

**Points to consider for patient education provided by nurses on methotrexate use. A
European consensus initiative**

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ABSTRACT

Background: Methotrexate (MTX) is the anchor and most prescribed disease-modifying anti-rheumatic drug (DMARD) for inflammatory rheumatic diseases (IRDs). MTX can be very efficacious but can also have serious, life-threatening side effects. Adequate education and follow-up of patients/carers are therefore essential, and dedicated rheumatology nurse consultations are an important part of this. However, many patients across European countries lack access to nurse consultations, and there are no agreed-upon, defined standards of care for this topic.

Objectives: To develop points to consider (PtC), based on the best available evidence and experts' opinion, on the nursing education of patients (or carers) with IRDs taking MTX.

Methods: A task force of adult and pediatric nurses (n=19) from 16 European countries, one rheumatologist, one pharmacist, and three patient-representatives, was established by the Portuguese Association of Health Professionals in Rheumatology. The group convened virtually to discuss the protocol for developing the PtC, including the research questions for a scoping review and for a European survey to collect patients'/carers', nurses' and rheumatologists' experiences and perceptions about MTX education. The results from these studies informed the development of the PtC statements, which were discussed and voted on in two virtual meetings and one online questionnaire. Modified EULAR Standard Operating Procedures for the development of recommendations/PtC were followed.

Results: The consensus resulted in three overarching principles and six PtC. All PtC were based on available scientific evidence, and all obtained high levels of agreement (>8/10). These PtC emphasize the need for continuous, tailored education by trained nurses, the availability of diverse educational methods, and the support for self-management and adherence strategies.

Conclusion: A set of PtC has been developed to improve the quality of care provided to patients with IRDs and their carers regarding the education and support nurses should provide on MTX use. The ultimate goal is to optimize MTX intake, improve efficacy, reduce side effects and ensure adherence to treatment. A plan is underway for the European implementation of these PtC, recognizing the crucial relevance of multi-professional rheumatology teamwork.

Keywords: Methotrexate; Health Education; Patient Education as Topic; Rheumatology; Self-management; Nurse's role.

Key-messages:

- Access to standardized rheumatology nurse-led education on methotrexate varies across Europe, with no clear standards on its provision.
- An international group of experts developed consensus-based Points to Consider for nurse-led methotrexate education.
- These suggestions aim to improve patient safety, treatment adherence, and overall quality of multiprofessional Rheumatology care.

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Introduction

Methotrexate (MTX) stands as a cornerstone in the management of inflammatory rheumatic diseases (IRDs). Its efficacy in controlling disease activity and preventing joint damage has been well documented, making it a first-line treatment option in international recommendations¹⁻⁵. These recommendations mainly focus on which disease-modifying anti-rheumatic drugs (DMARDs) to choose first and which to choose second. Given MTX's therapeutic potential and risk profile, proper administration and vigilant monitoring are essential to mitigate potential adverse effects⁶. A multicenter survey in the UK and Ireland reported that 57% to 86% of patients experienced side effects, including fatigue (53%), nausea (38%), mouth ulcers (23%), and hair loss (23%), which can compromise adherence⁷.

Given its widespread use, distinct pharmacological characteristics, and potential side effects, including serious dosing errors, MTX presents unique challenges that are less likely with other DMARDs. These include the need for folic acid supplementation, progressive dose escalation, and the risk of confusion between weekly and daily dosing, which has led to safety alerts by regulatory agencies^{8,9}.

In this context, patient education (PE) emerged as a pivotal component of care^{10,11}. Several European Alliance of Associations for Rheumatology (EULAR) recommendations advocate for PE tailored to individual needs, integrated as a self-management strategy, and embedded within shared decision-making processes¹²⁻¹⁵. Patients need to be aware of MTX risks, understand the importance of regular laboratory monitoring, and recognize symptoms that require medical attention. Addressing patients' fears of potential side effects is as important for this 'old' drug as it is for novel agents⁴.

