




**European
Reference
Network**

for rare or low prevalence
complex diseases

 **Network**
Genetic Tumour Risk
Syndromes (ERN GENTURIS)



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ERN GENTURIS

European Reference Network on GENetic
TUmour Risk Syndromes

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Contents

1. Introduction.....	3
2. Overview of guideline development process.....	4
3. Guideline development.....	5
Stage I Preparation.....	5
Stage II. Research	8
Stage III. Writing.....	12
Stage IV. Implementation.....	14
4. Supporting Methodology	16
4.1 AGREE II – Guideline Appraisal.....	16
4.2 GRADE – Evidence appraisal	17
5. Governance	18
6. Patient Involvement.....	21
7. Declaration and management of interests	22
Appendix 1: AGREE II – Guideline Appraisal Tool	23
Appendix 2: Guideline Document Template.....	24
Appendix 3: Project Milestones & Deliverables.....	25

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1. INTRODUCTION

The European Reference Network for Genetic Tumour Risk Syndromes (ERN GENTURIS) is committed to driving improvements in diagnosis, care and treatment for patients with a high hereditary risk of developing benign or malignant tumours. The Network proposes the clinical area and the rare genturis syndrome where a guideline should be developed.

Clinical Guidelines are statements, based on systematically evaluated evidence, for a specified clinical circumstance to support decision making.

Clinical Guidelines are not:

- Policies – these are positions adopted by organisations that must be adhered to
- Protocols – these specify exactly who does what, when and how in a defined situation
- Pathways – these are outlines of anticipated care typically incorporating multiple guidelines and cover all aspects of multi-disciplinary care for a defined portion or timeframe of a patient’s journey

The benefits of guidelines are only as good as the quality of the guidelines themselves. Appropriate methodologies and rigorous strategies used in the guideline development process are key for the successful implementation of the resulting recommendations.

ERN GENTURIS Task Force 3 together with Matt Bolz-Johnson and Tom Kenny developed this Network’s Policy for New Guideline Development based on internationally recognised methodology for guideline development (Grading of Recommendations Assessment, Development and Evaluation (GRADE)), although adapted to be applicable to rare diseases as well: the ‘enhanced-GRADE approach’ (more information: [Bolz-Johnson M, Kenny T, Gaasterland C, Omar MI, Engels M, van Eeghen A, et al. Evidence evaluation in rare disease guidelines: a methodological perspective. Rare Dis Orph Drug J. 2025;4\(4\)](#)). The guideline process underpinning this Network policy is structured into 4 core components: Preparation, Research, Writing and Implementation. The successful adoption of new clinical guidelines relies upon the value each component adds to the completed Clinical Guidelines.

The Network also has a separate policy for the endorsement of existing guidelines.

2. OVERVIEW OF GUIDELINE DEVELOPMENT PROCESS

Stage(s)	Step(s)
I. Preparation	1. ERN GENTURIS selects guideline topic area
	2. Set-up Project Governance
	3. Project planning and infrastructure
	4. Identify topics in the guideline
II. Research	5. Specify the topic - Key questions formulation
	6. Evidence retrieval and review
	7. Evidence quality assessment
	8. Draft recommendations
	9. Consensus building
III. Writing	10. Write guideline, finalise recommendations and editing
	11. Assessment against AGREE II criteria, final review
	12. ERN GENTURIS approval
IV. Implementation	13. Layout, proof reading and publishing
	14. Dissemination
	15. Updating

3. GUIDELINE DEVELOPMENT

Stage I Preparation

Table 1: Overview of steps and project actions in the preparation stage (stage I)

No.	Step	Actions
1	Prioritisation	<ul style="list-style-type: none"> Network selects guideline topic (disease), and Executive Committee Plus agrees on the priority areas
2	Set-up Project Governance	<ul style="list-style-type: none"> Appoint Project Lead and Core Working Group; note conflicts of interest
		<ul style="list-style-type: none"> Monthly Core Working Group meetings scheduled
		<ul style="list-style-type: none"> Establish Guideline Group, including a Patient Advisory Group, by identifying and inviting the experts and patient representatives, schedule meetings if necessary; note conflicts of interests
3	Project Planning & Infrastructure	<ul style="list-style-type: none"> Project Plan drafted
4	Identify the topics	<ul style="list-style-type: none"> The Core Working Group has to draft the scope of the clinical guideline and identify key area of expertise that is included in the scope of the guideline

Step 1. Prioritisation of Guideline Topic

The Network proposes the clinical area and the rare genturis syndrome where a guideline should be developed. The Executive Committee Plus makes the final decision on which guidelines are prioritised for developing.

