National Institute for Health and Care Excellence

Highly Specialised Technologies Evaluation

Burosumab for treating X-linked hypophosphataemia

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Birmingham Women's and Children's NHS Foundation Trust	I feel it is appropriate that this topic is referred to NICE	Comment noted.
	British Paediatric and Adolescent Bone Group (BPABG)	This is a very important disease area, where the currently available treatment is suboptimal. This new treatment is much more targeted to the underlying abnormality and therefore more effective. This is an opportunity to significantly improve the outcomes of children with this condition (XLH)	Comments noted.
	Brittle Bone Society (BBS)	Yes. Having inherited XLH from a family that currently has thirteen family members affected, through four generations, I have seen the significant impact that the condition can have in all areas of one's life. My personal experience includes requiring 18+ surgeries to correct bone abnormalities, as well as requiring multiple restorative dental treatments from having 15+ dental abscesses all over a period of 30 years. I'm now paying the price of having those surgeries as my bones do not heal well and as a result, are bolted together with rods, nails, plates, staples, fixators and ilizarovs. I'm now entering a time in my life where I have recurring pseudo fractures, from bone that won't respond to treatment, to other parts of my body where the bone deposits itself around the spine, hips, and knees. XLH is a debilitating chronic disorder, a treatment that offers the prospects of reducing the need for surgical intervention is incredibly important to reducing the impact of	Thank you for your comments. NICE will invite patient and professional organisations to submit evidence for the committee's consideration. The testimony of patient and clinical experts at the committee

Section	Consultees	Comments	Action
		XLH on patients' lives and reducing the costs associated with these interventions.	meeting is highly valued.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	[Would it be appropriate to refer this topic to NICE for evaluation?] [Yes] Agreed	Comments noted.
	Genetic Alliance UK	This is an appropriate topic for the HST programme, as it meets all the criteria for prioritisation.	Comments noted.
	Kyowa Kirin Limited	Yes it is appropriate for NICE to review this topic through the HST process. XLH is a seriously debilitating condition. Kyowa Kirin believes that burosumab meets an unmet medical need in the small number of children with XLH. In addition, there is an uneven distribution of patients due to geographical clustering, which would result in a potential impact on a small number of commissioning groups. Treatment of children with XLH is currently concentrated in a small number of specialist centres, often with expertise in other rare metabolic bone diseases and therefore burosumab is an appropriate candidate for highly specialised commissioning.	Comments noted.
	St Vincent's University Hospital / University College Dublin, on behalf of Society for Endocrinology	[Would it be appropriate to refer this topic to NICE for evaluation?] Yes	Noted.

Section	Consultees	Comments	Action
Wording	Birmingham Women's and Children's NHS Foundation Trust	Yes the wording is correct	Noted.
	Brittle Bone Society (BBS)	[Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider?] Yes, I have no comments to add.	Noted.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	No. The issues mentioned in the scope are primarily those related to childhood XLH. In adults with the condition there needs to be consideration of: • Bone pain • Fracture • Restriction of joint movement (a result of enthesopathy) • Development of neurological complications especially spinal cord compression as a result of intraspinal new bone formation	The background section of the scope, and the outcomes listed, have been updated based on consultation comments and discussion at the scoping workshop.
	Genetic Alliance UK	This is the standard wording.	Noted.
	Kyowa Kirin Limited	Please amend the scope to include the full description of ***X-linked*** hypophosphataemia, i.e.: To evaluate the benefits and costs of burosumab within its licensed indication for treating X-linked hypophosphataemia for specialist commissioning by NHS England.	The remit has been updated accordingly.
	St Vincent's University Hospital / University College Dublin, on	[Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider?] Yes	Noted.