Ample evidence supports the central role of nurses in delivering multidisciplinary PE, monitoring disease and treatment, managing adverse effects, and ensuring that patients understand the importance of adhering to the medication regimen¹⁶. Yet, despite all recommendations, significant variability persists across Europe in the accessibility and quality of MTX education and ongoing support. A recent survey across 24 European countries highlights these disparities, revealing that only 28% of patients had a dedicated nursing consultation at the start of oral MTX therapy, increasing slightly to 42% for subcutaneous MTX¹⁷. The lack of a standardized approach to the provision of MTX education by nurses has led to wide disparities in the content, timing, and depth of education, from informal discussions to structured programs, contributing to inconsistent patient knowledge, self-management skills, adherence, and safety^{10,17,18}.

Given the pivotal role of nurses in PE and follow-up support, and the observed variability in educational practices, there is a need to establish standardized guidance for nurse-led PE. To address this gap, a European task force coordinated by the Portuguese Association of Health Professionals in Rheumatology (APPSReuma) was formed to develop consensus-based Points to Consider (PtC) for nurse-led MTX education, drawing on the best available evidence and expert opinion. While this work focuses on methotrexate, the underlying principles of patient education and support are likely to be relevant to other DMARDs.

Methods

A task force group consisting of 19 adult and pediatric nurses from 16 European countries (Belgium, Cyprus, the Czech Republic, Denmark, Estonia, Germany, Greece, Hungary, Ireland, Italy, Norway, Portugal, Spain, Sweden, Switzerland, and the United Kingdom), one rheumatologist, one pharmacist, and three patient-representative partners was convened. Nurses were identified through the national Health Professionals in Rheumatology (HPR) organizations. An invitation outlining the study objectives and expert eligibility criteria was sent via email to the boards of 21 such organizations. Experts were defined as nurses with at least one year of clinical experience in MTX-related patient education (in adult or pediatric care) and the ability to participate in English-language virtual meetings and review written documents. Fifteen organizations responded, in some cases nominating more than one candidate. Final nurse selections were based on documented expertise. The non-nurse members of the task force were selected based on their experience, previous collaboration, and diversity. Among the three patient partners, one represented an adult umbrella organization for rheumatic and musculoskeletal diseases (RMDs), another represented a children's and youth organization, and the third was a young adult living with systemic lupus erythematosus—all with personal experience of MTX use.

The steering group comprised two nurses as convenors (RF and AM), one experienced nurse (PL), one pharmacist (CM), one rheumatologist with methodological expertise (EN), two patient partners (AP and BS), and two fellows (MOP and CM), who met monthly during the first semester of the project and twice a year thereafter. A comprehensive and structured protocol guided the process, which included: (1) a pre-assessment survey completed by all task force members prior to the first virtual meeting; (2) a scoping review to evaluate the existing evidence on nursing practices related to MTX education¹⁸ (3) a Europe-wide survey to gather perspectives and experiences from patients/carers, nurses, and rheumatologists regarding MTX education¹⁵; and (4) the definition of the consensus methodology. Findings from both the scoping review and

survey were instrumental in developing and refining the OPs and PtCs. The methodology process was conducted in accordance with a modified version of the EULAR Standard Operating Procedures for the development of recommendations/PtC¹⁹, adapted to the scope and context of this initiative. While this was not a formal EULAR-endorsed project, key elements of the SOPs were adopted, including the establishment of a multidisciplinary task force, systematic evidence collection, and structured voting procedures. Relevant modifications included conducting a pre-meeting survey among task force members, using a scoping review rather than a systematic literature review, conducting additional stakeholder surveys to inform the task force, holding three task force meetings (instead of two), and predefining voting thresholds.

Three virtual meetings were held, each lasting around 2-3 hours. Prior to the first meeting, a pilot survey was conducted among taskforce members to assess their experiences with PE regarding methotrexate, with 13 responses obtained (from nurses only), which were used to prompt discussion. During the first meeting, participants introduced themselves and shared their backgrounds and perspectives on the project. The study objectives were presented, followed by a discussion of the pilot survey results. Based on this discussion, the steering group refined the pilot survey, adding and updating questions to enable large-scale implementation among healthcare professionals (nurses and physicians) and patients/carers. It was also agreed that a scoping review on nurse-led methotrexate education would be appropriate, and preliminary research questions were discussed in this meeting.

