EuroBloodNet
European Reference Network in Rare Hematological Diseases

Criteria defined by the Network for Rare Red blood cell defects

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:
  - **X** **Rare Red blood cell defects**
    - Rare anaemias due to haematopoietic defects
    - Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis
    - Rare bleeding-coagulation disorders
    - Myeloid hemopathy
    - Lymphoid hemopathy

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
Rare Red Blood Cell (RBC) defects	Haemoglobinopathy	ICD10 D56.0 D56.1 D56.2 D56.3 D56.4 D56.8 D56.9 D57.0 D57.1 D57.2 D57.3 D57.8 D58.0 D58.1 D58.2 D58.8 D58.9 ORPHA68364, 621, 275745, 275749, 275752, 2132, 2133
Rare Red Blood Cell (RBC) defects	Hereditary erythroenzymopathies (chronic conditions)	ICD10 D55.0, D55.1, D55.2, D55.3, D74.0, E74.0, E74.1 ORPHA98369
Rare Red Blood Cell (RBC) defects	Hereditary RBC membrane defects	ICD10 D55.0, D55.1, D55.2, D55.3, D74.0, E74.1 ORPHA 98364
Rare Red Blood Cell (RBC) defects	Congenital Erythrocytosis	ORPHA 90042/ORPHA 98428 ICD10 D75.0, D75.1
Rare Red Blood Cell (RBC) defects	Diagnosis of haemoglobinopathies; phenotype and genotype, if needed: gene sequencing and large deletions identification	
Rare Red Blood Cell (RBC) defects	Genetic counselling and prenatal diagnosis for haemoglobinopathies	
Rare Red Blood Cell (RBC) defects	Diagnosis of membrane and enzyme defects: phenotype and genotype, if needed	
Rare Red Blood Cell (RBC) defects	Genetic counselling and prenatal diagnosis for enzymopathies/RBC membrane disorder	
Rare Red Blood Cell (RBC) defects	Bone-marrow transplant for haemoglobinopathies and rejection management	ICD10 T86.0; ORPHA99920/ORPHA99921/ORPHA39812
Rare Red Blood Cell (RBC) defects	Blood transfusion management. Care of immunised patient	
Rare Red Blood Cell (RBC) defects	Iron overload assessment: Iron chelation prescription and monitoring	
Rare Red Blood Cell (RBC) defects	MRI-T2* for iron monitoring.	
Rare Red Blood Cell (RBC) defects	Acute events management for sickle cell disease	
Rare Red Blood Cell (RBC) defects	Transcranial Eco-Doppler for stroke/prevention	
Rare Red Blood Cell (RBC) defects	Assessment of spleen function and splenectomy	

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

Specific diseases, conditions and highly specialized interventions	Measure	Evidence
Haemoglobinopathy	Number of patients per year	50
Haemoglobinopathy	Number of new patients per year	4
Hereditary erythroenzymopathies (chronic conditions)	Number of patients per year	10
Hereditary RBC membrane defects	Number of patients per year	25
Rare Erythrocytosis	Number of patients per year	2
Diagnosis of haemoglobinopathies; phenotype and genotype, if needed; gene sequencing and large deletions identification	Number of procedure per year	150
Genetic counselling and prenatal diagnosis for hemoglobinopathy	Number of procedure per year	20
Diagnosis of membrane and enzyme defects: phenotype and genotype, if needed	Number of procedure per year	50
Genetic counselling and prenatal diagnosis for enzymopathies/RBC membrane disorder*	Number of procedure per year	2
Bone-marrow transplant for haemoglobinopathies and rejection management	Number of procedure per year	2
Blood transfusion management. Care of immunised patient	Number of patients per year	30
Iron overload assessment. Iron chelation prescription and monitoring	Number of patients per year	30
MRI-T2* for iron monitoring.	Number of procedure per year	20
Acute events management for sickle cell disease	Number of patients per year	30
Transcranial Eco-Doppler for stroke prevention	Number of procedure per year	30
Endocrine assessment	Number of procedure per year	20
Splenectomy	Number of procedure per year	2

