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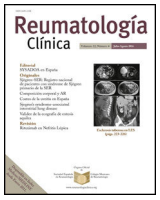

Special Article

Clinical practice guidelines for the management of patients with rheumatoid arthritis. GUIPCAR 2025

Guía de Práctica Clínica para el Manejo de Pacientes con Artritis Reumatoide. GUIPCAR 2025

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Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that has a predilection for the joints, with the synovial membrane being the primary target of the inflammatory process. Subsequently, it spreads to adjacent structures, affecting cartilage, ligaments, joint capsule, and bone. Furthermore, systemic inflammatory changes can affect other organs such as the heart, lungs, kidneys, skin, and eyes, among others, as well as the hematopoietic system and the neuropsychiatric system. If the patient does not receive appropriate treatment, it typically progresses to joint destruction, with a subsequent increase in functional impairment, and mortality.[1]

Although the aetiology of rheumatoid arthritis (RA) is unknown, it is accepted that it has a multifactorial origin with interactions between environmental factors and individual factors, particularly in people with a genetic predisposition. Host-related risk factors associated with the development of RA can be divided into genetic, epigenetic, hormonal, and neuroendocrine factors. Environmental risk factors include smoking, the gut microbiota, infectious agents, diet, and socioeconomic factors.[2]

A Clinical Practice Guideline (CPG) is a document that presents a šet of recommendations based on a systematic review of the evidence and an assessment of the risks and benefits of different alternatives, with the aim of optimising healthcare for patients."[3] Internationally, the recommendations of the European Alliance of Associations for Rheumatology (EULAR) and the American College of Rheumatology (ACR) for the diagnosis and treatment of these rheumatic diseases have been the most widely used.[4,5] In Spain, the reference guideline (Clinical Practice Guideline for the Management of Patients with Rheumatoid Arthritis [GUIPCAR for its initials in Spanish]) has been developed by the Spanish Society of Rheumatology (SER) since 2001 and has been updated three times: in 2007, 2011, and 2019.[6,7]

Given the time elapsed since the publication of the previous guideline,[7] and the significant advances that have emerged in recent years, mainly in the area of therapeutic innovations and risk management, the SER promoted its update, and in September 2025, the new "Guideline for the Management of Patients with Rheumatoid Arthritis"[8] was published. The objective has been to establish current recommendations, based on the best available evidence, aimed at improving the quality of care and quality of life of people with rheumatoid arthritis (RA), and to assist rheumatologists in making therapeutic decisions for this group of diseases.

The 2025 Clinical Practice Guideline (CPG) is the result of the work of a significant number of healthcare professionals (Development Group [DG]) from various autonomous communities involved in the management of patients with rheumatoid arthritis (RA), including specialists in rheumatology, cardiology, pulmonology, family medicine, specialised nursing, and representatives of patient associations. Methodology specialists, technicians from the Spanish Society of Rheumatology (SER) Research Unit, and several rheumatologists from the SER review working group, as well as other external reviewers, also participated, systematically reviewing the available scientific evidence. |For the first time the CPG has also incorporated the methodology of the international working group Grading of Recommendations Assessment, Development, and Evaluation (GRADE),[9] both for determining the quality or certainty of the evidence and for grading the strength and direction of the recommendations.

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The clinical practice guideline (CPG) includes sarilumab as a biologic therapy for the treatment of rheumatoid arthritis (RA), as well as upadacitinib and filgotinib, Janus kinase (JAK) inhibitors that were not included in the previous edition. It reviews treatment strategies for early-onset RA and continues to recommend methotrexate as a first-line drug if there are no contraindications, even though the availability of biosimilars provides further opportunities. The guideline also reviews therapeutic recommendations for patients who have failed a first biologic disease-modifying antirheumatic drug (DMARD), in which, since there are still no biomarkers of response, the approach remains open to all possibilities. Studies providing new evidence on the use and safety of glucocorticoids (GCs) in older adults and new treatments approved for interstitial lung disease in patients with RA have been added. The new approaches to risk management for JAK inhibitors in clinical practice have also been reviewed, considering both the occurrence of major cardiovascular and thromboembolic events, as well as tumours, following the recommendations of the Spanish Agency for Medicines and Health Products (AEMPS). The evidence regarding the association of different treatments with the development of cancer or tumour recurrence in patients with a history of cancer has been updated, vaccination recommendations have been updated, including those for herpes zoster and coronavirus, and finally, the recommendations for tapering treatment in patients in prolonged remission have been updated.

