

## Criteria defined by the Network for Lymphoid malignancies

The following information defines the specific criteria for our proposal for a European Reference Network (ERN) for Rare Hematological Diseases, EuroBloodNet. Each health care provider willing to be member of our ERN has to fulfil these criteria. These evidence based criteria intend to be realistic while ensuring a high level patient care.

The following information corresponds to the following points in the HCP application form:

**1) Point 7\_Table in Page 6** Diseases, conditions and highly specialized interventions: it includes not only diseases but also highly specialized interventions, treatments eg bone marrow transplantation

**2) Point 11\_Table in Page 9** 10 of the 16 “Diseases, conditions and highly specialized interventions” defined in point 7 needs to be quantified

**3) Point 12\_Table in page 11 “Multidisciplinary team”** Up to 16 Health care professionals have to be defined: position, training and number of patients/procedures by year (for assure expertise)

**4) Point 13\_Table in page 12 “Specialised equipment, infrastructure and IT”** Up to 16 Specialised equipment, infrastructure and IT used by the HCP to support diagnosis, care and treatment

**5) Point 21\_Table in page 18 “Clinical outcome data”** Up to 22 relevant clinical outcomes related to the Rare or complex disease, condition or highly specialized interventions defined

- Subthematic area of expertise:
  - Rare red blood cell defects
  - Bone marrow (BM) failure and rare haematopoietic disorders
  - Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis
  - Rare bleeding-coagulation disorders
  - Myeloid malignancies
  - X Lymphoid malignancies**

**1) Point 7\_Table in Page 6** Diseases, conditions and highly specialized interventions: it includes not only diseases but also highly specialized interventions, treatments eg bone marrow transplantation

Subthematic area of expertise	Rare or complex disease, condition or highly specialized interventions	ICD / Orphanet Code
Lymphoid malignancies	Acute lymphoblastic leukemia (ALL)	ICD 10 D91.0/ORPHA 513
Lymphoid malignancies	Marginal zone lymphomas	ICD 10 C83.0 C88.4 / ORPHA 300912
Lymphoid malignancies	Light chain Amyloidosis (AL amyloidosis)	ORPHA 85443, ORPHA 314701, ORPHA 314709
Lymphoid malignancies	Targeted therapies for marginal zone lymphomas including tyrosine kinase and immune checkpoints inhibitors	
Lymphoid malignancies	Expert Diagnosis and classification of amyloidosis.	
Lymphoid malignancies	Interventional therapeutic service: chemotherapy, autologous SCT (allo SCT does not have to be in the center)	
Lymphoid malignancies	Acute care (management of neutropenic fever, of acute compression by lymphoma...)	
Lymphoid malignancies	Phase I/II studies open for inclusion for ALL	
Lymphoid malignancies	Phase II/III studies open for inclusion for amyloidosis	

**2) Point 11\_Table in Page 9**

**10 of the 16 “Diseases, conditions and highly specialized interventions” defined in point 7 needs to be quantified as follows**

Specific diseases, conditions and highly specialized interventions	Measure*	Evidence
Acute lymphoblastic leukemia (ALL)	Number of patients / year	15
Interventional therapeutic service: allo SCT	Number of procedures per year	10
Phase I/II studies open for inclusion for ALL	Number of procedures per year	2
Marginal zone lymphomas	Number of patients per year	30
Targeted therapies for marginal zone lymphomas including tyrosine kinase and immune checkpoints	Number of procedures per year	10-20

inhibitors		
Light chain amyloidosis	Number of new patients per year	5
Diagnosis and classification of amyloidosis	Number of procedures per year	10
Phase II/III studies open for inclusion on amyloidosis	Number of procedures per year	2

**3) Point 12\_Table in page 11 “Multidisciplinary team”** Up to 16 Health care professionals have to be defined: position, training and number of patients/procedures by year (for assure expertise)

Healthcare professional	Training and qualifications	Nº procedures/patients per year
Haematologist (at least 3)	Experience in lymphoid malignancies > 3 years	50
Pathologist	expertise in hematopathology > 3 years	50
Hemato-biologist	Expertise in flow cytometry > 3 years	50
Nurses	Expertise in hemato-oncology > 3 years	50
Radiologist	Expertise in lymphoid malignancies > 3 years	50
Nuclear medicine physician	Expertise in lymphoid malignancies > 3 years	50
Surgeon	Expertise in splenectomy > 3 years	10

**4) Point 13\_Table in page 12 “Specialised equipment, infrastructure and IT”** Specialised equipment, infrastructure and IT used by the HCP to support diagnosis, care and treatment

