Neurofibromatosis Type 1 (NF1)

Paediatric Care Pathway

HSE National Rare Diseases Office

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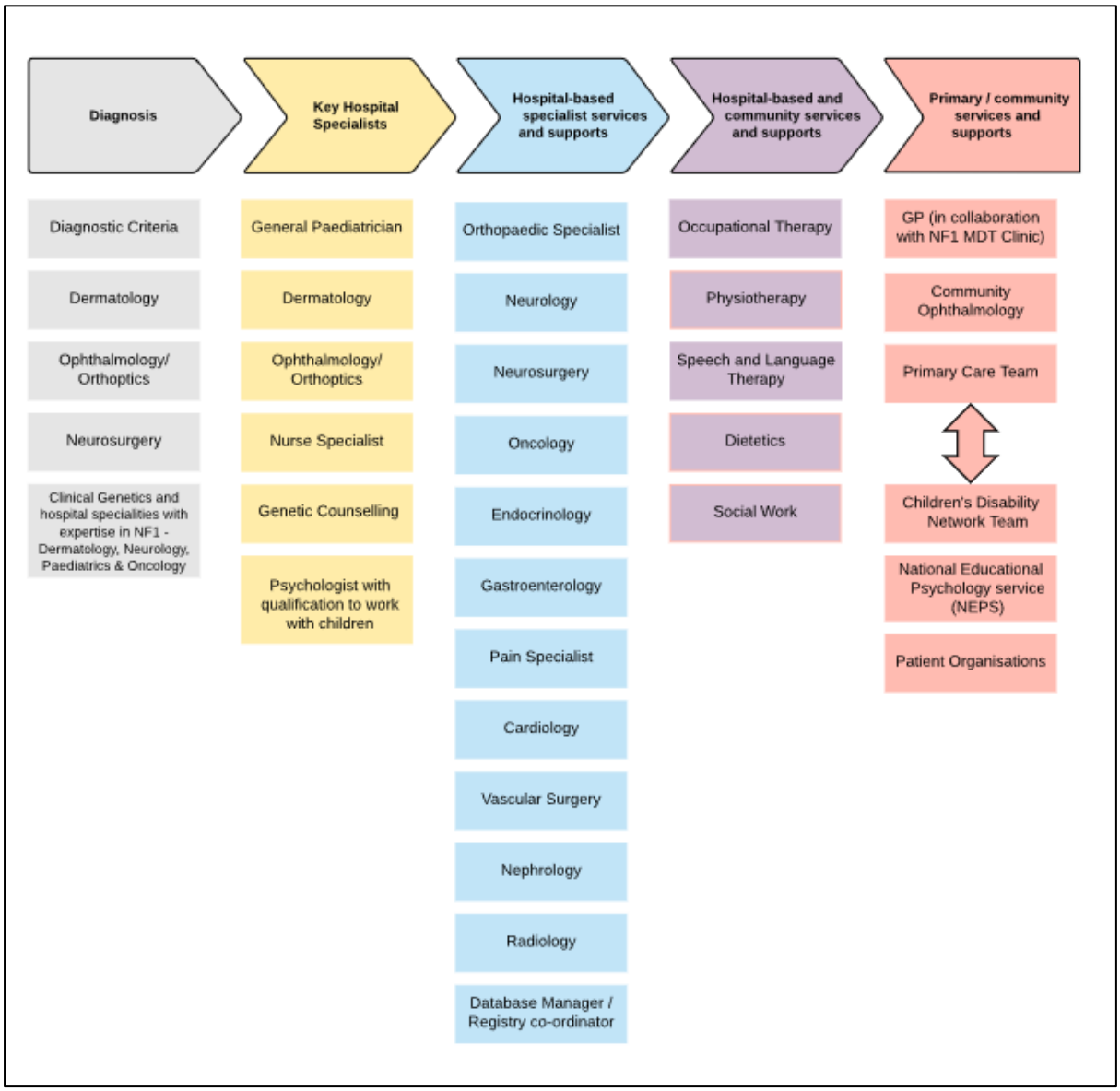