Step 2. Set up project governance: Convene the Core Working Group and identify the key stakeholder groups, convene the Guideline Group, including the Patient Advisory Group

The GENTURIS network will receive an invite to indicate their interest to participate in the Guideline Group. The ERN GENTURIS Network Board or the relevant Thematic Group may suggest the experts for the Core Working Group which should consist of approximately 3 to 8 people, of which representatives from at least 2 ERN GENTURIS HCPs from at least 2 Member States with expertise in the ERN GENTURIS thematic group to which the genturis disease belongs¹. If possible, a patient representative should be included in the Core Working Group as well. All involved should disclose any possible conflict of interests.

The development of a clinical guideline is a project, and it will need a lead (chair) to be responsible for delivering the final guideline, ensuring to undertake the Research, Writing and Implementation components of the guideline development. The leader should be a

¹ The HCP is recognised as an expert in Thematic Group following an application and assessment process, which includes proof of national endorsement as an expert centre as well as national endorsement for the application, a positive assessment by the ERN Board, and validation of the positive assessment by the ERN Board of Member States.

representative from an ERN GENTURIS Full Member or Affiliated Partner (ERN GENTURIS HCP).

The Core Working Group will identify the key stakeholder groups and get representatives of all relevant groups to participate in the Guideline Group. To determine who needs to be involved in the development of the guidelines it is useful to:

- Identify experts and multi-disciplinary specialists working in the field associated with the guideline topic and scope.
- Establish who will use the guideline within the multidisciplinary healthcare team.
- Identify the applicable patient group(s) with the aim to include at least one or two patient representative(s), if possible. A Patient Advisory Group of patient representatives will be established.
- Identify and involve key stakeholders that represent these various interest groups to ensure the relevance of the guideline.

The Guideline Group should include representation from 4-5 Member States, of which a minimum of 3 HCPs of ERN GENTURIS with expertise in the ERN GENTURIS thematic group to which the genturis disease belongs¹. The Patient Advisory Board should be included.

Specific criteria for membership to the Guideline Group include:

- established record of involvement in specialist clinical practice in the genturis on which the guideline will focus;
- commitment to engage with ERN GENTURIS, and to respond to requests in a timely manner;
- good communicator with command of written and oral English;
- ability to attend real or virtual meetings.

The Patient Advisory Group will advise on the scope, target population, clinical questions to the guideline, the aims to address, and will rate the outcomes in terms of their importance. The Patient Advisory Group will also undertake a patient centred literature review or survey the patient community where there are gaps in evidence, ensuring the views on the balance of benefit and harm of the recommendations is considered by the Guideline Group. The Patient Advisory Group will also develop a lay persons guide or information of the guideline.

Step 3. Project planning and infrastructure

One of the ERN GENTURIS project managers will oversee the administrative set up of the project, to ensure smooth development, documentation and central storage of evidence to support the clinical guideline.

The team, particularly those involved in direct research and content development should have access to the software and applications needed to conduct research.

The project manager is responsible for providing access to documents, relevant tools and templates, and for setting out the timeline for the project.

The process for developing guidelines detailed in this policy is based on the principles of Appraisal of Guidelines for Research & Evaluation (AGREE II, detailed in section 4 of this policy) and Grading of Recommendations Assessment, Development and Evaluation (GRADE, detailed in section 4 of this policy) to ensure the quality of the guidelines, but is tailored for rare disease guidelines, using an “enhanced GRADE’ approach to mitigate the challenges associated with rare disease research ([Bolz-Johnson M, Kenny T, Gaasterland C, Omar MI, Engels M, van Eeghen A, et al. Evidence evaluation in rare disease guidelines: a methodological perspective. Rare Dis Orph Drug J. 2025;4\(4\)](#)). This approach includes a comprehensive literature search with expert opinion (from clinicians with expertise in the guideline topic as well as patient representatives; described in step 7-9), to ensure that guidelines are both evidence-based and clinically relevant to the complex needs of rare disease populations.

Step 4. Identify the Topic(s)

Once the Core Working Group has been established, we will begin with defining the guideline topic of the clinical guideline.

Clinical care is often multidisciplinary. All disciplines from the multidisciplinary team should be involved in the Guideline Group to assure correct addressment of each guideline topic with the overall aim to provide the best recommendations for patient’s care.

During this stage, we plan to agree and clarify over the aim and scope of the clinical guideline that should be agreed by the Core Working Group.