At the second meeting, the group revisited the study objectives and reviewed the decisions made during the initial session. Practical information related to the Europe-wide survey was shared, and preliminary findings from the ongoing scoping review were presented and discussed.

The third meeting focused on reviewing preliminary survey results, the final scoping results, and drafting the initial set of OPs and PtC, working on a set of sentences drafted by the Steering Group. Each proposed statement was examined individually, discussed (evidence, understanding, wording, etc.), and revised for clarity. Participants voted on whether to retain each OP and PtC using a simple "yes" or "no" response. Statements receiving at least 65% affirmative votes were retained. A second round of discussion and voting followed, in which members rated their level of agreement with each statement on a scale from 1 (completely disagree) to 10 (completely agree). An agreement was considered if >75% of experts scored on one of the extremes of the Likert scale (8 to 10 or 1 to 3). After this meeting, a follow-up questionnaire was distributed to all members to confirm their level of agreement with each statement, using the same Likert scale, and to gather any final comments or suggestions for

modification. One statement (OP3), although receiving high levels of agreement, generated substantial feedback and was subsequently reformulated. A new round of voting was conducted only on the revised version of that statement.

The level of evidence supporting each PtC, informed by the scoping review findings, was discussed and rated during the final meeting. The level of evidence and the “strength of recommendation” were determined in accordance with the Oxford Centre for Evidence-Based Medicine standards²⁰.

The findings from the scoping review and from the survey conducted to inform this task force were published elsewhere^{17,18}. A summary of the methodological steps followed is presented in Figure 1.

Results

The task force developed three OPs and six PtCs regarding nurse-led education for patients and carers on MTX use. Table I presents the full list, including the level of evidence, strength of recommendation, and level of agreement, which was high for all statements.

Overarching Principles

OP1. All patients prescribed MTX and their carers should receive treatment-specific education. The task force strongly agreed that patients and carers must receive structured education at the initiation of MTX to ensure safe and effective use, as recommended in all treatment guidelines^{1-5,21}. This OP is not specific for nurses, as the taskforce recognized that MTX-specific education is provided by nurses, rheumatologists and, if applicable, a wider healthcare team, in close collaboration with the patient (and family/significant others, as appropriate), always according to national guidelines.

OP2. Education for patients prescribed MTX needs to be ongoing and requires continuous review by the rheumatology team.

MTX education is not a one-time event provided only at the beginning of treatment, but rather a dynamic and evolving process¹⁵. As patients’ needs and concerns change over time, educational content must be revisited and reinforced^{22,23}. During discussions, the group considered several phrasings, including “ongoing dynamic process” and “education and care,”

and agreed to retain a more focused formulation. There was consensus that follow-up should be the responsibility of the rheumatology team, acknowledging varied national practices and the multidisciplinary nature of care¹⁷. This OP also addresses the need to move beyond isolated or single-session education, which occurs in 70% of cases nowadays¹⁷, ensuring that patients have continuous access to updated information and support throughout the treatment journey. This is especially important for children and young patients.

OP3. Nurses should have access to training regarding methotrexate treatment and stay up to date through continuous education.

To effectively fulfil the role of educating and supporting patients prescribed MTX, nurses should have access to structured, specific training and ongoing education to stay up-to-date with new publications on the topic. This OP resonate with the professional obligations of nurses, who are required by regulatory bodies to engage in continuous education. Members emphasized that such training should cover both clinical content and educational skills and be supported by reliable resources. Examples of useful materials include patient leaflets, e-learning platforms, professional guidelines, and repositories like EULAR's eLearning courses or national rheumatology society tools. Ideally, these professional courses should be provided in conjunction with national associations/societies of rheumatologists, health professionals in rheumatology (HPRs), and patient organizations. For instance, the Royal College of Nursing (RCN) in the UK, in collaboration with national rheumatology experts, has developed comprehensive guidance on administering subcutaneous MTX for inflammatory arthritis²⁴. This RCN guidance includes an appendix listing "Example of specialist practitioner competence checklist", which is very useful to standardize training. Additionally, EULAR offers a range of online courses tailored to health professionals in rheumatology, focusing on various aspects of patient care and education. Lastly, reading more comprehensive manuals, such as the practical guide for health professionals by Taylor²⁵, is recommended.

