



1 17 June 2024  
2 EMA/CHMP/96250/2024  
3 Committee for medicinal products for human use (CHMP)

4 **Concept paper on the need for revision of the guideline**  
5 **on clinical investigation of medicinal products for the**  
6 **treatment of psoriatic arthritis**

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Agreed by Rheumatology/Immunology Working Party	April 2024
Adopted by CHMP for release for consultation	17 June 2024
Start of public consultation	1 July 2024
End of consultation (deadline for comments)	30 September 2024

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9 The proposed guideline will replace the Guideline on clinical investigation of medicinal products for the  
10 treatment of psoriatic arthritis (CHMP/EWP/438/04).

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the [EUSurvey Support](#).

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Keywords	Psoriatic arthritis, treat-to target, extra musculoskeletal disease manifestations, guidance
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14 **1. Introduction**

15 Psoriatic Arthritis (PsA) is a multifactorial, chronic inflammatory arthropathy of the peripheral and axial  
16 joints affecting synovium, tendons, entheses, skin and bone. Pain, inflammation and fatigue are a  
17 significant burden for patients. To prevent joint damage from persisting inflammation early treatment  
18 is indicated. In patients with Plaque Psoriasis (PsO) the prevalence of PsA is approximately 20%.<sup>1,2</sup>

19 The current Guideline on clinical investigation of medicinal products for the treatment of psoriatic  
20 arthritis<sup>3</sup> came into effect in 2007. Since then, several medicinal products have been approved in the  
21 EU for the treatment of PsA and consecutively there are also substantial updates in general treatment  
22 approaches and treatment goals for this condition<sup>4</sup>. Despite the number of existing treatment options  
23 for PsA, an unmet need still exists for patients experiencing poor efficacy and tolerability of current  
24 therapies.



## 25 **2. Problem statement**

26 The regulatory guidance on the treatment of PsA has not been updated since 2007 and does not take  
27 into account the regulatory experience with applications for scientific advice and for marketing  
28 authorisation since then, or the current approaches of the pharmacological management of PsA<sup>4</sup> nor  
29 recent developments within the field of 'early' disease detection in the population at risk.

30 In particular, the European League Against Rheumatism (EULAR) recommendations for the treatment  
31 of PsA have been published and most recently updated<sup>4</sup>. EULAR points to consider for the definition of  
32 clinical and imaging features suspicious for progression from psoriasis to PsA<sup>5</sup> also need to be  
33 considered.

34 Therefore, several important additions and changes are needed to explicit the current state of scientific  
35 knowledge in the guideline.

36 The purpose of this concept paper is to highlight the identified points for revision of the existing  
37 Guideline on Clinical Investigation of Medicinal products for the treatment of psoriatic arthritis<sup>3</sup>. The  
38 guideline update concerns the adult form of PsA. The paediatric form is addressed by the Guideline on  
39 clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis<sup>6</sup>, that is not  
40 within the scope of the current guideline update.

## 41 **3. Discussion (on the problem statement)**

42 The following critical aspects have been identified and would need to be addressed in the revised  
43 guideline:

44 • Since the current EMA PsA guideline<sup>3</sup> came into effect, the PsA (and PsO) treatment  
45 armamentarium has expanded. Currently, many different medicinal products are approved for  
46 PsA in the EU. These include both conventional synthetic disease-modifying anti-rheumatic  
47 drugs (csDMARDs) and various biologics targeting tumour necrosis factor (TNF), Interleukin  
48 (IL)-17, IL-12/23, IL-23, and modulation of T lymphocyte-dependent antibody responses. An  
49 additional drug class comprises targeted synthetic DMARDs (tsDMARDs), that inhibit  
50 phosphodiesterase-4 (PDE4); and the Janus kinase (JAKs) i.e. JAK-inhibitors interfering with  
51 the JAK-STAT signalling pathway.

52 Importantly, the regulatory experience from recent approvals in the PsA field may have  
53 generated essential insights that should be reflected in an update of the EMA PsA guideline  
54 including what can be considered reasonable standard of care, concomitant study treatment or  
55 rescue therapy, as well as potential active comparators in PsA-studies.

56 • The current EMA PsA guideline<sup>3</sup> states that there are no generally accepted validated case  
57 definitions of PsA and at present, the diagnosis is based on clinical judgement.

58 The additional experience that has been gained since the guideline was issued may allow an  
59 update of this section of the guideline. The Classification criteria for Psoriatic Arthritis<sup>7</sup> is  
60 currently widely used, including in recent clinical trials in marketing authorisation applications  
61 for PsA.