Section	Consultees	Comments	Action
	behalf of Society for Endocrinology		
Timing Issues	Birmingham Women's and Children's NHS Foundation Trust	This is a new treatment option for the condition and therefore feel it is appropriate to be reviewed by NICE over the next year.	Comment noted.
	Brittle Bone Society (BBS)	The delay of treatment of those with XLH, especially in those who are still growing, can have a significant impact on patients' lives. The earlier the treatment can be given, the better the prospects of patients having less severe symptoms and requiring the need for surgical intervention.	Comments noted.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	Only suitable for those patients registered in the trial the manufacturer has not been minded to provide it on a compassionate use basis	Comments noted.
	Genetic Alliance UK	We understand that the decision by the CHMP is expected in the second half of 2017. Given the substantial unmet need, it is appropriate that this evaluation be carried out as soon as possible.	Comment noted.
	Kyowa Kirin Limited	[redacted] If the technology is not evaluated in a timely manner this would lead to children with a significant unmet need being denied access to the treatment.	Comment noted.
	St Vincent's University	Trial patient access to this drug currently available through extension study	Comments noted.

Section	Consultees	Comments	Action
	Hospital / University College Dublin, on behalf of Society for Endocrinology		
Additional comments on the draft remit	Kyowa Kirin Limited	Please note that X-linked hypophosphataemia is a subset of hypophosphataemic rickets. Clinical data are available for X-linked hypophosphataemia, but not for other types of hypophosphataemic rickets.	Comments noted. The remit has been updated to specify **X-linked** hypophosphataemia. NICE can only issue recommendations that are within a technology's marketing authorisation.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Birmingham Women's and Children's NHS Foundation Trust	It is stated that there is no treatment for this condition which is incorrect	The background section has been updated to clarify that there are no existing treatments which **target the underlying cause** of XLH.
	British Paediatric and Adolescent Bone Group (BPABG)	More recent epidemiological evidence suggests a lower disease prevalence of 1:60,000 doi:10.1530/EJE-15-0515. Rafaelsen et al European Journal of Endocrinology. 2016:174:125-136	Comments noted. The epidemiology estimates have been updated based on input and agreement from scoping

Section	Consultees	Comments	Action
			workshop attendees.
	Brittle Bone Society (BBS)	I feel the following symptoms are not adequately covered by the background information: currently only mentions dental anomalies in children, however dental issues such as abscesses and high occurrences of cavities and the need for restorative treatments occur in many XLH patients of all ages; the background info does not cover the occurrence of excess mineralisation of tendons at the sites of muscular attachments and the background info does not cover the social impact and potential frequency of hospital visits.	Thanks you for your comments. The background section has been updated based on consultation comments and discussion at the scoping workshop. Please note that this section of the scope is intended to provide a brief summary of the disease and how it is managed, and is not designed to be exhaustive.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	Also concerns expressed by some (esp Prof W Fraser) that giving too much phosphate to adults might actually stimulate FGF23 production which could make things worse: a) By increasing renal tubular losses of PO_4 and hence causing a paradoxical fall in plasma PO_4 b) By increasing the drive to enthesopathy and new bone formation	Comments noted. The background section of the scope has been updated.
	Kyowa Kirin Limited	Due to uncertainties in the incidence of X-linked hypophosphataemia (XLH), Kyowa Kirin is currently undertaking work to evaluate the number of children who are currently being treated in the UK, which the company believes to be fewer than would be calculated from the incidence of 4 - 5 per 100,000 live births. [redacted]there are fewer than 250 children currently being treated for this condition in the whole of the UK.	Comments noted. The epidemiology estimates have been updated based on input and agreement from scoping workshop attendees.
	St Vincent's University Hospital / University	Does not mention potential of phosphorus supplementation to result in tertiary hyperparathyroidism and renal impairment	Comments noted. The background section of the

Section	Consultees	Comments	Action
	College Dublin, on behalf of Society for Endocrinology	(although does mention poor tolerability)	scope has been updated. Please note that this section of the scope is intended to provide a brief summary of the disease and how it is managed, and is not designed to be exhaustive.
The technology/ intervention	Birmingham Women's and Children's NHS Foundation Trust	[Is the description of the technology or technologies accurate?] Yes	Noted.
	Brittle Bone Society (BBS)	No comments.	Noted.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	[Is the description of the technology or technologies accurate?] [Yes] Agreed	Noted.
	Kyowa Kirin Limited	The information is correct. Please note that we will refer to KRN23 as burosumab in this document as this is now the approved International Nonproprietary Name (INN).	Comment noted. The technology name has been updated throughout the scope.
	St Vincent's University Hospital / University College Dublin, on behalf of Society for Endocrinology	[Is the description of the technology or technologies accurate?] Yes	Noted.
Population	Birmingham Women's and Children's NHS Foundation Trust	It will be important to distinguish the use of this technology separately in children and adults	Comments noted. The current evaluation with consider burosumab for treating children and young people only.