Clinical Characteristics:

ORPHAcode: 636

Disease Definition: Neurofibromatosis type 1 (NF1) is a clinically heterogeneous, neurocutaneous genetic disorder characterized by café-au-lait spots, iris Lisch nodules, axillary and inguinal freckling, and multiple neurofibromas

Diagnosis	Diagnostic Criteria	Clinical diagnosis based on presence of two of the following: 1. Six or more café-au-lait macules over 5 mm in diameter in prepubertal individuals and over 15mm in greatest diameter in postpubertal individuals, bilaterally localised. 2. Two or more neurofibromas of any type or one plexiform neurofibroma. 3. Bilateral freckling in the axillary or inguinal regions. 4. Two or more Lisch nodules (iris hamartomas), or two or more choroidal abnormalities. 5. Optic glioma. 6. A distinctive osseous lesion such as sphenoid dysplasia, anterolateral bowing of tibia (tibial dysplasia) or pseudarthrosis of a long bone. 7. A pathogenic NF1 variant. 8. A parent with NF-1 by the above criteria. Legius, E., Messiaen, L., Wolkenstein, P. *et al.* Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. *Genet Med* (2021)
Diagnosis	Dermatology	Woods light examination -cafe au lait macules; Axillary or inguinal freckling, neurofibromas Clinical assessment of parents/adult screening
Diagnosis	Ophthalmology/ Orthoptics	Lisch nodules - first noticed in children aged 5-10 years, almost all adults have these; Optic gliomas, Plexiform Gliomas and associated glaucoma, choroidal abnormalities
Diagnosis	Neurosurgery	Neurofibromas and plexiform neurofibromas
Diagnosis	Clinical Genetics and hospital specialities with expertise in NF1 - Dermatology, Neurology, Paediatrics & Oncology	Clinical diagnosis based on Legius et al 2021 revised diagnostic criteria. Genetic testing for NF1 pathogenic variants in those with a confirmed clinical diagnosis where molecular diagnosis is required for management of the proband / family for diagnostic and / or reproductive issues. Genotype /phenotype correlations may inform specific tumour risk and developmental trajectories. Less likely to detect pathogenic variant in cases of segmental NF1. Clinical assessment of parents and siblings to determine if affected to inform recurrence risk for couple and identify at-risk family members. Genetic testing (if familial pathogenic variant known) if required for diagnostic and / or reproductive issues. Predictive testing of at-risk relatives (if familial pathogenic variant known) by Genetic Counsellor If clinical diagnosis is uncertain a referral to Clinical Genetics should be considered to assess for differential diagnosis

