Phenylketonuria (PKU) Paediatric and Adult Care Pathway

HSE National Rare Diseases Office

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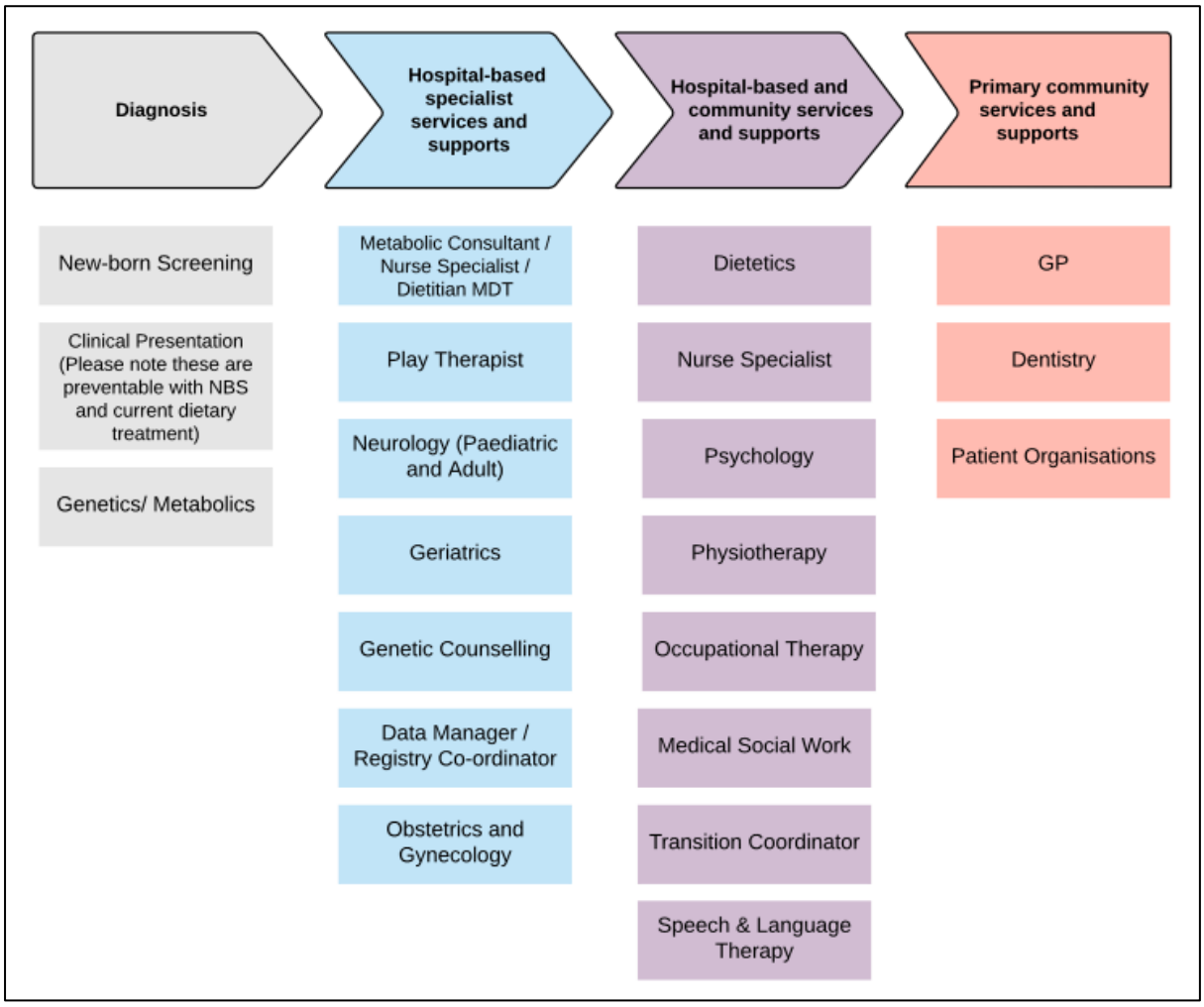

Clinical Characteristics:

Orphacode: 716

Disease Definition: Phenylketonuria (PKU) is the most common inborn error of amino acid metabolism and is characterized by elevated blood phenylalanine and low levels or absence of phenylalanine hydroxylase enzyme. If not detected early or left untreated, the disorder manifests with mild to severe mental disability