Points to Consider

PtC1. Patients prescribed MTX and their carers should be offered education by a nurse when starting treatment, changing the route and when required by the patient.

The initiation of MTX therapy is a key moment to provide comprehensive education about the treatment's goals, potential side effects, monitoring requirements, and self-management strategies. Education is equally important when there is a change in the route of administration (e.g., from oral to subcutaneous), or when a significant event is planned or occurs (e.g. surgery,

pregnancy), which may raise new concerns or challenges. Dose adjustments present valuable opportunities to reassess patient understanding and reinforce education. This point applies to both oral and subcutaneous MTX and should be adapted to each patient's context and preferences.

PtC2. Patients prescribed MTX should have access to a nurse for needs-based education to improve treatment knowledge, enhance satisfaction with care and quality of life.

Access to a nurse for needs-based education allows information and support to be tailored to individual circumstances, preferences, and levels of understanding. This is particularly relevant for patients living with comorbidities, physical limitations, or emotional distress, which may affect how they manage their condition and treatment^{26,27}. Needs-based approaches help patients better understand MTX, improve satisfaction with care, and enhance quality of life²⁷. Tools such as the Educational Needs Assessment Tool (ENAT)^{28,29}, can support health professionals in identifying and prioritizing patients' educational needs²⁹. A retrospective study showed that a single therapeutic education session with a nurse improves patients' knowledge about MTX at 6 and 12 months³⁰.

PtC3. Nurses should support patients and carers with relevant self-management skills related to MTX treatment, to ensure safety and improve self-efficacy.

Self-management of MTX includes a range of tasks and decisions that patients and carers must carry out safely and confidently, such as monitoring for side effects, remembering doses, and—in the case of subcutaneous administration—managing injection technique³¹. These responsibilities can present challenges and lead to poor adherence if not adequately supported. Nurses play a central role in promoting self-efficacy by equipping patients and carers with the necessary knowledge and practical skills^{16,30,32,33}. Supporting self-management not only improves safety but also empowers patients to actively participate in their care, ultimately enhancing treatment outcomes^{29,34}.

It was also discussed the importance of signing patients up to patient associations, because most patients find this helpful and supportive²³, helping them to access peer support, share experiences, and gain practical strategies to manage their condition, in line with the EULAR recommendations for the implementation of self-management strategies¹³.

PtC4. Education about MTX should be tailored to the individual patient/carer needs.

Patients and carers vary in their health literacy, cultural background, emotional state, and disease experiences. Rheumatic diseases can also manifest differently in each individual and

may exhibit varying periods of activity. As a result, patients and carers have unique concerns related to both the condition and its treatment. A tailored educational approach allows healthcare professionals to address their most relevant concerns, improve understanding, and enhance self-efficacy³⁵. Results from our European survey showed significant differences in educational priorities among patients/carers, nurses and Rheumatologists¹⁷. While all groups valued information about side effects and their management, nurses emphasized administration techniques, rheumatologists prioritized discussing treatment rationale and family planning, and patients gave less importance to the latter¹⁷. These differences underline the need to adapt the content and timing of MTX education to the individual's context, preferences, and level of understanding.

PtC5. Education on MTX for patients and carers can be delivered through face-to-face or online interactions, supplemented where necessary by telephone consultations, written or online resources.