Section	Consultees	Comments	Action
	British Paediatric and Adolescent Bone Group (BPABG)	All infants, children and adolescents should be considered as one whole group (ie they all have actively growing bones). It is not possible to apply a disease severity assessment, as very there is deterioriation with time on current standard treatment. Ie a paediatric patient with XLH per se should be the whole group considered.	Comments noted.
	Brittle Bone Society (BBS)	No comments.	Noted.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	[Is the population defined appropriately? Are there groups within this population that should be considered separately?] [population is defined] Agreed. Also adults with symptoms related to enthesopathy/new bone formation	Comments noted. The current evaluation with consider burosumab for treating children and young people only.
	Genetic Alliance UK	It is not clear at this stage whether the licensed indication will include adult patients, or be limited to children. If adults are included, it would be appropriate to consider them separately, as it is likely that patients are likely to receive greater clinical benefit if treated before the growth of their long bones is complete.	Comments noted. The current evaluation with consider burosumab for treating children and young people only.
	Kyowa Kirin Limited	Based on the data currently available from completed and ongoing clinical trials and the submitted indication, the appropriate population should be [redacted]	Comments noted.
	St Vincent's University Hospital / University College Dublin, on behalf of Society for Endocrinology	Population is defined. Adults who are P-dependant, have pain or non-healing fractures theoretically most likely to benefit	Comments noted. The current evaluation with consider burosumab for treating children and young people only.
Comparators	Birmingham Women's	The current standard of care in children is the combination of	Comments noted. The

Section	Consultees	Comments	Action
	and Children's NHS Foundation Trust	Phosphate supplements and a Vitamin D analogue	background of the scope has been updated accordingly.
	Brittle Bone Society (BBS)	No comments.	Noted.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	[Note not all adult patients require P supplementation] Agreed	Comments noted. The background of the scope has been updated accordingly.
	Kyowa Kirin Limited	There is no approved treatment that targets the underlying cause of X-linked hypophosphatemia (XLH). The description of current clinical management is accurate. We would add that current clinical management uses large multiple daily doses of phosphate (4-5 times daily) and active vitamin D analogues (2-3 times daily). Reported doses vary widely, from 30 to 180 mg/kg/d of elemental phosphorus and 10 to 80 ng/kg/d of calcitriol, reflecting uncertainty regarding optimal doses and concerns regarding the side effects of nephrocalcinosis, hypercalciuria, and hyperparathyroidism. Due to the potential risks, close individual monitoring is required. Unlike burosumab, this approach relies on increasing the intake of phosphate rather than directly addressing phosphate wasting and results in fluctuating phosphate blood levels, which may contribute to the incidence of treatment related adverse effects.	Comments noted. The background of the scope has been updated. Please note that this section of the scope is intended to provide a brief summary of the disease and how it is managed, and is not designed to be exhaustive.
	St Vincent's University Hospital / University College Dublin, on behalf of Society for Endocrinology	Note not all adult patients require P supplementation	Comments noted. The background of the scope has been updated accordingly.
Outcomes	Birmingham Women's and Children's NHS	Yes these are appropriate outcome measures	The outcomes in the scope have been updated based on

Section	Consultees	Comments	Action
	Foundation Trust		discussion at the scoping workshop.
	Brittle Bone Society (BBS)	Also should consider: incidence of dental abscesses; frequency of restorative dental treatment; incidence of fractures; need for corrective surgery.	Thank you for your comments. The outcomes in the scope have been updated based on discussion at the scoping workshop. Outcome descriptions are broad to allow the evaluation to cover all relevant aspects of the condition and treatment.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	[Must include a measure of mobility in the motor skills assessment] Agreed also self caring ability	Thank you for your comments. The outcomes in the scope have been updated based on discussion at the scoping workshop. Outcome descriptions are broad to allow the evaluation to cover all relevant aspects of the condition and treatment.
	Genetic Alliance UK	The outcomes listed are appropriate, however we would also add: fractures/pseudofractures, enthesopathy, arthritis, muscle weakness, mobility, and fatigue.	Thank you for your comments. The outcomes in the scope have been updated based on discussion at the scoping workshop. Outcome descriptions are broad to allow flexibility in the evaluation.
	Kyowa Kirin Limited	The outcome measures to be considered might also include reduction in complications of XLH or current clinical management e.g. nephrocalcinosis, hyperparathyroidism and corrective surgery. The scoping could also consider the inclusion of the residual	Thank you for your comments. The outcomes in the scope have been updated based on discussion at the scoping workshop. Outcome