<table>
<tr><td>Diagnosis</td><td>Newborn Screening (NBS)</td><td>In accredited laboratory:
Phe >140µmol/L
Testing for disorder of synthesis or recycling of Tetrahydrobiopterin (BH4)
Confirmed biallelic pathogenic variants in PAH gene or BH4 pathway
Kuvan load testing on newborn babies for 48 hours</td></tr>
<tr><td>Diagnosis</td><td>Clinical Presentation (Please note these are preventable with NBS and current dietary treatment)</td><td>Severe intellectual disability in older people with PKU (born prior to newborn screening) who may be in residential care or cared for at home;
Epilepsy;
Any level of intellectual disability and behaviour problems, including autistic features;
Parkinson-like features (particularly in an adult);
Decreased skin and hair pigmentation;
Maternal PKU syndrome - female with no prior normal offspring who has a history of recurrent pregnancy loss and/or offspring with malformations including any combination of small size, microcephaly/ brain malformations, congenital heart defect, limb malformations and/or tracheoesophageal fistula</td></tr>
<tr><td>Diagnosis</td><td>Genetics/ Metabolics</td><td>Cascade testing of at-risk siblings or investigation of developmental delay in an untreated Individual (infancy to adulthood);
PAH pathogenic variants (if confirmed in family) and BH4 responsiveness testing;
Phenylalanine levels for possible late-treated or untreated people with PKU</td></tr>
<tr><td>Hospital-based specialist services and supports</td><td>Metabolic Consultant / Nurse Specialist / Dietitian MDT</td><td>Specialised metabolic accredited laboratory – phenylalanine (phe) and tyrosine (tyr) monitoring and quantitative amino acids;
Maintain blood phe < 360 µmol/L to age 12, <600 µmol/L teenagers and for life. Maternal targets 120-360 µmol/L;
Recommended frequency of testing:
0-2 year: weekly
2-12 years: fortnightly
> 12 years: monthly

Pre-conception counselling of female adolescents and women with PKU about teratogenic effects of high phenylalanine on embryo

Females pre-pregnancy monitoring: weekly
During pregnancy: twice weekly
Post-partum breast feeding: weekly
Unwell regimes

Outpatient Department (OPD) visit frequency:
<table>
<tr><th>Age (years)</th><th>OP Review Frequency</th><th>Medical Review (or as required)</th></tr>
<tr><td>0-2y</td><td>Every 2 months</td><td>Every visit</td></tr>
<tr><td>2-4y</td><td>4 monthly</td><td>Once every 2 years</td></tr>
<tr><td>4-18y</td><td>6 monthly</td><td>Once every 2 years</td></tr>
<tr><td>> 18y</td><td>6-12 monthly (as</td><td>Once every 2 years</td></tr>
</table></td></tr>
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		Anthropometric monitoring at each visit – weight, height, paediatric growth charts / adult BMI; Bone health monitoring – bone mineral density (BMD) at adolescence, then yearly if low; Monitor vitamin D, calcium and micronutrients; For adults only consider - monitor lipid profile and HbA1c; Treatments other than diet - Trial BH4 in newborn period if genotype amenable or suspected; BH4 trials in children, adolescents and adults; Liaise with hospital and community pharmacy
Hospital-based specialist services and supports	Play Therapy	Play therapy to assist diet adherence in children
Hospital-based specialist services and supports	Neurology (Paediatric and Adult)	Developmental/neurological condition; Brain MRI (as clinically indicated)
Hospital-based specialist services and supports	Geriatrics	Management of late treated and untreated individuals - sarcopenia requiring protein supplementation, co-existing conditions
Hospital-based specialist services and supports	Genetic Counselling	Genetic counselling for parents of affected children and affected females and males of reproductive age; mode of inheritance - autosomal recessive; recurrence risk; identification of at-risk relatives; cascade testing; reproductive options
Hospital-based specialist services and supports	Data Manager / Registry Co-ordinator	Create and maintain database of service users attending service; Record service users biographical, clinical and research data; Audit and quality improvement; Ensure minimum data set standards for ERN registry
Hospital-based specialist services and supports	Obstetrics and Gynaecology	Menstrual health; Reproductive and obstetric issues; High risk pregnancy and admission resource; Effects of menopause on bone health
Hospital-based and community services and supports	Dietetics	Ensure nutritional adequacy (monitor micro-nutrient and essential fatty acid status) and energy intake to promote optimum development, growth and healthy body weight;