Educational delivery should adapt to the individual's preferences, needs, and circumstances³⁶. This may involve one-on-one or group sessions, conducted either in person or virtually, and complemented by telephone consultations, printed materials, or digital resources. Face-to-face formats allow for personalized, interactive discussions, while online and telephone options enhance accessibility, particularly for those with mobility or geographic barriers, and are also handy for quick clarification^{37,38}. Supplementary written or online resources also provide opportunities for repeated access and self-paced learning¹⁰. This flexible, multimodal approach increases patient engagement, supports understanding, and respects each patient's preferred method of receiving information^{36,39}. According to the EULAR PtC for telehealth, virtual consultations could be used in cases of infection, adverse events or abnormal lab results, where temporal or permanent discontinuation of DMARDs is needed (PtC 4)⁴⁰. The same document refers that "Telehealth should be considered for non-pharmacological interventions including but not limited to disease education, advice on physical exercise, self-management strategies and psychological intervention" (PtC 7)⁴⁰. Pragmatic recommendations and guidance on telecare can be followed^{41,42}.

PtC6. Nurses should promote and support adherence to MTX by identifying and discussing potential barriers and facilitators.

Nurses are uniquely positioned to promote adherence through their ongoing, trusted relationships with patients¹⁶. Regular conversations can help uncover individual concerns or misunderstandings—such as fear of side effects, logistical barriers, or a lack of perceived

benefit—and also highlight facilitators, such as support networks or patient motivation⁴³. Using a structured approach, such as a checklist or a guided discussion tool, can help ensure that these factors are routinely explored and addressed⁴⁴. Examples of MTX-specific or more general checklists can be found in the appendices from the Royal College of Nursing²⁴ and Ritschl¹⁴, respectively. Very importantly, education should not focus solely on the transmission of information, but rather prioritize creating space for meaningful interaction and clarification of patients' doubts and barriers—elements that are often overlooked due to time constraints in clinical practice⁷. Even the language used during these interactions matters; for instance, referring to possible “symptoms” rather than “adverse events” can influence patients’ perceptions and improve the effectiveness of the education session⁴⁵.

Discussion

These points to consider represent the first European initiative specifically aimed at guiding nurses' educational role in supporting patients and carers prescribed MTX. Developed through a structured process, they reflect the perspectives of a multidisciplinary task force composed mainly of nurses, grounded in current evidence and stakeholder experience.

The OPs emphasize the importance of structured education at treatment initiation (OP1), its continuity throughout the treatment journey (OP2), and the need for nurse-specific training (OP3). These statements highlight a paradigm in which education is not limited to a single moment or professional role but rather embedded across the care continuum, delivered by a competent, informed team. However, problems remain regarding the training of nurses and patient access. For instance, the training received by UK nurses to educate patients on starting MTX is highly varied, influencing nurses' confidence and competencies^{7,46}. Findings from the international survey conducted by this taskforce¹⁷ indicated that only 48% of European nurses had received specific training to advise patients about MTX. Regarding patients' access to and follow-up, according to the same survey, only 28% of patients prescribed oral MTX received a nurse-dedicated consultation, which increased slightly to 42% for the subcutaneous form. The survey results also revealed that a single educational session remains the most common practice across Europe (71%). Nonetheless, in some settings, two or more sessions are provided. Regarding follow-up, only 20% of nurses reported systematically scheduling a second contact for all patients, while 42% do so selectively. These follow-ups are conducted either face-to-face or remotely, and approximately 90% of nurses offer patients support contact details—most commonly direct phone numbers for the nursing team (52%). Notably, there is considerable

variation in practice across different European regions and countries¹⁷, underscoring the need for harmonized guidance and system-level support.

The six PtCs provide operational guidance for clinical practice. They recognize key moments for educational delivery (PtC1), the importance of individualized and needs-based approaches (PtC2 and PtC4), and the role of nurses in enabling self-management and promoting adherence (PtC3 and PtC6). The emphasis on different educational formats (PtC5) reflects a pragmatic view that education must be flexible, accessible, and respectful of patient preferences and health literacy. The PtC encourages nurses to be mindful of their interactions with patients and carers, supporting the notion of 'Making Every Contact Count' (MECC), a well-established initiative in the NHS across England, Scotland, Wales and Northern Ireland. In MECC, all health and care professionals are encouraged to use every appropriate interaction with patients to help them make positive changes to their health and wellbeing, for example, by highlighting medication adherence⁴⁷.