Key Hospital Specialists	General Paediatrician	Yearly review (or more frequently, if indicated) Developmental assessment Growth monitoring (height, weight and head circumference) Blood pressure monitoring Monitoring for signs of scoliosis Monitoring of neurological symptoms including headaches, ataxia An assessment of educational attainment increased incidence of learning difficulties, attention-deficit hyperactivity disorder, autism spectrum disorder At diagnosis - family referral to Clinical Genetics for assessment Referral to specialities as indicated https://nervetumours.org.uk/images/downloads/NTUK_0046_NF1_Review_Guidelines_v4.pdf At transition - refer to Clinical Genetics to support young person in managing their condition, understanding their tumour risk and genetic counselling for reproductive risk and options
Key Hospital Specialists	Dermatology	Annual screening for neurofibromas, laser treatment, surgical removal Annual screening for plexiform neurofibromas Malignant peripheral nerve sheath tumours – monitor & refer to neurosurgery, if indicated Participation in clinical trials
Key Hospital Specialists	Ophthalmology/ Orthoptics	Annual review up to age 10 years (or more frequently if indicated), after age 10 years Community Ophthalmology Services Screen for optic gliomas (lifetime risk: 15-20%, - occur most commonly in children < age 8), orbital plexiform with associated glaucoma. Early detection of brain tumours with monitoring of visual development, visual fields, ocular motility, orbital assessment, corneal examination
Key Hospital Specialists	Nurse Specialist	Service user and family education, advice and support Liaise with health service professionals Link for the family and between all teams to acute and community nursing services Main point of contact for service user and family Co-ordination of services and supports Link to patient organisations Transition Planning
Key Hospital Specialists	Genetic Counselling	Autosomal dominant inheritance Genotype/Phenotype correlation, if relevant 50% cases are *de novo* - note small risk of gonadal mosaicism (not more than 1%) in the parents of an affected child may increase recurrence risk slightly above general population risk 50% risk for offspring of affected individuals Identify at-risk relatives Cascade testing, as appropriate Discuss all available reproductive options including pre-implantation genetic testing, prenatal diagnosis and neonatal genetic testing Provide information and signpost to additional support services to support adaption to diagnosis
Key Hospital Specialists	Psychologist with qualification to	Cognitive/ IQ Assessment - educational assessments pre-school, mid-school, transition to secondary, pre leaving school-vocational planning) Educational needs/ learning supports

	work with children	School placements Autism Spectrum Disorders (ASD) Assessment Support for chronic condition and anxiety management ADHD supports and interventions Behavioural support Developmental delay assessment Pain management Ideally hospital-based liaison service Specialist Rare Disease Centres of Expertise will aim to provide specialised psychology support and liaison psychiatry (when available). An outreach shared care model can be established (when requested) at community level (with support as needed from the specialist centre)
Hospital-based specialist services and supports	Orthopaedic Specialist	Scoliosis assessment and management – bracing, surgery Assessment and treatment of bone abnormalities - Pseudarthrosis; Long Bone dysplasia
Hospital-based specialist services and supports	Neurology	Screen for central nervous system tumours Pain control - gabapentin and pregabalin Treat epilepsy (8% prevalence) MRI brain. NB: MRI surveillance is not routine, performed when symptoms suggest
Hospital-based specialist services and supports	Neurosurgery	Neurofibromas and plexiform neurofibromas – assessment and removal, if indicated
Hospital-based specialist services and supports	Oncology	Management and treatment of symptomatic optic pathway gliomas, low grade gliomas, malignant peripheral nerve sheath tumours (MPNST)
Hospital-based specialist services and supports	Endocrinology	Pubertal and growth disorders
Hospital-based specialist services and supports	Pain Specialist	Pain evaluation and management
Hospital-based specialist services and supports	Cardiology	Monitor and manage hypertension Diagnose and manage cardiovascular anomalies (e.g pulmonary artery stenosis)
Hospital-based specialist services and supports	Vascular Surgery	Manage NF-associated vasculopathy: cerebral artery stenosis, aortic coarctation
Hospital-based specialist services and supports	Nephrology	MRA (magnetic resonance angiography) for suggested renovascular hypertension
Hospital-based specialist services and supports	Radiology	Musculoskeletal and neuroradiology Tumour surveillance and assessment
Hospital-based specialist services and supports	Database manager/ Registry co-ordinator	Create & maintain database of service users Record service user biographical, clinical and research data Audit and quality improvement