Section	Consultees	Comments	Action
		effects in adults of childhood skeletal deformities which may result in significant long term morbidities such as damaged lower limb joints requiring replacement.	descriptions are broad to allow flexibility in the evaluation.
	St Vincent's University Hospital / University College Dublin, on behalf of Society for Endocrinology	Must include a measure of mobility in the motor skills assessment	Thank you for your comments. The outcomes in the scope have been updated based on discussion at the scoping workshop. Outcome descriptions are broad to allow flexibility in the evaluation.
Equality and Diversity	Birmingham Women's and Children's NHS Foundation Trust	I have no concerns in relation to equality	Comment noted.
	British Paediatric and Adolescent Bone Group (BPABG)	Equality of opportunity should apply across the whole group of affected infants, children and adolescents.	Comment noted. The committee will consider whether its recommendations could have a different impact on people protected by the equality legislation than on the wider population.
	Brittle Bone Society (BBS)	No comments.	Noted.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	[Patients not attending highly specialised bone centres may be labelled Vitamin D resistant rickets without formal testing for XLH and thus might not be identified as candidates] Agreed but not sure that this involves any specific protected characteristic	Comment noted. Issues related to under-diagnosis cannot be addressed in a highly specialised technologies evaluation.
	Kyowa Kirin Limited	XLH is a genetic disease in which the majority of cases are familial. Patients will be managed by a small number of specialist centres with appropriate expertise. Due to the genetic inheritance there is a likelihood of geographical clustering of family members,	Comment noted.

Section	Consultees	Comments	Action
		with associated variations in service requirements and, in the absence of national commissioning, different budgetary impacts in local areas. In the absence of specialist national commissioning, there would therefore be a significant risk of inequality of availability of this treatment.	
	St Vincent's University Hospital / University College Dublin, on behalf of Society for Endocrinology	Patients not attending highly specialised bone centres may be labelled Vitamin D resistant rickets without formal testing for XLH and thus might not be identified as candidates	Comment noted. Issues related to under-diagnosis cannot be addressed in a highly specialised technologies evaluation.
Innovation	Birmingham Women's and Children's NHS Foundation Trust	Yes I think the technology is innovative and is consistent with our current understanding of the physiology in this condition.	Comment noted. The company and other consultees will be able to fully describe why they consider burosumab to be innovative in their evidence submissions, which will then be considered by the committee.
	British Paediatric and Adolescent Bone Group (BPABG)	Yes, the current approach to treatment has been the only available option for at least 3-4 decades. Clinical outcomes are still problematic with current treatment. This new approach more correctly targets the underlying abnormalities. So this represents a step change in how we can improve the health of these growing children. (We have not addressed adults in great detail, as they are not the age group that we are involved in treatment of. But enabling children to reach adulthood with better built spines would be expected to have a contribution to their adult health as well).	Comment noted. The company and other consultees will be able to fully describe why they consider burosumab to be innovative in their evidence submissions, which will then be considered by the committee.
	Brittle Bone Society (BBS)	No comments.	Noted.