Specific diseases, conditions and highly specialized interventions	Specific equipment, infrastructure and information technology (IT)
<b>Acute lymphoblastic leukemia</b>	
Medical care organization	Access to radiotherapy facilities. JACIE accreditation for Allogeneic/Autologous stem cell transplants Availability of transfusion care 24 hours a day, seven days a week. Availability of an Intensive Care unit. Adequate facilities for immune-incompetent patients: separated rooms or ward, active infection prevention protocol with involvement of a hospital hygiene specialist. Availability of in-house consultants for neurology and pneumology. Intensive in-house support of medical-microbiologists with

	<p>experience in problems caused by disrupted immune response: weekly consultations with the physicians, able to perform weekly cultures for infection surveillance with results available within 72 hours.</p> <p>Multidisciplinary meetings between physicians and persons responsible for the execution and interpretation of diagnostic tests.</p>
Pharmacy	<p>In-house KNMP registered hospital pharmacist available. Pharmacy staff is aware of GCP requirements regarding study drug handling and drug accountability.</p> <p>Pharmacy has facilities to adequately store study drug: no unauthorized access, separate from regular medication, refrigerated with temperature log if necessary.</p> <p>Access to facilities for pharmacological assays (drug blood levels)</p> <p>Availability of pharmacy 24 hours a day, seven days a week for preparation and dispensing of medication.</p>
Diagnostic facilities	<p>Availability of in-house CKL accredited facilities for hematology and blood chemistry with the ability to provide test results within 24 hours.</p> <p>Access to facilities for cytogenetics and FISH, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 72 hours.</p> <p>Access to facilities for molecular biology (mutational analysis by NGS)</p> <p>Access to facilities for pathology, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 72 hours.</p> <p>Availability of in-house imaging facilities (x-ray and CT) for surveillance of infections and complications with the ability to provide imaging results and interpretation of those results within 24 hours.</p>
<b>Marginal zone lymphoma</b>	
Diagnostic facilities	<p>CT scan and 18-FDG PETscan</p> <p>Flow cytometry</p>
<b>Light chain Amyloidosis</b>	
Medical care organization	<p>Availability of an Intensive Care unit.</p> <p>Availability of in-house consultants for cardiology, nephrology and neurology.</p> <p>Multidisciplinary meetings between physicians and persons responsible for the execution and interpretation of diagnostic tests and treatment's decisions.</p> <p>Available guidelines for treatment of AL amyloidosis patients</p> <p>Physician expert in amyloidosis available by phone or mail to give advices to all particular cases of other centers in the reference center's network</p>
Pharmacy	<p>In-house KNMP registered hospital pharmacist available. Pharmacy staff is aware of GCP requirements regarding study drug handling and drug accountability.</p> <p>Pharmacy has facilities to adequately store study drug: no unauthorized access, separate from regular medication, refrigerated with temperature log if necessary.</p> <p>Access to facilities for pharmacological assays (drug blood levels)</p> <p>Availability of pharmacy 24 hours a day, seven days a week for</p>

	preparation and dispensing of medication.
Diagnostic facilities	<p>Availability of in-house CKL accredited facilities for hematology and blood chemistry with the ability to provide test results within 24 hours.</p> <p>Access to facilities for cytogenetics and FISH for characterization of plasma cell dyscrasias</p> <p>Access to facilities for pathology, participating in review rounds (all dubious samples reviewed) and with the ability to provide test results within one week</p> <p>Availability of in-house imaging facilities (echocardiography and MRI) diagnosis and evaluation of cardiac amyloidosis</p> <p>Expert Diagnosis and classification of amyloidosis. with:</p> <p>Morphology with Congo Red</p> <p>Immunohistochemistry and immunofluorescence for amyloidosis typing</p> <p>Immuno-electron microscopy or proteomic if necessary.</p> <p>Immunology laboratory expert in characterization of monoclonal gammopathies able to practice:</p> <p>Serum and urine Immunofixation</p> <p>serum Free Light chain assays with both available tests (Freelite and N-Latex)</p>

**5) Point 21\_ Table in page 18 “Clinical outcome data”**

Rare or complex disease, condition or highly specialized interventions	Clinical outcome	Evidence (per year)
Marginal zone lymphoma	<p>Mortality rate</p> <p>Survival free of disease</p> <p>Quality of life under treatment and after treatment</p> <p>Specific tolerance of treatment for elderly patients</p> <p>Secondary malignancies</p> <p>Secondary immune deficiency</p>	