		Report Phe/Tyr levels and modify nutrition care plans to ensure optimal metabolic control and nutritional adequacy in conjunction with medical team; Educate service users and healthcare professionals on achieving / maintaining Phe levels within treatment range. Advise on provision / adjustment of Phe intake from natural protein and supplementation with Phe free amino acids (synthetic protein), use of low protein products and micronutrients supplementation, as required; Support / educate families at key stages e.g. weaning, starting school; Monitor and educate people with PKU planning a pregnancy/ during pregnancy /post-partum to ensure optimum metabolic control prior to conception and maintain blood Phe concentrations within recommended maternal range and ensure adequate maternal nutritional intake for optimal fetal growth / development; Liaise with medical / dietetic staff in maternity hospitals on dietary requirements pre and post-delivery, promote / support breastfeeding Incorporate dietary requirements for co-existing conditions requiring dietary manipulation e.g. diabetes, sarcopenia, heart disease and bone health; Advise on optimising exercise and sports performance; Develop PKU dietary resources; Management of late treated / untreated individuals - sarcopenia requiring protein supplementation
Hospital-based and community services and supports	Nurse Specialist	Core multidisciplinary team (MDT) member; Care co-ordination; Service users education, advice and support; Liaise with health care professionals to accomplish holistic personal care pathways in hospital and community; Main point of contact for service users; Transition planning; Link service users to patient organisations
Hospital-based and community services and supports	Psychology	Children* and adults (*requires person with professional qualification to work with children and adolescents) for emotional difficulties, feeding abnormalities, adherence issues, pregnancy compliance; Psychological evaluation at 12 years and 18 years; Full Scale Intelligent Quotient (FSIQ), adaptive functions, executive function (inhibitory control, working memory, cognitive flexibility) and motor control; Screen for anxiety, attention deficit hyperactivity disorder (ADHD), autism; Seek additional educational psychology support, as required

Hospital-based and community services and supports	Physiotherapy	Parkinson-like features – Falls prevention: Balance and gait training strength training; Decreased motor skills – Neuro rehab: Remediate performance problems; Facilitate normal movement patterns to help achieve functional tasks; Osteopenia/Osteoporosis: Exercise therapy to enhance BMD, slow, or prevent loss of BMD. Advice on high impact exercise; sarcopenia: Strength and Resistance Training
Hospital-based and community services and supports	Occupational Therapy	Assessment and intervention for difficulties participating in activities of daily living; including sleep, self-care, productivity and leisure Environmental assessments and adaptations, if required Education / Occupation supports Postural management assessment and intervention, including specialist seating and equipment provision, if required Assistive technology
Hospital-based and community services and supports	Social Work	Psychosocial support: Assess social and family supports, safeguarding; Issues with mental health and PKU diet; Assess and provide counselling support: Offer 1-1 counselling or GP referral to Counselling in primary care (CIPC) www.hse.ie/eng/services/list/4/mental-health-services/counsellingpc/ Link with Psychology (if required); Link with community supports as required e.g GP, Public Health Nurse, Primary Care SW, Local authority SW, Mental Health SW, Disability SW, TUSLA Assess all maternal PKU patients (high risk) for good support system and self-management of PKU levels; 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/
Hospital-based specialist services and supports	Transition Coordinator	Start programme before age 14 – National Clinical Programme for Rare Disease (NCPRD) Model of Care for Transition in Rare Diseases www.hse.ie/eng/about/who/cspd/ncps/rare-diseases/resources/
Hospital-based and community services and supports	Speech & Language Therapy	Support early language development for those who spent a lot of early life in hospital environments with less stimulation for language and learning Link to parent resources: www.ncse.ie/parent-early-years-speech-language-communication www.enableireland.ie/parent's-resources Assess and support speech, language and communication needs (SLCN) and / or feeding, eating, drinking & swallowing skills based on individual needs / priorities; Support adults living in congregated residential care with intellectual disability, behaviours of concern or Parkinson-like features
Primary community services and supports	GP	Management of intercurrent conditions; Co-ordination of local services and supports; Refer/Communication across services
Primary community services and supports	Dentistry	Dentist - annual review; Hygienist – every 6 months
Primary community services and supports	Patient Organisations	Advocacy, support and information: PKUAI (PKU Association of Ireland (www.pku.ie) Rare Diseases Ireland (www./rdi.ie) Rare Ireland Family Support Network (www.rareireland.ie)

Clinical Leads:

Prof. Ahmad Monavari, CHI Temple Street Dr. James O'Byrne, Mater Misericordiae University Hospital

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National Centre for Inherited Metabolic Disorders PKU handbook

www.metabolic.ie/wp-content/uploads/2021/08/PKU-Handbook.pdf