Section	Consultees	Comments	Action
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	[Yes this is the first specific therapy for this disorder] Agreed	Comment noted. The company and other consultees will be able to fully describe why they consider burosumab to be innovative in their evidence submissions, which will then be considered by the committee.
	Genetic Alliance UK	As the medicine is the first to treat the underlying basis of the condition, we consider it to be innovative in its potential to make a significant and substantial impact on the health of these patients.	Comment noted. The company and other consultees will be able to fully describe why they consider burosumab to be innovative in their evidence submissions, which will then be considered by the committee.
	Kyowa Kirin Limited	Kyowa Kirin believes that burosumab is a highly innovative technology which represents a 'step-change' because it is the first treatment to address the underlying pathophysiology in patients with X-Linked Hypophosphatemia (XLH) by directly targeting excess FGF23 to improve phosphate homeostasis. Early intervention with burosumab has the potential to be disease modifying through the avoidance of significant deformities, which are a feature of the condition and which may be carried through to cause long-term morbidity in adulthood.	Comment noted. The company and other consultees will be able to fully describe why they consider burosumab to be innovative in their evidence submissions, which will then be considered by the committee.
	St Vincent's University Hospital / University College Dublin, on behalf of Society for Endocrinology	Yes this is the first specific therapy for this disorder	Comment noted. The company and other consultees will be able to fully describe why they consider burosumab to be innovative in their evidence submissions, which will then be considered by the

Section	Consultees	Comments	Action
			committee.
Other considerations	Birmingham Women's and Children's NHS Foundation Trust	Another aspect to consider would be the prevention of osteoarthritis in adults with the condition	Comments noted. The outcomes in the scope have been updated based on discussion at the scoping workshop. Outcome descriptions are broad to allow flexibility in the evaluation.
	Brittle Bone Society (BBS)	Should also consider that the administering of the new treatment by subcutaneous injection is likely to see higher compliance compared to the administering of multiple daily doses of phosphate and alfacalcidol. This is because injections are required less frequently and do not have the unpleasant taste and potential gastrointestinal effects that the current treatments do.	Comments noted.
	Central Manchester University Hospitals NHS Foundation Trust, on behalf of the Society for Endocrinology	As intimated above I suspect that the remit and scope have been written from a paediatric perspective and more discussion and consultation needs to be offered from an adult viewpoint	Comments noted. The scope has been updated to include issues and treatment relevant to adults. The current evaluation with consider burosumab for treating children and young people only.
	Kyowa Kirin Limited	The following additional issues might also be considered by the proposed evaluation: Provision of shared care services led by specialist centres to provide safe, effective high quality care nationally, despite the clustering effects of inherited disease in families (service delivery should also include consideration of the proposed dose regimen in children of twice monthly subcutaneous injections). Alignment of potential service with existing or planned specialist services for children with rare metabolic bone diseases by NHSE.	Comments noted.

Section	Consultees	Comments	Action
Questions for consultation	Birmingham Women's and Children's NHS Foundation Trust	The current established clinical management will differ between children and adults – many of the latter do not currently receive medical treatment.	Comments noted. The scope has been updated accordingly.
	Brittle Bone Society (BBS)	No additional comments.	Noted.
	Kyowa Kirin Limited	*What is the anticipated population in whom burosumab will be used? Is it likely to be used in adults? Please provide an estimate of patient numbers if possible.* Kyowa Kirin anticipates that burosumab will be granted conditional approval for use in the treatment [redacted] there are fewer than 250 children currently being treated for this condition in the whole of the UK. Clinical development is continuing in adult patients. [redacted] Please note that there is great uncertainty regarding the number of adult patients in the UK who are currently receiving treatment for X-Linked Hypophosphataemia (XLH). *What is established clinical management without KRN23? Is this likely to differ for children and adults?* Current clinical management of children with X-Linked Hypophosphataemia (XLH) is multiple daily doses of oral phosphate (4-5 times daily) and active vitamin D analogues (2-3 times daily). This approach results in suboptimal outcomes and a higher incidence of undesirable effects. Whilst in some patients it can partially improve rickets, growth,	Thank you for your comments. The scope has been updated based on consultation comments and discussion at the scoping workshop.

