Clinical Commissioning Policy Proposition: MO00X01 Commissioning Medicines in Children

Reference: NHS England XX XX XX

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First published: Month Year

Prepared by NHS England Specialised Services Medicines Optimisation Clinical Reference Group

Published by NHS England, in electronic format only.

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1 Executive Summary

Equality Statement

NHS England has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. NHS England is committed to fulfilling this duty as to equality of access and to avoiding unlawful discrimination on the grounds of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, NHS England will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which NHS England is responsible, including policy development, review and implementation.

Plain Language Summary

About commissioning medicines in children

Recommendations made by the National Institute for Health and Care Excellence (NICE) within their Technology Appraisals (TA)/Highly Specialised Technology Appraisals (HST) only provide guidance on using a medicine in the group of patients for which the medicine has been granted a licence (this may also be the case within NHS England policy). Medicines often only have a licence for patients who are 18 years and above because these are the group of patients on whom the medicine has been researched. Although a patient under 18 years may be in the situation outlined by the TA/HST or policy, they may not be able to access the medicine because the guidance/policy does not cover people of their age and so is not routinely funded.

About current process

Currently, as patients under 18 years of age may not be able to access a medicine because a NICE TA/HST or NHS England policy only covers patients over 18 years of age, the only way they are able to receive these treatments is by applying via the NHS England Individual Funding (IFR) request process which will consider whether

the NHS will fund this for the patient because the treatment would be effective for them. This process often excludes applications as the patient is often part of a group of similar patients and therefore funding such a patient would be considered part of a new service which requires a national policy.

About the new process

This policy proposes that patients less than 18 years of age who meet the criteria set out in a NICE TA/HST or NHS England policy relating to adults will be able to receive the medicine without going through the IFR process, if they meet certain conditions outlined within this document.

What we have decided

NHS England has carefully reviewed the evidence to treat patients under 18 years with medicines available for adults by a NICE TA/HST or NHS England policy. We have concluded that there is enough evidence to consider making these treatments routinely available to patients less than 18 years of age, in certain situations.

2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to routinely commission medicines for children within specialised services where the specific commissioning criteria within a NICE TA or NHS England policy are met and the medicine is clinically appropriate for use in a child.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether this policy will allow routine commissioning of medicines in children is planned to be made by NHS England following a recommendation from the Clinical Priorities Advisory Group.

3 Background

Paediatric patients should have access to medicines that have been appropriately evaluated for their use. However, safe and effective pharmacotherapy in paediatric patients requires the timely development of information on the proper use of medicinal products in various age ranges and, often, the development of paediatric formulations of those products.

The paediatric patient population should ideally be included when a product is being developed for a disease or condition in adults. An EU paediatric regulation was published in 2007 by the European Medicines Agency (EMA), which seeks to drive licensing of medicines for children through an incentive/reward system of patent extension. Companies seeking a license for their product in the EU/UK are obliged to develop a Paediatric Investigation Plan or obtain a waiver excluding them from developing a PIP. However, a paediatric license is often sought after the adult indication has received a Marketing Authorisation and sometimes is never obtained.

The NHS England Individual Funding Requests (IFR) team receive requests for treatment involving paediatric patients where the treatment requested is either approved by NICE or NHS England in the adult setting. Examples of such requests include:

- Request for MS treatment in a 12 year old where the medicine in question is supported by NICE in adults
- Request for a treatment for ulcerative colitis in a 16 year old where the medicine in question is approved by NICE

Following the IFR Standard Operating Procedure (IFR SOP) these requests are screened and in general will be considered as part of a cohort request and will not be progressed further. Some requests are also made under the Clinically Critically Urgent process. There can be significant delays in accessing treatment and treatment may not be approved at all.

The key issue is that NHS England does not have a commissioning position in such circumstances and is unlikely to have clinical commissioning policies in place for every possible scenario.