Notably, and as expected, several PtCs are interlinked. For example, tailored education (PtC4) is inherently tied to needs-based models (PtC2) and supports both self-management (PtC3) and adherence (PtC6). The survey conducted during this initiative¹⁷ reinforced the need for such personalization: while all stakeholders valued safety information, significant variation existed in other priorities, underscoring that a one-size-fits-all model is inadequate.

While the evidence base for nurse-led education on MTX remains limited in some European countries, the task force addressed this by conducting a broader literature search and a robust survey of patients' and clinicians' experiences and perspectives across Europe. The Steering Group included experts with extensive experience in developing recommendations and influencing European policy, which contributed to the rigour of the process and provided strong leadership throughout the project. The inclusion of patient representatives and both adult and pediatric representatives ensured that the recommendations are grounded in real-world experiences and priorities of diverse groups. Despite these strengths, some limitations should be acknowledged. These PtC were developed within a European framework, which may limit their relevance to countries with different regulatory, educational, or healthcare delivery structures. Some educational principles may overlap with existing European or national guidance for broader inflammatory arthritis care. Additionally, focusing exclusively on MTX, although methodologically pragmatic and clinically justified, could also apply to other DMARDs. Nonetheless, this narrowed scope allowed for a more coherent and feasible process. Strategically, we believe that establishing robust educational standards for MTX could have a ripple effect, paving the way for broader improvements in patient education for other DMARDs.

These PtCs are intended as a reference to support local implementation strategies, training initiatives, and future research. As clinical contexts, legislation, and scopes of practice vary across Europe, their adaptation should involve national professional bodies and patient organizations. Given the evolving evidence on the safe use of MTX, it is essential that nurses remain up to date with clinical guidance and support patients accordingly. For instance, in the context of vaccination against influenza or COVID-19, short-term pausing of MTX (1–2 weeks) is increasingly considered as a strategy to improve immunogenicity, particularly in older adults. However, such decisions should always be individualized, weighing infection prevention against disease control^{48,49}.

The use of structured tools—such as educational checklists, the ENAT, or eLearning modules—may support consistency and quality in implementation. For example, previous guidance on MTX, such as the UK Royal College of Nursing ‘Administering Subcutaneous Methotrexate for Inflammatory Arthritis’²⁴ includes a useful checklist for home administration, listing 15 skills to be demonstrated by patients or carers. Likewise, a Spanish position statement for primary care nurses provides concise recommendations on MTX preparation, administration, disposal and management of extravasation, which can also support patient and carer education⁵⁰. This initiative applied a modified version of the EULAR SOPs, with adaptations that may inform future consensus processes. These included a nomination of (most of) taskforce members by national associations (based on predefined criteria), a pre-meeting survey, early co-definition of scoping review questions by all task force members, three online meetings instead of two face-to-face, and the inclusion of three patient research partners. While these changes enhanced inclusiveness and feasibility, they also reduced informal interactions and increased reliance on digital communication. Nonetheless, this participatory and digitally enabled model offers a viable alternative for initiatives facing resource or geographical constraints.

Future studies should evaluate the impact of these recommendations on patient outcomes and care processes, ideally through collaborative implementation research. Meanwhile, this work provides a foundation for improving the educational role of nurses and advancing shared decision-making in MTX care.

Conclusion

A set of Points to Consider has been developed to guide nurses in delivering education and support on methotrexate use for patients with IRDs and their careers. These orientations aim to optimize treatment efficacy, minimize side effects, and enhance adherence. Implementation across Europe is planned, acknowledging regional variations in health care system provision and

underlying infrastructure, reinforcing the importance of collaborative, multi-professional rheumatology care.

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Polytechnic of Coimbra (116_CEIPC/2022_IPC registry).