Section	Consultees	Comments	Action
		and osteomalacia, the efficacy of this treatment is limited because phosphate levels cannot be consistently maintained at appropriate levels to allow mineralization of bone and improve skeletal outcomes. The use of high doses of oral phosphate results in fluctuating phosphate blood levels, which may contribute to the incidence of treatment related adverse effects, which include diarrhoea, hypercalcemia, hypercalciuria, nephrocalcinosis, and hyperparathyroidism. In addition, this approach requires continual monitoring and dose adjustment to balance efficacy and safety. Frequent daily dosing, gastrointestinal tolerability issues, and the need for regular clinical and laboratory monitoring add to treatment burden and may compromise therapeutic benefit due to poor concordance with prescribed treatment. The limitations of the current management strategy are evident. This approach can only increase supply of phosphate, but no current treatment option can target the excess FGF23 and improve phosphate homeostasis by addressing the underlying cause of XLH, which is phosphate wasting. *Are patients likely to be treated at specialist centres?* There is a limited number of expert clinicians with the necessary training and experience in rare metabolic bone diseases to appropriately identify and manage children with X-linked hypophosphataemia. It is anticipated that treatment would be initiated by specialist centres and clinicians and managed via shared care service provision. *Are the outcomes listed appropriate? Should any other outcomes*	

Section	Consultees	Comments	Action
		be included? The outcome measures to be considered might also include reduction in complications of XLH or current clinical management e.g. nephrocalcinosis, hyperparathyroidism and corrective surgery. The scoping could also consider the inclusion of the residual effects in adults of childhood skeletal deformities which may result in significant long term morbidities such as damaged lower limb joints requiring replacement. *Are there any subgroups of people in whom KRN23 is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?* Kyowa Kirin is not aware of any genetic or biochemical markers to allow disease severity to be predicted before the development of skeletal deformities. *Equality of opportunity* XLH is a genetic disease in which the majority of cases are familial. Patients will be managed by a small number of specialist centres with appropriate expertise. Due to the genetic inheritance there is a likelihood of geographical clustering of family members, with associated variations in service requirements and, in the absence of national commissioning, different budgetary impacts in local areas. In the absence of specialist national commissioning, there would therefore be a significant risk of inequality of availability of this treatment. *Do you consider the technology to be innovative in its potential to*	

Section	Consultees	Comments	Action
		make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? Kyowa Kirin believes that burosumab is a highly innovative technology which represents a 'step-change' because it is the first treatment to address the underlying pathophysiology in patients with X-Linked Hypophosphatemia (XLH) by directly targeting excess FGF23 to improve phosphate homeostasis. Early intervention with burosumab has the potential to be disease modifying through the avoidance of significant deformities, which are a feature of the condition and which may be carried through to cause long-term morbidity in adulthood.	
Additional comments on the draft scope	Consultant Physician, Society for Endocrinology	I have several comments which relate primarily to the draft scope and especially why this has been targeted as a highly specialised appraisal rather than an STA: 1. The number of patients is grossly underestimated. In the document the paediatric population is stated as a very limited age range when the actual target children's population should be aged 1 – 16 and so will be three times that estimated 2. The adult population will be much higher still. I have well over 50 patients in my clinic with the condition and there are presumably similar numbers at the clinics at Birmingham [redacted], Sheffield [redacted], Oxford [redacted], London [redacted] with lower numbers at Liverpool [redacted], Newcastle [redacted], Norwich [redacted] and Leeds [redacted]The majority of these adults will be looked after in endocrine or metabolic clinics and not as seems to be implied in the scope by rheumatologists	Thank you for your comments. The current evaluation with consider burosumab for treating children and young people only. The background section of the scope and epidemiology data have been updated based on discussion and agreement at the scoping workshop.

Section	Consultees	Comments	Action
		3. The scope states that there is no treatment which is just not true. Many of the children transitioned to me by my paediatric colleagues have reasonable stature and straight legs on just phosphate and active vitamin D 4. The spectrum of clinical outcomes in the scope really relates only to paediatric disease. In adults the issues are different with bone pain and fracture being the predominant skeletal symptoms. However the main adult problems relate to new bone development as the result of prolonged action of FGF23 which leads to a painful enthesopathy with restriction of joint movement and new bone formation with nerve entrapment of which the most severe form is spinal cord compression as a result of ossification of the ligament flavum. 5. A lot of adults go on to develop tertiary hyperparathyroidism which limits treatment options. Most of these do not seem to have been considered in the draft scope which looks to have been written by paediatricians who seem to have forgotten that the m`majority of patients with this condition are adults.	

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Department of Health