NICE will review medicines in relation to their Marketing Authorisation and therefore

if the medicine only has a license for use in adults, NICE will not make recommendations for the paediatric population. This will also be the case within an NHS England clinical commissioning policy unless it is specific to the paediatric population.

This policy proposition addresses NHS England's position on commissioning medicines for children within specialised services where a medicine is approved for use by NICE TA or NHS England policy in the adult population but not within the paediatric population.

4 Definitions

British National Formulary (BNF) for Children - The BNF for Children is for rapid reference by UK health professionals engaged in prescribing, dispensing, and administering medicines to children.

NICE Technology Appraisal - A specific form of guidance issued by NICE. Where NICE makes a positive recommendation, commissioners must make funding available to support the recommendation within the period specified, usually three months from the date of publication. For the purposes of this policy any reference to a TA also applies to a Highly Specialised Technology Appraisal.

Off label – a term used to describe the use of a licensed medicine outside the terms of its marketing authorisation e.g. on the basis of age, dose, route, indication

Paediatric patient – any patient below the age of 18

Pharmacokinetics - this refers to the movement of a medicine into, through and out of the body – the time course of its absorption, distribution, metabolism and excretion.

Specialised service – a service that is directly commissioned by NHS England i.e. not CCG commissioned as listed in The Manual for specialised services (found at https://www.england.nhs.uk/commissioning/spec-services/key-docs/)

5 Aims and Objectives

This policy proposition considers the circumstances where recommendations made in a NICE TA or NHS England clinical commissioning policy for an adult patient can be used to inform a commissioning position in the paediatric population within a specialised commissioned service.

It aims to reduce the need for such cases to be considered through the IFR process and allow rapid access to treatment where appropriate.

6 Epidemiology and Needs Assessment

There are about 13 million children below the age of 18 in England - nearly a quarter of England's 53 million population (2011 census). About 650,000 of these children (5%) are post pubertal.

Every year about 10% of hospital admissions are in children below the age of 18 years.

Many medicines used to treat children are either not licensed for any indication – adult or children (as an imported medicine, an extemporaneously prepared

medicine, a medicine prepared under a specials manufacturing licence, or a manipulated medicine) or are prescribed outside the terms of the product license applying to indication, age, dose or route of administration (off label). Unlicensed and off label use of medicines in children has been reported to range from 11% in the community to about 90% in specialist areas such as Neonatal Intensive Care Units and on average 50% of children admitted to hospital receive either an unlicensed or off label medicine during their admission with the most common reason for off label prescribing being the age of the patient.

The need and use of unlicensed and off label medicines has not been formally reviewed in the delivery of Specialised Services in NHS England. In the year 2014/2015, the NHS England IFR team documented 80 requests to use medicines outside the license or off-label.

7 Evidence Base

NHS England has concluded that there is sufficient evidence to support a proposal for the routine commissioning of medicines/indications for children if the treatment meets the criteria with the NICE TA/NHS England clinical commissioning policy for adults and the child meets the additional criteria set out in this policy.

In 1994, as a first step toward ensuring the most efficient use of all relevant data in the planning of paediatric medicine development programs specifically, the Food and Drugs Administration (FDA – the US equivalent of the EMA) finalised a set of rules for the extrapolation of efficacy to the paediatric population from adequate, well controlled studies with adults. Such extrapolation depends on a series of evidence-based assumptions. These include the following fundamental assumptions:

1. There are similar disease progressions in the adult and paediatric population
2. There are similar responses to the intervention in the adult and paediatric populations.
3. That the adult and paediatric populations have similar exposure-response relationships.

The FDA examines several factors before making assumptions of similarity, including disease pathogenesis, criteria for disease definition, clinical classification, measures of disease progression, and pathophysiological, histopathological, and pathobiological characteristics. Support for these assumptions may be derived, for example, from sponsor data, published literature findings, expert panels, workshops, or consensus documents, or previous experience with other products in the same class; the FDA decides whether the available evidence is sufficient for authorisation of a medicine for paediatric use. This reduces the number and complexity of clinical trials necessary to achieve a paediatric label.

