?
- Which patients should not be offered PRP?





AVAILABLE RECOMMENDATIONS IN 2025

Knee Surgery, Sports Traumatology, Arthroscopy (2021) 29:3195–3210 https://doi.org/10.1007/s00167-020-06102-5

KNEE



Intra-articular injections of platelet-rich plasma in symptomatic knee osteoarthritis: a consensus statement from French-speaking experts

Florent Eymard¹ · Paul Ornetti² · Jérémy Maillet³ · Éric Noel⁴ · Philippe Adam⁵ · Virginie Legré-Boyer⁶ · Thierry Boyer⁷ · Fadoua Allali⁸ · Vincent Gremeaux⁹ · Jean-François Kaux¹⁰ · Karine Louati¹¹ · Martin Lamontagne¹² · Fabrice Michell¹³ · Pascal Richette¹⁴ · Hervé Bard¹⁵ on behalf of the GRIP (Groupe de Recherche sur les Injections de PRP, PRP Injection Research Group)

Recommendations for action	Expert opinion	Median	≤3	4-6	≥7	Level of evidence
PRP should not be mixed with an anesthetic or intra-articular corticosteroid	Appropriate with relative agreement	9	0	1	14	5
Anti-inflammatory treatment should be avoided in the days before and after PRP treatment	Appropriate with strong agreement	9	0	0	15	5
Treatment of knee osteoarthritis with PRP should be done away from an intra- articular injection of a corticosteroid	Appropriate with relative agreement	8	0	1	14	5
Recent neoplasia (malignant tumors, hematological diseases) may be a contraindication to intra-articular PRP injections	Appropriate with relative agreement	7	0	6	9	5
Antiplatelet aggregation therapy is not a contraindication to PRP injections but may alter its efficacy by preventing platelet activation.	Appropriate with strong agreement	9	0	0	15	5
The presence of radiographic chondrocalcinosis is not a contraindication to intra-articular injections of PRP	Appropriate with strong agreement	8	0	0	15	5

KNEE

Knee Surgery, Sports Traumatology, Arthroscopy WII FY

The use of injectable orthobiologics for knee osteoarthritis: A European ESSKA-ORBIT consensus. Part 1—Blood-derived products (platelet-rich plasma)

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                                                             Mikel Sanchez<sup>7,8</sup>
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                                                                                      Ricardo Bastos 14,15
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Ramon Cugat<sup>16,17</sup>
                            Micahel losifidis 18,19
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                               ESSKA-ORBIT Group
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- Contraindications due to local problems in the injection area: any contraindication for knee injections, such as infection, skin problems, others.
- Contraindications due to systemic problems (they can be grouped in four main groups):
- Infections

Besides the well-known reasons not to perform a knee injection in a patient with active systemic infections, systemic infections also affect negatively the PRP performances/functionalities because in addition to the immune and inflammatory process they generate at the systemic level, platelets are modified in these processes and may be more hyper-reactive, altering their functionality.

Cancer

Specific contraindications exist for the use of PRP in patients with active malignancies.

In terms of malignancies, current literature has

not demonstrated a clear link between PRP contents and the risk of turnour proliferation, either locally or remotely. However, due to the theoretical risk that PRP and growth factors may contribute to turnour growth promotion in situations where either a benign or malignant turnour exists in the knee joint, the consensus group considers these conditions a contraindication for injecting PRP. Due to similar concerns and until further evidence is available, the consensus group recommends this recommendation should also apply to turnours with or without metastasis located in other locations, outside/even remote from the knee, although consultation should be made with the managing oncologist/physician in specific cases.

- Inflammatory diseases

The presence of local or systemic inflammatory diseases (rheumatoid arthritis, Chron's disease and or other autoimmune diseases) does not prevent the possibility of injecting PRP in the knee. However, the nature of these diseases can lead to a plasma with a high content of proinflammatory molecules that may lead to lower results.

 Blood and quantitative and qualitative platelet disorders



METHODOLOGICAL GUIDE



EDITORIAL

Development of Good Practice Guidelines

"Formal Consensus" Method

December 2010 Updated: March 2015

Knee Surgery, Sports Traumatology, Arthroscopy

High scientific value of consensus is based on appropriate and rigorous methodology: The ESSKA formal consensus methodology

Beaufils et al.