Stage II. Research

Table 2: Overview of steps and project actions in the research stage (stage II)

No.	Step	Actions
5	Specify the topic	• Specify the guideline topic
		• Guideline Group, including Patient Advisory Group to provide feedback on guideline scope
		• Final Scope and Clinical questions after incorporation of feedback
6	Evidence retrieval and review	• Conduct an objective search of important and relevant databases and search engines for relevant literature.
		• Start review
		• Complete master table of publications
7	Evidence quality assessment	• Grade and record the evidence. Create a spreadsheet to record the key search terms and the evidence using the ERN GENTURIS grading of recommendations.
8	Draft Recommendations	• Write draft recommendations based on the literature review
9	Consensus building	• Complete a modified Delphi process

Research forms a large part of developing clinical guidelines and can be carried out by different people whose skills vary. The research stages can be carried out in parallel, but it is **important to record how decisions were made, who was consulted and what their responses were.**

The Core Working Group should be supported by a methodologist lead to ensure the literature review is conducted to a high-quality level. The methodologist will be assigned by the Network Coordinator's management team.

Step 5. Specify the topic

The guideline topic that was identified and selected, now needs to be expanded into a detailed guideline scope, based on detailed clinical questions.

The Core Working Group will conduct an engagement exercise on the draft guideline scope with the Guideline Group, including the PAG. The guideline scope is revised based on feedback from the wider stakeholders' comments and feedback.

Step 6. Evidence retrieval and review

The Core Working Group supported by a methodologist will use the guideline scope to design the literature review search strategy. In rare disease research, it is common for authors to consolidate multiple stages of the diagnostic and therapeutic process within a single publication, unlike studies on more prevalent conditions, which typically focus on specific interventions. Consequently, the keywords utilized for literature searches in rare diseases need not be as narrowly defined as those employed for common diseases. This broader scope reflects the nature of rare disease guidelines, which often encompass an integrated continuum of diagnosis, care, and treatment.

When searches are conducted using individual PICO components or are narrowly focused on specific topics within rare disease guidelines, they frequently yield minimal or no evidence. To address this limitation, an emerging strategy involves conducting broader searches using only the disease term itself. This approach increases the number of retrieved articles and mitigates the risk of omitting pertinent evidence due to excessively restrictive search criteria. All publications will be collected (for example in Endnote). Papers considered in each topic for the recommendations will be assessed (step 7) and should be structured accordingly.

Step 7. Evidence quality assessment

The quantification of strength for a recommendation involves careful consideration of harms and benefits. As a general note for these recommendations, the harms that a recommendation seeks to address are often clear, but the benefits of a specific recommendation may not be as clear.

As the volume of peer-reviewed evidence for rare diseases is typically limited due to the small population sizes, and it is unlikely that the evidence will ever reach a fraction of that for a more common disease, it creates a difficulty when considering the grading of the strength of evidence using GRADE – please see chapter 4.

As is typical for many rare diseases, the volume of peer-reviewed evidence available for consideration for ERN GENTURIS guidelines is generally small and articles are typically based on small samples or series. If the evidence is categorised and then graded using standard approaches, that are designed to differentiate evidence, in circumstances when there are large numbers of papers and there are likely to be more trials with larger cohorts, then all knowledge of rare diseases would be assessed as low-grade evidence. This is not an accurate reflection of the combination of the experts' experience and clinical consensus with the available evidence. This is further compounded as there is a low likelihood of additional volumes of evidence that could change the recommendations.

For this reason, and to **balance the weight of both published evidence and quantify the wealth of expert experience and knowledge**, ERN GENTURIS have agreed to use the follow scale to grade the recommendation:

Strength	Grading of Recommendation
Strong	Expert consensus AND consistent evidence
Moderate	Expert consensus WITH inconsistent evidence AND/OR new evidence likely to support the recommendation
Weak	Expert majority decision WITHOUT consistent evidence

Expert consensus (an opinion or position reached by a group as whole) or expert majority decision (an opinion or position reached by the majority of the group) is established after reviewing the results of the modified Delphi approach (step 9) within the Core Working Group.

To summarise, for our grading of the recommendations, we assess all available evidence, comprising not only the published observational studies, but also the real-world evidence based on experience of clinical experts and patients. The guideline group assesses all these sources of evidence and quantifies if the evidence points in the same direction (consistent) or not (inconsistent). The guideline group then decides to issue strong or conditional draft recommendations. These draft recommendations are then graded in a modified Delphi survey to reach structured expert consensus, including active engagement of affected individuals and patient representatives, specifically balancing the desirable and undesirable consequences of surveillance and alternative care strategies, quality of evidence, and values and preferences held by the patient representatives.

The findings of the literature review will be organised against the clinical questions and outcomes and the evidence graded regarding consistency. This should be added to the master table.