* This service could be agreed with a second HCP – Letter of agreement required

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	Expertise in haemoglobinopathies > 3 years	50
Pediatrician or Hematologist with proven pediatric experience	Expertise in haemoglobinopathies > 3 years	50
Transfusion Medicine expert	Expertise in chronic transfusion > 3 years	20
Pediatrician/Haematologist	Expertise in Bone marrow transplant in haemoglobinopathies > 3 years	2
Nurse	Expertise in haemoglobinopathies > 3 years	33
Laboratory specialist	Expertise in haemoglobinopathies > 3 years	150
Radiologist	Expertise in haemoglobinopathies > 3 years	30
Genetic counsellor	Expertise in haemoglobinopathies > 3 years	20
Endocrinologist	Expertise in haemoglobinopathies > 3 years	20
Surgeon	Expertise in splenectomies > 3 years	2
Neurologist/Transcranial Doppler expert	Expertise in haemoglobinopathies > 3 years	30
Cardiologist	Expertise in haemoglobinopathies > 3 years	30
Pneumologist	Expertise in haemoglobinopathies > 3 years	5

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

Specific diseases, conditions and highly specialized interventions	Specific equipment, infrastructure and information technology (IT)
Diagnosis of haemoglobinopathies; phenotype and genotype: gene sequencing and large deletions identification	HPLC, Capillary electrophoresis, horizontal electrophoresis equipments, thermocycler, sequencer.
Diagnosis of membrane and enzyme defects: phenotype and genotype	Spectrophotometer with temperature module and continuous measurement, vacuum pump, flow cytometer Osmotic gradient ektacytometry or Laser-assisted Optical Rotational Cell Analyzer, Sodium Dodecyl Sulphate Polyacrylamide gel electrophoresis equipments, thermocycler, sequencer.
Diagnosis of erythrocytosis	HPLC, Capillary electrophoresis, horizontal electrophoresis equipments,. Measurements of serum EPO. Thermocycler, sequencer.
Bone-marrow transplant for haemoglobinopathies and rejection management	BMT Unit: Availability for bone marrow transplant for haemoglobinopathies. Implementation of European guidelines and recording and assessment of clinical outcomes.
Blood transfusion management. Care of immunised patient	Serological and molecular viral tests for the diagnosis of hepatitis viruses and HIV
Iron overload assessment. Iron chelation prescription and monitoring	MRI system calibrated for iron quantification, such as heart and liver T2*; experienced personnel. Iron absorption, intake and excretion balance.
Acute events management for sickle cell disease	Intensive care Unit: Treatment of acute events, i.e. blood transfusion for acute stroke or acute chest syndrome, antibiotics for infection, tailored analgesia for a painful crisis… Prevention of acute or chronic events, i.e. treatment by erythrocyte-apheresis and/or hydroxycarbamide
Transcranial Eco-Doppler for stroke/prevention	Transcranial Doppler technology
Endocrine assessment	Equipment for basal and dynamic endocrine tests, bone density evaluation, female/male fertility assessment
Assessment of spleen function and splenectomy	Hematological and non-invasive assessment of spleen activity. Preparation to splenectomy. OPSI prevention. Thrombotic risk assessment.

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 and quantification

Rare or complex disease, condition or highly specialized interventions	Clinical outcome	Evidence
Rare anaemias due to red blood cell disorders	Mortality rate	< 5% per year
Thalassemia major	% patients with mean pre-transfusion Hb >9	80%
Thalassemia major	% patients with mean serum ferritin <1000	30%
Thalassemia major	% patients heart T2* <20ms	20%
Thalassemia major/intermedia	% patients achieving graduation	as in MS controls
Thalassemia major/intermedia	% employment	as in MS controls
Sickle cell disease	% of patients followed that performs at least one hematology visit per year	>50%
Sickle cell disease	% of patients on penicillin prophylaxis	>50%
Sickle cell disease	% of patients undergoing annual influenza vaccination	>50%
Sickle cell disease	% of patients that have up to date vaccination schedule against pneumococcus	>50%
Sickle cell disease	% of children undergoing annual TCD	>60%