Journal of Experimental Orthopaedics (2023) 10:10

https://doi.org/10.1186/s40634-023-00664-2

Journal of Experimental Orthopaedics

REVIEW PAPER

Open Access

ESSKA consensus initiative: why, when and how?



Philippe Beaufils^{1*}, David Dejour², Giuseppe Filardo³, Joan Carles Monllau^{4,5,6}, Jacques Menetrey^{7,8}, Romain Seil⁹ and Roland Becker¹⁰



HAS 2015

FORMAL CONSENSUS METHODS

The methods for development of good practice guidelines described by HAS are:

- the "Clinical practice guidelines" (CPG) method (20); and
- the "Formal consensus" (FCG) method.

The choice between these two methods is determined during the GPG outline phase 4.

Use of the "Formal consensus" method may be considered if at least two of the following conditions are met:

- absence or insufficiency of literature with a high level of evidence, specifically addressing the questions raised;
- possibility of applying the subject in easily identifiable clinical situations (lists of indications, of criteria, etc.);
- controversy, with the need for an independent group to identify and select among several alternatives the situations in which a practice is deemed appropriate.



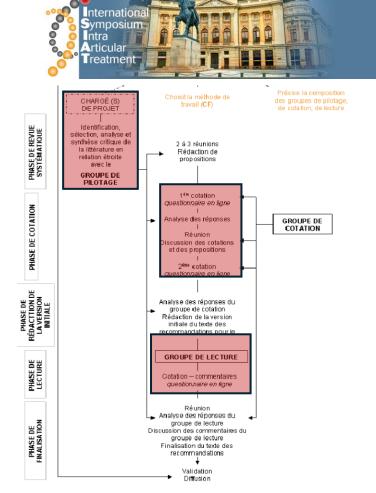
FORMAL CONSENSUS METHODS

METHODOLOGICAL GUIDE

Development of Good Practice Guidelines

"Formal Consensus" Method

December 2010 Updated: March 2015





STEERING GROUP

- Pr Florent Eymard
- Dr Karine Louati
- Dr Eric Noel

3 GRIIP members who:

- discussed the clinical situations that warranted inclusion in these recommendations
- performed a targeted literature search
- · drafted an initial set of recommendations



EXPERTS OF THE RATING GROUP

- Dr Philippe Adam
- Pr Fadoua Allali
- Dr Hervé Bard
- Dr Hervé Collado
- Pr Christelle Darrieutort-Laffite
- Dr Alain Frey
- Pr Vincent Grémeaux-Bader
- Pr Jean François Kaux

- Pr Martin Lamontagne
- Pr Jeremy Magalon
- Pr Fabrice Michel
- Pr Paul Ornetti
- Dr Ghislaine Robert
- Pr Mikel Sanchez
- Dr Alain Silvestre



- > Rheumatologists x 4
- Radiologists x 2
- Sports medicine x 3
- ➤ PRM x 4
- Orthopaedists x 1
- Pharmacist x 1







EXPERTS OF THE RATING GROUP

Hematology:

- o Dr. Mathieu Leclerc (CHU Mondor)
- Pr. Jo Caers (CHU Liège)
- Dr. Mael Heiblig (CHU Lyon)
- Dr. Gabriel Antherieu (CHU Lyon)
- Dr. Mathilde Gavillet (CHU Lausanne)

Oncology:

- Dr. Charlotte Joly (CHU Mondor)
- Dr. Daniel Lopez-Trabada-Apaz (CHU Saint Antoine)
- Pr. Guy Jerusalem (CHU Liège)
- Dr. Elvire Pons Tostivint (CHU Nantes)

- Infectious diseases:

- o Dr. Raphaël Lepeule (CHU Mondor)
- Pr. Redouane Abouqal (CHU Rabat)
- Dr. Philippe Léonard (CHU Liège)

Scientists

- Dr. Fernando Real (CNRS Lille)
- Dr. Cécile Oury (CHU Liège)
- Dr. Fabrice Cognasse (EFS Grenoble)
- Pr. Corinne Frère (CHU Pitié Salpêtrière)





RATING PROCESS

First meeting:

 To present the initial list of overarching principles and recommendations, together with the literature review

First rating:

- The 15 experts in MSK diseases and the 4 scientists rated all items
- The hematologists, oncologists and infectious disease specialists rated only those items related to their speciality

Second meeting:

- To review the experts' ratings and arguments
- To modify in substance or form the recommendations.