Another important theme addressed in the GUIPCAR is the importance of empowering patients to participate in decisions about their disease treatment. These measures can improve treatment adherence. Hence the inclusion of patients and nursing professionals in the GUIPCAR.

The SER's GUIPCAR 2025, like the EULAR recommendations, presents some key differences when compared to the ACR recommendations for RA. Essentially, the final recommendations on disease management and treatment are similar in the GUIPCAR and EULAR, although the methodology used in their development differs, employing the GRADE[9] and SIGN[10] systems, respectively. The GRADE methodology explicitly structures the process of formulating recommendations. Among its novel features and strengths is the evaluation of the quality or certainty of evidence for each outcome of interest. These outcomes will have been previously prioritised by the research team. The assessment of quality goes far beyond the usual risk of bias, extending to other factors such as the consistency or inconsistency of results or their imprecision. It explicitly separates the quality of evidence (confidence in the estimate of an effect to support a recommendation) from the strength of recommendations (the degree to which we can be sure that implementing a recommendation will bring more benefits than risks). Furthermore, other relevant factors are incorporated into the development of recommendations, such as patients' values and preferences, the balance between desirable and undesirable effects of interventions, aspects such as equity, acceptability, and feasibility of implementation, and the use of resources and costs. Integrating all these factors, the research group proceeded to formulate specific recommendations based on a f̈ormal assessmentör ïeasoned judgment,äfter having previously summarised the evidence for each clinical question.

One of the most important, though predictable, conclusions of the GUIPCAR 2025 guidelines is the need for further studies to improve the quality of evidence in certain areas, such as the relationship between infections and treatment with biologic and targeted DMARDs, especially in patients who have previously experienced a serious infection. As mentioned earlier, biomarkers of response are required for selection of the most appropriate treatment, and the relationship between cardiovascular events and cancer and the various JAK inhibitors needs clarification. These and other unmet needs are addressed in the GUIPCAR 2025 research agenda.

To conclude, the GUIPCAR 2025 Guidelines for the Management of Patients with Rheumatoid Arthritis were developed using a rigorous, evidence-based methodology and aim to promote effective, safe, and coordinated decision-making among healthcare professionals regarding therapeutic interventions for RA, focusing on patients with these diseases.

CRediT authorship contribution statement

The authors have made substantial contributions based on the data analysis, the draft article, and the final approval of the submitted version.

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Declaration of competing interest

Alejandro Balsa has received funding from AbbVie, Lilly, Pfizer, and Sandoz to attend courses/conferences; fees from AbbVie, Biogen, BMS, Galápagos, Lilly, Nordic, Pfizer, Sandoz, Sanofi, and UCB for presentations; funding from Pfizer and UCB for educational programs or courses; financial support from AbbVie, Novartis, and UCB for participating in research, and fees from AbbVie, Biogen, Galápagos, Lilly, Nordic, Pfizer, Sanofi, Sandoz, and UCB for consulting services provided to a pharmaceutical company/other technology company. Petra Díaz del Campo Fontecha has declared no conflicts of interest related to this Clinical Practice Guideline.

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Appendix A. List of members of the GUIPCAR Drafting Group

José Luis Andreu Sánchez, Laura Cano García, Carlos González Juanatey, M. Vanesa Hernández Hernández, Fernando León Vázquez, Francisco Javier Narváez García, Mª Asunción Nieto Barbero, Ana Ortiz García, Lucía Silva Fernández. The complete declarations of interests of all members of the drafting group, as well as GUIPCAR 2025, can be found at the following link: https://www.ser.es/guipcar/.

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