Step 8. Writing Draft Recommendations

Literature was reviewed along with expert opinion to draft recommendations based on literature and experts' experiences and knowledge. Recommendations should be consistent across ERN GENTURIS guidelines, mainly using one of the following four stylistic formats: Should, Should Probably, Should Probably Not, Should Not

Should & Should Not, were taken to mean - most well-informed people (those who have considered the evidence) would take this action

Should Probably & Should Probably Not, were taken to mean - the majority of informed people would take this action, but a substantial minority would not

In day-to-day practice, clinicians will not have the time to explore the evidence as thoroughly as a guideline group, nor devote as much thought to the trade-offs, or the possible underlying values and preferences in the population. To ensure clinicians have a complete overview, the core working group has made recommendations even when confidence in effect estimate is low and/or when desirable and undesirable consequences are closely balanced.

Step 9. Consensus building

Where there is limited or low-quality evidence, recommendations should be developed based on expert opinion and consensus, based on methodology that safeguards against bias. Consensus building must be undertaken in a structured, transparent and planned way – drawing on the expertise of multiple experts and patient representatives. The consensus exercise should be carried out after a literature review has been conducted and in areas where there is low quality evidence or inconsistent evidence.

Consensus building can be a lengthy process and should be structured using a modified Delphi methodology. In principle, two to three rounds of survey (online) will be organized followed by a workshop if necessary. Each survey round involves all relevant multidisciplinary experts and patients and is based on predefined draft recommendations (based on the literature review findings). Each Delphi participant should rate the statements based on a 4-point Likert scale from totally disagree to totally agree and is able to fill out their comments and remarks in a text box.

Subsequent survey rounds include the overall score of each statement from the previous round and changes to the recommendations should be indicated.

The strength of this approach that its anonymously without the influence of authoritative voices or dominant personalities, as well as allowing a controlled way for the overall opinions of the group seen and considered for each individual to consider their original opinion.

A threshold for consensus should be defined by the Core Working Group before the survey is launched e.g.: >60% of participants 'strongly agree' with the statement. The results of each round are shared with all participants. If no consensus is reached a consensus meeting will be organized to enable participants to check the accuracy of the results, query and discuss any significant areas of variation, re-vote in areas where there is no consensus and to ratify the final statements.

The final grading of the recommendations is established by the Core Working Group after reviewing the results of the modified Delphi approach.

Stage III. Writing

Table 3: Overview of steps and project actions in the writing stage (stage III)

No.	Step	Actions
10	Writing Guideline	• 1st draft of the full guideline
		• Guideline Group reviews 1st draft
11	Review	• Complete assessment of guideline against AGREE II criteria
		• Final version (plus lay-persons' version) to Guideline Group
12	Approval	• Approval of the guideline by ERN GENTURIS Network Board

Step 10. Writing Guideline, finalise recommendations and editing

During the modified Delphi approach, draft recommendations will be adapted and should be finalised after the modified Delphi approach has finished.

The guideline should be presented well and using accessible user-focused language for unambiguous recommendations. The ERN GENTURIS template should be used to write the guideline. The guidelines should be developed in three formats: a pocket guide, an 'concise version', which can be published in a Journal and a Full Guideline Report with supporting evidence in the appendixes – please see Appendix 2. Members of the Guideline Group will be co-authors of the guideline, in which the Core Working Group will occupy first and last authorships. European Reference Network for Genetic Tumour Risk Syndromes will be added in the title, and in the acknowledgement of the journal publication. If possible, the phrase "on behalf of European Reference Network for Genetic Tumour Risk Syndromes" will be added to the author list or affiliations to ERN GENTURIS will be added.

It would be also important to list all sources of evidence used from the research.

The guideline should be comprehensive and concise and only what is essential is kept in the guideline to ensure it is complete. All extra supporting documentation should form a separate resource pack (appendix) and can include links to external materials, reference list (this can be taken from the research phase), tables and charts.

When writing the guideline, keep the intended audience in mind and refer back to stakeholder co-design process to ensure recommendations are accurately communicated.

Terminology used is not interchangeable. The content may be used by people from different disciplines so consistent use of terminology, phrases make it easier to follow. Avoid generating and using abbreviations. Where there is the possibility for doubt produce an accompanying glossary.

Step 11. Review

The Core Working Group will complete an internal assessment of the quality of the guideline against AGREE II criteria – please see Appendix 1. This assessment will provide assurance on the quality and independence of the guideline.

Following internal review, the Core Working Group will actively involve external experts from different specialty areas and patient groups, relevant to the scope of the guideline (Guideline Group), to review the initial recommendations and first and final draft of the guideline.

The Core Working Group will review the existing ERN GENTURIS care pathway and patient journey or will draft a new care pathway and patient journey based on the results of the developed guideline if possible.

In addition, the Core Working Group will engage with the European Journal of Human Genetics and European Society of Human Genetics (or other journals and societies that are appropriate for the guideline topic) to review the guideline and consideration for publication.