Final rating

	1 2 3 4 5 6 7 8 9	
Completely	↓	Completely
inappropriate	Undecided	appropriate

Proposal jud	ged	Median value	Distribution of responses to 2 nd round	Distribution of responses to 2 nd round				
			(9 to 15 raters)	(16 to 30 raters)				
Appropriate	Strong agreement	≥ 7	All responses are between [7-9], except one, missing or < 7.	All responses are between [7-9], except two, missing or < 7.				
	relative agreement	≥ 7	All responses are between [5-9], except one, missing or < 5.	All responses are between [5-9], except two, missing or < 5 (two missing or two responses < 5 or one missing and one response < 5).				
Inappropriate	strong agreement	≤ 3	All responses are between [1-3], except one, missing or > 3.	All responses are between [1-3], except two, missing or > 3.				
	relative agreement	≤ 3.5	All responses are between [1-5], except one, missing or > 5.	All responses are between [1-5], except two, missing or > 5.				
Uncertain	undecided	between [4 – 6.5]	Whatever the distribution of the responses.	Whatever the distribution of the responses.				
	lack of consensus	≥7	At least two values < 5 or two missing (or at least one missing value and one value < 5).	At least three values < 5 or missing.				
		≤ 3.5	At least two values > 5 or two missing (or at least one missing value and one value > 5).	At least three values > 5 o missing.				



READING GROUP

The reading group gives a formal opinion on the content and form of the initial version of the guidelines, in particular its applicability, acceptability, and readability. The members offer an advisory opinion on an individual basis and do not meet together as a group.

31 GRIIP members





OVERARCHING PRINCIPLES



		After exclusion of 2 extreme ratings				
		Nb of ratings	Median	Range	Judgment and degree of agreement	Grade
OP1	The indication of PRP injection for joint or tendon disease must be established by a specialist in musculoskeletal diseases.	29	9	9 - 9	Appropriate with strong agreement	Grade D
OP2	Each injection of PRP must be preceded by an assessment of the benefit-risk balance, taking into account the indication for injection and the characteristics of the lesion as well as the patient's history, comorbidities and treatments while systematically considering injectable therapeutic alternatives (corticosteroids, hyaluronic acid, etc.).		9	8 - 9	Appropriate with strong agreement	Grade D
OP3	In the presence of co-morbidities that may compromise platelet function or be transmitted by PRP, this treatment should be considered only in the absence of efficacious alternative therapeutic options or following their failure.		9	7 - 9	Appropriate with strong agreement	Grade D
OP4	Patients must receive clear, personalised information about the potential benefits and risks of PRP injection, taking into account the medical history and comorbidities, and the patient's informed consent must be recorded in the medical file.		9	9 - 9	Appropriate with strong agreement	Grade D



INFECTIOUS DISEASES



			After exclusion of 2 extreme ratings			
		Nb of ratings	Median	Range	Judgment and degree of agreement	Grade
R1	In patients with HIV infection, PRP injection may be performed if the viral load is undetectable and the CD4 count is >350/mm ³ .	20	8	7 - 9	Appropriate with strong agreement	Grade C
R2	In patients with hepatitis B virus infection, PRP injection may be performed if the viral load is undetectable.	20	8.5	7 - 9	Appropriate with strong agreement	Grade D
R3	In patients with hepatitis C virus infection, PRP injection should be performed only after antiviral treatment has been completed.	20	9	7 - 9	Appropriate with strong agreement	Grade D
R4	In patients with an acute viral infectious syndrome, PRP injection may be performed if the patient has no general symptoms (fever, chills, etc.) or signs of bacterial infection and if the viral syndrome is improving.	20	8	7 - 9	Appropriate with strong agreement	Grade D
R5	In patients with a bacterial infection requiring antibiotic therapy of less than 3 months, PRP injection may only be performed once the treatment has been completed.	20	9	8-9	Appropriate with strong agreement	Grade C
R6	In patients with a controlled bacterial infection requiring antibiotic therapy for more than 3 months, a PRP injection may be performed only after infectiologist agreement.	20	9	8-9	Appropriate with strong agreement	Grade D
R7	In patients with chronic renal failure requiring dialysis, PRP injection may be considered, but the patient should be carefully monitored for signs of bacteremia and the injection must be avoided on the day of dialysis.	20	8	5 - 9	Appropriate with relative agreement	Grade C
R8	In patients with prolonged and stabilized prescription of immunosuppressive agents, PRP injection may be performed, but particular attention must be paid to the presence of concomitant infection.	20	8.5	7-9	Appropriate with strong agreement	Grade C
R9	In patients with dental infection or invasive oral procedures, PRP injection should not be performed until the completion of treatment and healing.	20	9	9-9	Appropriate with strong agreement	Grade C
R10	In asymptomatic patients with no known infectious pathology, no additional tests for infection are needed.	20	9	9 - 9	Appropriate with strong agreement	Grade D