62 • The EULAR developed recommendations for the pharmacological management of PsA in 2011<sup>8</sup>  
63 and updated them in 2015<sup>9</sup>, 2019<sup>10</sup> and 2023<sup>4</sup>. The EULAR recommendation includes some  
64 important points that are either not reflected or not sufficiently addressed in the current EMA  
65 PsA guideline.

66           ○ First, the most recent EULAR publication<sup>4</sup> includes the following recommendation  
67 'Treatment should be aimed at reaching the target of remission or, alternatively, low  
68 disease activity, by regular disease activity assessment and appropriate adjustment of  
69 therapy' i.e. a treat-to-target (T2T) approach. Also 'The taskforce members  
70 emphasised that disease activity should be regularly assessed across individual  
71 involved manifestations (eg, joints, skin, enthesitis, dactylitis, axial disease), and that  
72 treatment adjustments will depend on the predominant manifestation of the disease at  
73 a given moment.'

74           To be noted, the EMA recently published a Letter of support for Minimal Disease  
75 Activity Score as primary outcome instrument for clinical studies in PsA<sup>11</sup> .

76           Overall, a rather substantial revision of the guideline section on '*Methods to assess  
77 efficacy*' is expected, reflecting also validation and use of new endpoints in  
78 authorisation studies as compared to 2007 when the current guideline came into effect.  
79 It is foreseen that the recommendation for the primary endpoint (PEP) will be updated.

80           ○ Secondly, the most recently updated EULAR publication<sup>4</sup> also stresses that the choice  
81 of drug should take into account not only the musculoskeletal PsA subtype but also  
82 extra (non)- musculoskeletal manifestations related to PsA, including skin psoriasis,  
83 uveitis, and inflammatory bowel disease.

84           This topic is to some extent covered by the current EMA PsA guideline but could be  
85 further highlighted in an updated version.

86           It is thus becoming increasingly clear that PsA comprises a number of different clinical  
87 domains which manifest their own unique clinical features and immune phenotypes,  
88 including arthritis (synovitis), enthesitis, dactylitis, spondylitis, psoriasis and nail  
89 disease<sup>12</sup>.

90           ○ Finally, the most recent EULAR publication<sup>4</sup> includes the following recommendation: 'In  
91 patients in sustained remission, tapering of DMARDs may be considered'. The EULAR  
92 publication clarifies that tapering means 'dose reduction' not drug discontinuation since  
93 the latter usually leads to flares.

94           This is not a topic explicitly covered by the existing EMA PsA guideline. The EMA PsA  
95 guideline may thus be updated to encourage studies on this topic to better guide use of  
96 new PsA treatments over time.  
97

98           • The EULAR points to consider for the definition of clinical and imaging features suspicious for  
99 progression from psoriasis to PsA<sup>5</sup> includes nomenclature that could be relevant for studies  
100 looking at PsA prevention / detection of early PsA, or interception with two potential new  
101 outcomes in the field of transition: (i) the regression of joint symptoms and imaging features in  
102 patients with PsO with subclinical PsA and (ii) reduction of new clinical PsA cases.

103           This is a topic not mentioned in the current EMA PsA guideline that could be considered to be  
104 included in an updated version.

105           • In 2020, the ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to  
106 the guideline on statistical principles for clinical trials<sup>13</sup> came into effect.

107           Advice on how the estimand concept is best applied in PsA should be considered for inclusion in  
108 the updated guideline.

## 109 **4. Recommendation**

110 The RIWP of the Committee for Human Medicinal Products (CHMP) recommends revising the Guideline  
111 on Clinical Investigation of Medicinal products for the treatment of PsA taking into account the issues  
112 identified above.

## 113 **5. Proposed timetable**

114 Release for consultation on 1 July 2024, deadline for comments 30 September 2024.

## 115 **6. Resource requirements for preparation**

116 The update of the guideline will involve representatives of the RI-WP, including one Rapporteur. It is  
117 anticipated that at least one plenary session discussions at the RI-WP will be needed.

## 118 **7. Impact assessment (anticipated)**

119 The update of the guideline will have an impact on the clinical development of medicinal products for  
120 the treatment of PsA. It will aim to consolidate the current regulatory view on the design of the clinical  
121 development programs of these medicinal products and is expected to be helpful to achieve consensus  
122 in the evaluation of such products by regulatory authorities.

## 123 **8. Interested parties**

124 Pharmaceutical Industry, Academia, EU Competent Authorities and patients and health care  
125 professional groups. Consultation with other working parties or committees (e.g. SAWP, PDCO) will be  
126 initiated, as appropriate.

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