Step 12. ERN GENTURIS Approval

The final version of the guideline will be approved by the ERN GENTURIS Network Board and circulated to all ERN GENTURIS members.

Stage IV. Implementation

Stage 4. Project Actions:

Table 4: Overview of steps and project actions in the implementation stage (stage IV)

Task No.	Task	Actions
13	Publishing Guideline	• The ERN GENTURIS guideline will be published on the website of ERN GENTURIS
		• Draft and submit concise version to journal, for example European Journal of Human Genetics
		• Develop and circulate pocket guide
14	Communication & Launch	• Draft Communication Plan
		• Guideline Group should promote the guideline on conferences, (virtual) meetings, and workshops
15	Updating	• Collect new evidence annually; for consideration for updating thereafter

The research and writing have been completed, and the final component is to implement the clinical guidelines. Careful planning for implementation leads to better uptake and use of the guideline. Uptake of guidelines, no matter how robust the evidence is, requires careful management of expectations.

Step 14. Publishing Guideline

The ERN GENTURIS guideline will be published on the website of ERN GENTURIS. Members of the Guideline Group will be co-authors of the guideline, in which the Core Working Group will occupy first and last authorships.

A concise version will be submitted to the European Journal of Human Genetics or similar journal for publication. European Reference Network for Genetic Tumour Risk Syndromes will be added in the title, and in the acknowledgement of the journal publication. If possible, the phrase “on behalf of European Reference Network for Genetic Tumour Risk Syndromes” will be added to the author list or affiliations to ERN GENTURIS will be added.

A Pocket Guide of the guideline will also be developed and circulated to the ERN GENTURIS members.

Step 15. Communication & Launch (disseminating)

ERN GENTURIS will publish the guideline as well as the related documents on its website and will disseminate the guideline, for example using the newsletter and LinkedIn. If relevant, professional societies will be notified of the published guideline as well. The Guideline Group should promote the guideline developed by ERN GENTURIS on conferences, (virtual) meetings and workshops thereby promoting high quality patient care and engagement as well as dissemination in their country.

Step 15. Updating

The Guideline Group, in particular the Core Working Group, will collect any new evidence that has been published on annual basis and consider the guideline for updating thereafter.

4. SUPPORTING METHODOLOGY

4.1 AGREE II – Guideline Appraisal

Appraisal of **Guidelines for REsearch and Evaluation (AGREE II)** is the chosen methodology to assess the quality of a guideline through assessing the rigor and transparency of the process for development the Networks guidelines. The benefits of guidelines are only as good as the quality of the guidelines themselves, and the quality of many published guidelines can significantly varies.

The AGREE II instrument was originally developed to assess the quality of clinical practice guidelines retrospectively, however this approach also provides a robust methodology to guide the development of guidelines. The AGREE II checklist is structured under 23 items and grouped under the following 6 domains:

- D1 Scope and Purpose is concerned with the overall aim of the guideline, the specific health questions, and the target population (items 1-3).
- D2 Stakeholder Involvement focuses on the extent to which the guideline was developed by the appropriate stakeholders and represents the views of its intended users (items 4-6). Who was involved in creating the guideline(s).
- D3 Rigour of Development relates to the process used to gather and synthesize the evidence, the methods to formulate the recommendations, and to update them (items 7-14). The approach serves to search the literature and use the evidence in order to create recommendations.
- D4 Clarity of Presentation deals with the language, structure, and format of the guideline (items 15-17). The suitability and usefulness to the intended audience
- D5 Applicability pertains to the likely barriers and facilitators to implementation, strategies to improve uptake, and resource implications of applying the guideline (items 18-21). Realistic consideration of the effort needed to use the guideline in clinical services
- D6 Editorial Independence is concerned with the formulation of recommendations not being unduly biased with competing interests (items 22-23). Honest, transparent declaration of factors outside the evidence that may have influence the nature of strength of the recommendation.

The overall assessment includes the rating of the quality of the guideline(s) and whether the guideline(s) would be recommended for use in practice.

ERN GENTURIS has added two additional questions to rate: Is the guideline up to date (yes/no) and are the recommendations applicable to European healthcare setting (yes/no).

The Core Working Group will complete an internal assessment of the quality of the guideline against AGREE II criteria. This assessment will provide assurance on the quality and independence of the guideline.

4.2 GRADE – Evidence appraisal

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group developed a methodology for quality assessment of evidence, through a common and transparent approach, that can be applied to all evidence used to support the strength of recommendation used in guidelines. The final quality assessment, which applies to the body of evidence is classified one of four possible levels: high, moderate, low, or very low – depending on the type and size of study - high quality and that non-randomised (observational) studies start out as low quality.