ONCOLOGY



		After exclusion of 2 extreme ratings				
		Nb of ratings	Median	Range	Judgment and degree of agreement	Grade
R11	PRP should not be injected in the vicinity of benign or malignant tumors (bone, synovial or soft tissue) or metaplasia (such as primary synovial chondromatosis).	21	9	8 - 9	Appropriate with strong agreement	Grade D
R12	In patients with solid cancers undergoing diagnosis or considered active, PRP injection should not be performed, except in exceptional situations to be discussed with the oncologist.	21	9	9-9	Appropriate with strong agreement	Grade D
R13	In patients with non-metastatic solid cancer considered in remission by the oncologist after the end of treatment, PRP injection may be performed.	21	9	7 - 9	Appropriate with strong agreement	Grade C
R14	In patients with metastatic solid cancer under treatment or not and considered in remission, PRP injection may be performed only after oncologist agreement.	21	9	8 - 9	Appropriate with strong agreement	Grade D
R15	In patients with a history of solid cancer that the oncologist considers cured, PRP injection may be performed.	21	9	7 - 9	Appropriate with strong agreement	Grade D



HEMATOLOGY



		After exclusion of 2 extreme ratings				
		Nb of ratings	Median	Range	Judgment and degree of agreement	Grade
R16	A significant abnormality in the blood count should be investigated before PRP injection.	22	9	9 - 9	Appropriate with strong agreement	Grade D
R17	Previously investigated thrombocytopenia > 50,000/mm3, excluding hematologic malignancies, is not a contraindication to PRP injection.	22	8	7 - 9	Appropriate with strong agreement	Grade D
R18	In patients with a hematologic malignancy undergoing diagnosis or not considered stabilized, PRP injection should not be performed, except in exceptional situations to be discussed with the hematologist.	22	9	8 - 9	Appropriate with strong agreement	Grade D
R19	In patients with a hematologic malignancy considered in remission by the hematologist after the completion of treatment (including post-transplant immunosuppressive therapy), PRP injection may be performed if there are no platelet count abnormalities.	22	9	7-9	Appropriate with strong agreement	Grade D
R20	In patients with stabilized chronic lymphoid hemopathy under treatment or not, PRP injection may be performed if there are no platelet count abnormalities.	22	9	8 - 9	Appropriate with strong agreement	Grade D
R21	In patients with a stabilized chronic myeloid hemopathy under treatment or not, PRP injection may be performed only after hematologist agreement.	22	9	8 - 9	Appropriate with strong agreement	Grade D
R22	In patients with monoclonal gammopathy of undetermined significance, PRP injection may be performed.	22	9	6 - 9	Appropriate with relative agreement	Grade D
R23	In patients with a hematologic malignancy that the hematologist considers cured, PRP injection may be performed.	22	9	8 - 9	Appropriate with strong agreement	Grade D



CONCLUSION

First recommendations on contraindications to PRP injections in patients with infectious, oncologic or hematologic diseases

>Strengths:

- Validated methodology (followed in the ESKKA-ORBIT consensus)
- Large panel of experts in MSK conditions and in the various comorbidities considered.
- > International

>Limitations:

- > Lack of scientific evidence for most recommendations
- Likely bias related to the origin of the expert
- ➤ Need to collect real-life data+++ (register)





KNAL OF ESSKA Sport





Edited by: Michael Hirschmann
IOURNAL METRICS >

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Indications and contraindications to PRP injections in case of infectious, oncological and hematological comorbidities:

A 2025 formal consensus from the GRIIP