		Ensure minimum data set standards for National and International Skin Registry Solutions (NISR) and ERN NF1 registries
Hospital-based and community services and supports	Occupational Therapy	Assess and support full functional capacity and promote community inclusion through: Activities of Daily Living support Cognitive Development and Training Postural Stability and Motor Performance - assessment and intervention Visual Deficits and Compensation Behavioural / attention intervention Parent & caregiver education Equipment and Assistive Technology provision, where required Rehab post-surgical intervention
Hospital-based and community services and supports	Physiotherapy	Skeletal Abnormalities: Scoliosis, Genu Varum, Spontaneous fractures +/- delayed healing (pseudoarthrosis) Joint contractures and muscle imbalances, movement disorders Tumours: Plexiform Neurofibromas, Malignant Peripheral Nerve Sheath Tumours Promote normal patterns of movement - improve gross motor performance and function. Balance, co-ordination, and gait & proprioception training. Strength training and stretching. Postural monitoring and management - prevention of contractures and postural correction through bracing and orthotics. Supportive devices and adaptive equipment. Rehabilitation post-surgical correction. Pain management Regular Screening – Recognising and treating impairments that manifest due to underlying pathology, education of patients and carers (clinical features of Spinal Cord Compression) Adaptive approach with possible cognitive, speech, sight and hearing difficulties
Hospital-based and community services and supports	Speech and Language Therapy	Assess and support speech, language and communication needs (SLCN) and / or feeding, eating, drinking & swallowing (FEDS) skills based on individual needs / priorities Motor and cognitive difficulties may impact SLCN / FEDS

Hospital-based and community services and supports	Dietetics	Nutrition assessment including monitoring of growth to ensure nutritional adequacy - prevention of under-nutrition and aid in management of overweight / obesity Dietary counselling to optimise calcium and vitamin D intake to aid in management of osteopenia Assist in the management of feeding and food-related difficulties Provision of texture modified diets if swallowing impairments Essential hypertension: dietary advice in aid of management GI stromal tumour: Dietary counselling for gastrointestinal symptoms management. Nutrition support including enteral tube feeding, as required
Hospital-based and community services and supports	Social Work	Psychosocial support: Assess social and family supports, safeguarding Link with community supports as required e.g., GP, Public Health Nurse, Primary Care SW, Local authority SW, Mental Health SW, Disability SW, TUSLA Offer 1-1 counselling or GP referral to Counselling in primary care (CIPC) www.hse.ie/eng/services/list/4/mental-health-services/counsellingpc/ Financial support (as required): Patient advocacy, support applications for Medical card, Disability allowance, Supplementary Welfare allowance, Exceptional Needs payment, Long-term illness card, direct to Citizens' information www.citizensinformation.ie/ Housing and/or mobility issues: Advocacy and support Home Care Packages: if issues with activities of daily living - arrange application for inpatients, liaise with Public Health Nurse to arrange for out-patients Respite Care: liaise with public health nurse or community disability services to arrange Employment issues: Link to Intreo public employment and EmployAbility services www.gov.ie/en/campaigns/fb84c0-intreo/ www.gov.ie/en/service/8578c4-access-the-employability-service/
Primary/community services and supports	GP (in collaboration with key hospital specialists)	NF1 is a tumour predisposition syndrome – monitor & refer for red flag features as outlined: https://nervetumours.org.uk/images/downloads/NTUK_0046_NF1_Review_Guidelines_v4.pdf Management of inter-current conditions Co-ordination of local services and supports

		Refer/communication across services
Primary/community services and supports	Community Ophthalmology	Follow-up screening from 10 years of age
Primary/community services and supports	Primary Care Team	Children with NF1 may have difficulties or delays in development. Some can have their needs met by their local Primary Care services
Primary/community services and supports	Children's Disability Network team	Children with NF1 who have more complex needs should be referred to their local Children's Disability Network Team (Find a children's disability network team - HSE.ie) in accordance with the National Access Policy (Introduction (hse.ie)) using the attached Referral forms (Get a referral for a children's disability network team - HSE.ie)
Primary/community services and supports	National Educational Psychology service (NEPS)	School referral to National Educational Psychological Service (NEPS) Developmental Delay Assessment Cognitive / IQ assessment Educational Needs / Learning Support School Placements Link with Children's Disability Network Team (CDNT) Psychology
Primary/community services and supports	Patient Organisations	Advocacy, support and information: NF Association Ireland www.nfaireland.ie Rare Ireland www.rareireland.ie/ Rare Diseases Ireland www.rdi.ie

Clinical Lead:

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