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system identified its five categories; risk of bias, imprecision, inconsistency, indirectness, and publication bias.

5 Questions to help identify important strength of evidence categories.

1. Imprecision - How many studies were pooled to get this estimate; how many patients did they include?
2. Risk of bias - Were they randomized controlled trials? Did the studies have important limitations?
3. publication bias - Is there evidence that more studies of this treatment were conducted?
4. Inconsistency - Did the trials have similar or widely varying results?
5. Indirectness - Was the outcome measured at an appropriate time, or were the studies too short in duration to have much relevance? (see Appendix I for scoring approach)

These categories help to determine the degree to which you can trust that results reported in the literature are likely to be those you will see if you were to use the interventions for ‘real’ patients. **However, GRADE is not appropriate for making guidelines recommendations when there is no evidence, conflicting evidence, or very low-quality evidence, and consensus statements are more appropriate in these scenarios.**

Due to many of the genetic tumour risk syndromes being very low prevalence and therefore has a limited published evidence base, the Network developed its own grading system which considers the consistency of the published evidence, expected new evidence and **also**, uses a modified Delphi approach to quantify the experience, expertise and knowledge of the Networks Members to also be used to define guideline recommendations. More information on the need for a tailored methodology for rare diseases and the enhance-GRADE approach is described in: [Bolz-Johnson M, Kenny T, Gaasterland C, Omar MI, Engels M, van Eeghen A, et al. Evidence evaluation in rare disease guidelines: a methodological perspective. Rare Dis Orph Drug J. 2025;4\(4\).](#)

5. GOVERNANCE

ERN GENTURIS will decide on the topic of the next guideline and suggest members of the Core Working Group. The Core Working Group is a group of experts who have profound expertise in this area and (if possible) experience in guideline development. The Core Working Group will be the operational arm of the Guideline Group to drive the development of the guideline. The Core Working Group will appoint a leader for the guideline who will be the Chair of the Core Working Group as well as of the Guideline Group. The Guideline Group of expertise is established to oversee and advise on the development of each specific guideline. The Core Working Group will suggest internal and external experts and patient representatives to join the [disease name] Guideline Group.

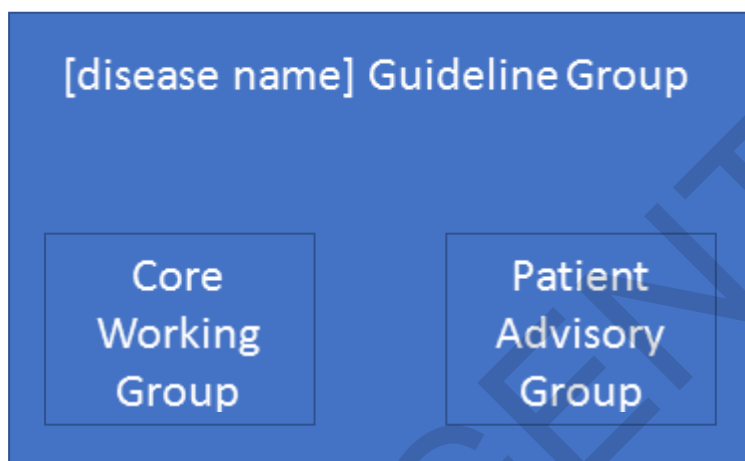


Figure A: Schematic representation of the Guideline Group. The Guideline Group consists of internal and external experts of the disease, including patient representatives. The Core Working Group is firstly established and the operational arm of the Guideline Group. They will suggest other members of the Guideline Group, including patient representatives that will form a subgroup: the Patient Advisory Group.

Core Working Group

The Core Working Group is established first but will be one of the subgroups of the Guideline Group. The Core Working Group will be the operational arm of the Guideline Group and will engage with the Guideline Group for advice on the scope of the guideline, research carried out and in writing the guidelines and recommendations.

The GENTURIS network will receive an invite to indicate their interest to participate in the Guideline Group. The ERN GENTURIS Network Board or the relevant Thematic Group may suggest the experts who will form the Core Working Group and who will lead on the research and writing of the guideline. The Core Working Group should consist of approximately 3 to 8 people, of which representatives from at least 2 ERN GENTURIS HCPs from at least 2 Member States with expertise in the ERN GENTURIS thematic group to which the genturis disease belongs¹. If possible, a patient representative should be included in the Core Working Group as well. The leader should be a representative from a ERN GENTURIS HCP.

The Core Working Group will engage with, either virtually or face to face, to secure consensus for recommendations.