The FDA uses the following age group categorisation when extrapolating adult trial data to the paediatric population:

- preterm new born infants
- term new born infants (0 –27 days)
- infants and toddlers (28 days to 23 months)
- children (2 to 11 years)
- adolescents (12 to 16 –18 years)

It should be noted that this classification is used to discuss characteristics of the paediatric population in different developmental stages. Some age classes are wide and include a large range of maturation levels. In addition to age, other factors may need to be taken into consideration such as gestational age, renal function, metabolic function etc. The pharmacokinetic processes in adolescent patients is often similar to the pharmacokinetic processes in adults and monitoring the onset of puberty could be considered as a relevant threshold for determining whether an adult commissioning position could be extrapolated to a paediatric patient.

For the purposes of policy, and, in the absence of a recognised published dose in the BNF for Children, a threshold where the child is post pubescent can be used to approve funding.

It is proposed that NHS England adopts the process as described above along with other agreed criteria (i.e. post pubescent) to determine whether a medicine should be routinely available in the paediatric population where a NICE or NHS England position recommends the use of the medicine within a children's specialised commissioned service.

8 Proposed Criteria for Commissioning

NHS England will fund medicines approved in adults by a NICE TA or NHS England policy for children when one of the following conditions apply:

- The medicine has a license for use in children and both the indication for use and the age of the child fall within those specified in the license **or**
- The medicine is listed in the BNF for Children with a recommended dosage schedule relative to the age of the child **or**
- The child is post pubescent **or**
- An expert working group for the particular medicine/indication using methodologies described by the FDA provides robust data to support an appropriate dosing schedule

It should be noted that where a product has a marketing authorisation for use in children it should be considered prior to a funding request for a product that does not have a marketing authorisation for use in children.

In addition **ALL** of the following conditions must apply:

- The patient meets all the NICE TA/NHS England policy criteria for the proposed medicine/indication
- The patient does not meet any exclusion criteria for the medicine/indication in question
- Approval for use of the medicine has been agreed by an appropriately constructed Multi-disciplinary Team (MDT) at the specialised paediatric centre involving, where appropriate, the adult service

In all cases the use of the medicine when off label must go through internal Trust approval systems to ensure the request is clinically safe and approved by the Trusts governance process e.g. MDT, Drugs and Therapeutics Committee (DTC).

Patients who do not meet the criteria outlined above or approved through the NICE TA or NHS England clinical commissioning policy can have their case considered through the IFR process in the usual manner. In such cases, the clinician would

need to demonstrate that the child has exceptional clinical circumstances (meeting the criteria of the IFR policy) and there is robust evidence that supports the case for funding.

9 Proposed Patient Pathway

It is proposed that decisions about the commencement, monitoring and stopping of a treatment approved as meeting the access criteria within this policy will be made by a specialised commissioned children's service in conjunction with the appropriate adult service if appropriate. The decision to prescribe the medicine must be made by an appropriately constructed MDT.

10 Proposed Governance Arrangements

Each Trust treating children with a medicine approved under this policy will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics Committee (or similar) and NHS England can ask for documented evidence that these processes are in place.

11 Proposed Mechanism for Funding

NHS England will be responsible for commissioning treatments prescribed in line with this policy on behalf of the population of England within specialised commissioned children's services. The medicine will be funded through local specialised commissioning teams.

12 Proposed Audit Requirements

All use of a biologic medicine must be entered onto the appropriate biologic registry.

13 Documents That Have Informed This Policy Proposition

ICH E11 Clinical Investigation of medicinal products in the paediatric population (CPMP/ICH/2711/99).

Role of Pharmacokinetics in the development of medicinal products in the Paediatric Population (CHMP/EWP/147013/2004).

14 Date of Review

This document will be reviewed in 2020 or sooner if any specific legislation related to this policy is published.

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