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Tables and Figures

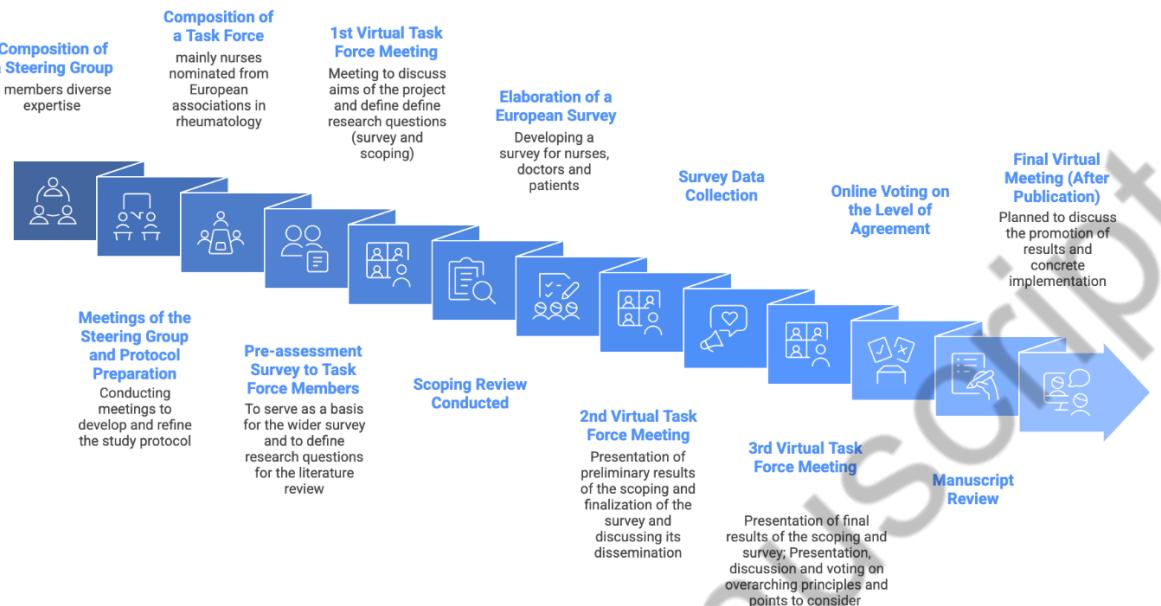
Table I. Points-to-consider for the nursing education of patients/carers taking methotrexate.

#	Overarching Principles	Level of Evidence ^a	Strength of recommendation ^b	Agreement (1-10) ^c	
				Mean (SD)	% ≥8
1	All patients prescribed MTX and their carers should receive treatment-specific education.	--	--	9.4 (1.5)	94
2	Education for patients prescribed MTX needs to be ongoing and requires continuous review by the rheumatology team.	--	--	9.5 (1.1.)	94
3	Nurses should have access to training regarding methotrexate treatment and stay up to date through continuous education	--	--	9.5 (0.9)	94
	Points to Consider				
1	Patients prescribed MTX and their carers should be offered education by a nurse when starting treatment, changing the route and when required by the patient.	3	C-D	9.7 (0.6)	100
2	Patients prescribed MTX should have access to a nurse for needs-based education to improve treatment knowledge#, enhance satisfaction with care and quality of life*	#3 *4	#C *D	9.8 (0.5)	100
3	Nurses should support patients and carers with relevant self-management skills related to MTX treatment, to ensure safety and improve self-efficacy.	3	C	9.8 (0.4)	100
4	Education about MTX should be tailored to the individual patient/carer needs.	3	C	9.7 (0.7)	100
5	Education on MTX for patients and carers can be delivered through face-to-face or online interactions, supplemented where necessary by telephone consultations, written or online resources.	3	C	9.4 (1.7)	94
6	Nurses should promote and support adherence to MTX by identifying and discussing potential barriers and facilitators.	3	C	9.7 (0.6)	100

a. *Level of Evidence* refers to the quality and reliability of the supporting evidence, graded according to the Oxford Centre for Evidence-Based Medicine (CEBM) system, ranging from high (e.g. randomized controlled trials, Level 1) to low (e.g. expert opinion, Level 5). b. *Strength of Recommendation* reflects the degree of agreement among experts and the balance between benefits and harms, ranging from strong (A) to weak (D) recommendations.

c. Agreement scores from the final voting round (by email).

Figure 1 - Stepwise Process Followed to Develop the Points to Consider



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