Guideline Group

The Guideline Group will be formed of experts who are respected in their field of expertise for each specialty and will be selected based on the guideline scope and on the following considerations:

- Consideration on which countries have a recognised guideline and consideration of which experts are experienced in writing guidelines;
- Experts from ERN GENTURIS, preferably with experience in writing guidelines;
- Experts from other ERNs where there is any overlap in scope;
- External people from Europe, who should be endorsed by a professional society;
- External people from outside Europe if necessary, and only if expertise cannot be found in Europe;
- Representative of relevant professional societies should be involved.

The Guideline Group(s) will consist of representatives from:

- Minimum representation from 4-5 Member States, of which a minimum of 3 HCPs of ERN GENTURIS with expertise in the ERN GENTURIS thematic group to which the genturis disease belongs¹.
- Minimum of two patient representatives with experience of or representing the clinical areas of the guideline, if possible; and linking back to the wider patient community when required.

The membership of the Guideline Group shall be determined by the Core Working Group based on the recommendations of the Chair – taking account of appropriate diversity and representation necessary to deliver the Guideline Group's remit.

Specific criteria for membership to the Guideline Group shall normally include:

- Established record of involvement in specialist clinical practice in genetic tumours;
- Commitment to engage with ERN GENTURIS and the Guideline Group, and to respond to requests in a timely manner;
- Good communicator with command of written and oral English;
- Ability to attend real or virtual meetings of the Guideline Group.

Members of the Guideline Group will be co-authors of the guideline, in which the Core Working Group will occupy first and last authorships.

Tasks

The Guideline Group is to:

- Oversee the writing of and the publication of the guideline and its recommendations;
- Provide specialist advice on new guideline scope – population, intervention, comparator and outcomes;
- Review and grade published and unpublished evidence, mainly performed by the Core Working Group;
- Secure consensus on recommendations and clinical opinion where there are gaps in published evidence through an evidence-based approach (e.g.: Delphi);
- Review patient and lay-person information and guidelines;
- Advise and communicate with wider stakeholders when agreed, maintaining links with national and European societies.
- Promote the guideline developed by ERN GENTURIS on conferences, (virtual) meetings and workshops and thereby promoting high quality patient care and engagement.

6. PATIENT INVOLVEMENT

Patient representatives can help to ensure that the guideline meets the needs of patients and ultimately improves the use of the guideline in healthcare services. Their input is important at each step in the guideline process, and it ensures the final guidelines answer the needs of patients.

Patient's insights are invaluable as they are 'experts living with the condition' and can provide insights from a different angle to clinicians. Patient representatives are the best people to say what outcomes are important when making decisions about health and to balance the different benefits and side effects from some treatments. Patient representatives can be involved to review the evidence and recommendations, which ultimately improve the relevance of the guidelines for respective patient population and improve implementation and use. Patients developing a patient-targeted version of the guidelines is effective in ensuring patients have access to treatment information.

ERN GENTURIS will enable meaningful patient involvement into guideline development through the establishment of a Patient Advisory Group of patient representatives that have experience in the clinical area of the guideline. The Patient Advisory Group will appoint a chair, preferably the member of the Core Working Group, who will be present as representative of the Patient Advisory Group in all Core Working Group meetings. The Patient Advisory Group will advise on the scope, target population, clinical questions to the guideline aims to address and rate the outcomes in terms of their importance.

The Patient Advisory Group will:

- Advise on what is important for them in the area the guideline will cover – this will be through advising on the clinical questions the guideline will address, also rating the importance of the outcomes expected from the new guideline.
- Review the evidence and the recommendations, undertaking a patient centred literature review or survey the patient community where there are gaps in evidence, ensuring their views on the balance of benefit and harm of the recommendations is considered by the Core Working Group.
- Review any gaps in the evidence that are discovered in the literature review and can help to fill in these gaps in evidence to recommend support that they feel they need at these points.
- Review the recommendations that are developed in the guideline, as patients are in the best place to balance the different benefits and side effects from some treatments.
- Provide practice advice that can be included either in the guideline or in separate supporting information that accompanies the guideline.

- Be supported by the Core Working Group in order to develop a lay persons guide or information of the guideline.
- If no ERN GENTURIS patient journey on the guideline topic (genturis-disease) exists yet, the Patient Advisory Group can initiate drafting such document.

7. DECLARATION AND MANAGEMENT OF INTERESTS

A conflict of interest occurs when a set of conditions in which professional judgement concerning a primary interest tends to be unduly influenced by a secondary interest. The declaration of a secondary interest does not automatically mean the presence of a conflict of interest that precludes participation in a Guideline Group or expert review group.

A 'conflict of interest' can be defined as any interest held by an expert that may affect or reasonably be perceived to affect the expert in their duties or providing advice to ERN GENTURIS. The conflict-of-interest rules are designed to avoid potentially compromising situations that could undermine or otherwise affect the work done by ERN GENTURIS.

All members of the Guideline Group, including the Core Working Group and patient representatives involved in the development of guidelines must declare if they have any potential conflict. All conflicts of interest – actual, potential or perceived – must be managed under the ERN governance procedure.

Declaration of any potential conflict must be made at the start of the project or establishment of the Guideline Group, Core Working Groups and Patient Advisory Group and reported at any stage, thereafter throughout the project.

Potential conflicts will be noted, recorded and assessed by the Guideline Group chair and project manager. Once an actual conflict of interest related to a specific activity has been evaluated, then the person must abstain from that specific activity.

APPENDIX 1: AGREE II – GUIDELINE APPRAISAL TOOL

Guideline Name:

	Item	AGREE II Rating						
		1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree
1.	The overall objective(s) of this guideline is (are) specifically described.							
2.	The health question(s) covered by the guideline is (are) specifically described.							
3.	The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.							
4.	The guideline development group includes individuals from all the relevant professional groups.							
5.	The views and preferences of the target population (patients, public, etc.) have been sought.							
6.	The target users of the guideline are clearly defined.							
7.	Systematic methods were used to search for evidence.							
8.	The criteria for selecting the evidence are clearly described.							
9.	The strengths and limitations of the body of evidence are clearly described.							
10.	The method for formulating the recommendations are clearly described.							
11.	The health benefits, side effects and risks have been considered in formulating the recommendations.							
12.	There is an explicit link between the recommendations and the supporting evidence.							
13.	The guideline has been externally reviewed by experts prior to its publication.							
14.	A procedure for updating the guideline is provided.							
15.	The recommendations are specific and unambiguous.							
16.	The different options for management of the condition or health issues are clearly presented.							
17.	Key recommendations are easily identifiable.							
18.	The guideline described facilitators and barriers to its application.							
19.	The guideline provides advice and/or tools on how the recommendations can be put into practice.							
20.	The potential resource implications of applying the recommendations have been considered.							
21.	The guideline presents monitoring and/or auditing criteria.							
22.	The views of the funding body have not influenced the content of the guideline.							
23.	Competing interests of guideline development group members have been recorded and address.							
	The guideline is up to date.							
	The recommendations are applicable to the European healthcare system.							
	Rate the overall quality of this guideline.	1 Lowest quality	2	3	4	5	6	7 Highest quality
	I would recommend this guideline for use.	No						Yes

Reviewer:

Date:

APPENDIX 2: GUIDELINE DOCUMENT TEMPLATE

The template documents will be provided by the project manager.

Version	Contents
Journal publication (Concise)	<ul style="list-style-type: none"> • Abstract • Introduction - Overall objectives of the guideline <ul style="list-style-type: none"> • Pathway module + target population & users of Guidelines • Health questions • Methods: Strengths and limitation of evidence • Clinical / Molecular aspects: Health benefits, side effects and risks • Care & Management: Clear Key Recommendations (include present different management options) • Conclusion • Publisher's notes
Pocket guide	<ul style="list-style-type: none"> • Title guideline • Statements on 'best available evidence' • Main recommendations / guideline summary
Full Guideline Report	<ul style="list-style-type: none"> • Abstract • Guideline summary • Introduction • Conflict of interests • Scope & Purpose - Overall objectives of the guideline: Health questions and target population, care setting and epidemiology and aetiology • Key Findings & Recommendations (incl. different management options) • Methodology • Summary of Evidence (may be moved to appendix) • Psychological needs • What do other guidelines state? • Suggestions for future research • Appendix: References, plain language summary, link with evidence and recommendations, disclosures, references etc.

APPENDIX 3: PROJECT MILESTONES & DELIVERABLES

Stage / step	Milestones / deliverables	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20	M21	M22	M23	M24
Step 2	Set up project governance	█	█	█	█																				
	monthly meetings				█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█	█
Step 4	Scope of the guideline defined by CWG Identify topics in the guideline				█																				
Step 5	Finalise guideline scope					█	█																		
Step 6	Evidence retrieval and review							█	█	█															
Step 7	Evidence quality assessment							█	█	█															
Step 8	1 st draft of recommendations										█	█													
Step 9	Consensus building																								
	Delphi round 1												█	█	█	█									
	Delphi round 2													█	█	█									
	Delphi round 3															█	█	█	█	█	█	█	█	█	█
Step 10	Write guidelines																		█	█	█	█	█	█	█
Step 11	Review																						█		
Step 12	ERN GENTURIS approval																							█	

M=Month

After ERN GENTURIS approval the guideline publication can be submitted to the selected journal. Depending on the peer review process this can take a couple of months. After acceptance the full guideline document and related documents will be published on the ERN GENTURIS website and disseminated in the network.