Joint Committee on Health

Houses of the Oireachtas

Leinster House

Dublin 2

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OPENING STATEMENT

Processes and Criteria Used by the NCPE when evaluating Orphan Drugs

This document includes an update to our previous submission on 6th June 2017 and considers developments in the joint evaluation of medicines by other EU Member states.

The NCPE assessment process considers the clinical effectiveness and health related quality of life benefits and all relevant costs including potential savings from reduced healthcare resource use (e.g. hospitalisation), which a new treatment may provide and whether the price requested by the manufacturer is justified. The NCPE will then advise the HSE in relation to the cost effectiveness [value for money] and budget impact associated with the specific pharmaceutical product.

A medicinal product is designated as an orphan medicinal product if it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 persons in the European Union at the time of submission of the designation application.

The NCPE has a standardized process and criteria for the evaluation of pharmaceutical products including Orphan Drugs. All assessments are conducted in accordance with published Health Technology Assessment [HTA] guidelines by the Health Information and Quality Authority [HIQA]. These guidelines were produced by the HTA Directorate in HIQA in consultation with it's HTA Scientific Advisory Group. The guidelines were first published by the Authority in 2010 and subsequently updated in 2014 and are available on the HIQA website www.hiqa.ie. A further update of these guidelines is underway and will be completed in November 2017.

The NCPE HTA process is well established and usually commences when the relevant pharmaceutical company receives notification from the HSE Corporate Pharmaceutical Unit [HSE-CPU] of the requirement for a Rapid Review Submission following a price application for a new medicine. The manufacturer submits the Rapid Review document according to the template available on the NCPE website [www.ncpe.ie]. The document includes a range of information on the relevant product including the regulatory status, the clinical condition, the proposed licensed indication, anticipated place in therapy, relevant comparators,

clinical evidence, safety and tolerability in addition to economic considerations. The NCPE reviews this document within a four week period to determine whether a full pharmacoeconomic assessment is required or not. If a full pharmacoeconomic assessment is not required the product is usually reimbursed.

Since the beginning of 2017 some 45 products have been reviewed under the rapid review process and 10 (22.2 %) were recommended as not requiring a full HTA, 20 (44.4%) required a full HTA assessment, 14 (31.1%) required a full HTA at the submitted price and the remaining product was not considered until further clinical evidence was available.

If a full pharmacoeconomic assessment [HTA] is required the manufacturer is directed to the applicant template for submission of a full assessment which is available on the NCPE website. A full HTA investigates in detail the value for money proposition associated with medications. Orphan Drugs are assessed through the same mechanism as other drugs, but mindful of the particular challenges that orphan drugs may have in satisfying the requirements of a full HTA.

The assessment includes a description of the relevant condition and its management and a detailed outline of the intervention under assessment. The clinical evidence supporting the efficacy of the product is reviewed. The manufacturer is required to outline in detail the health economics in relation to the product and provide an estimate of the incremental cost effectiveness of the drug i.e. the added benefit for the additional cost. A budget impact analysis is also required in addition to the status of HTA assessments in other jurisdictions.

The HTA submission process also facilitates submissions by patient groups who wish to have their views taken into consideration during the assessment process. The patient group submission template is also available on the NCPE website. Patient submissions were received for 7 of the 18 full HTAs conducted in 2016. Having reviewed all the available documentation the NCPE submits its report to the HSE Corporate Pharmaceutical Unit (HSE-CPU) following a check for factual accuracy by the manufacturer.

The HSE-CPU will forward the NCPE Report and any other relevant information to the HSE Drugs Group for their consideration. The final decision on reimbursement of any drug, including Orphan drugs, is made by the HSE, not the NCPE.

Examples of Orphan Drugs that have been considered by the NCPE include Agalsidase alpha [Replagal] and Agalsidase beta [Fabrazyme] for Fabry disease [2004], Eculizumab [Soliris] for Paroxysmal Nocturnal Haemoglobinuria [PNH] in 2010 and 2013, Ivacaftor [Kalydeco] for Cystic Fibrosis [2013], Ataluren [Translarna] for Duchenne Muscular Dystrophy [2016], Lumacaftor/Ivacaftor [Orkambi] for Cystic Fibrosis [2016], Elosulfase alpha [Vimizim] for mucopolysaccharidosis, type IV A (Morquio A syndrome) [2016], Human alpha 1 proteinase inhibitor [Respreeza] for emphysema in adults with documented alpha 1 proteinase inhibitor deficiency [2016], Migalastat [Galafold] for Fabry disease [2017] and Sapropterin [Kuvan] for Phenylketonuria [2017].

In relation to patient access Replagal, Fabrazyme, Soliris, Kalydeco and Orkambi are all reimbursed and available for those patients who would benefit from therapy. Respreeza is also available to patients following continuation of the compassionate access scheme. Galafold was deemed cost-effective and should be reimbursed in due course and Kuvan is currently being assessed. Vimizim (Morquio A syndrome) and Translarna for Duchenne Muscular Dystrophy are not reimbursed at this point in time.

A recent development in the area of rare diseases involves the HSE setting up the Rare Diseases Medicinal Products/Technology Review Committee which will be expected to play a role in the evaluation of drugs for Rare Diseases similar to that of the National Cancer Control Programme (NCCP) Technology Review Group in the assessment of cancer drugs.

Over the past 20 years the majority of EU Member States have developed National HTA agencies e.g. NCPE in Ireland 1998 and NICE in the UK in 1999. The debate on harmonizing European HTA has been discussed for some time and in 2004 the European Commission and Council of Ministers highlighted the need for a sustainable European network on HTA leading to the setting up of the European Network for Health Technology Assessment (EUnetHTA).

EUnetHTA aims to support the efficient production and use of HTA and does this by providing methodological support for HTA and facilitating the exchange of information in relation to shared HTA assessments. The NCPE is an active participant in the EUnetHTA process. This ongoing collaboration will inform the future of joint assessments in Europe.

Another important development is seen with the BeNeLuxA initiative which began in April 2015 when the health Ministers of Belgium and the Netherlands considered a collaboration on pharmaceutical policy. Luxembourg joined the cooperation in September 2015 and Austria joined in June 2016. One of the aims of the BeNeLuxA initiative was to ensure sustainable access to innovative medicine at an affordable cost. The cooperation is linked to four domains including (1) horizon scanning (2) information sharing and policy exchange (3) Health Technology Assessment (HTA) and (4) pricing and reimbursement.

The first joint HTA included Belgium and the Netherlands collaborating on a joint assessment of Orkambi (Lumacaftor + Ivacaftor). This HTA was completed in May 2017 which led to unsuccessful negotiations with the manufacturer. As a result Orkambi is not reimbursed in either Belgium or the Netherlands today. Over 300 CF persons with the 508del mutation are receiving Orkambi in Ireland. It is anticipated that further joint HTAs will be conducted as part of the BeNeLuxA initiative.

The Valletta declaration was signed on the 8th May 2017 by the Ministers of Cyprus, Greece, Italy, Malta, Portugal and Spain who agreed to explore collaboration in relation to ensuring patient access to new and innovative medicines while ensuring the sustainability of health systems.

It is proposed to set up a Technical Committee to explore areas for collaboration including but not limited to sharing of information, identifying best practices, horizon scanning of new and innovative medicines and possible mechanisms for price negotiations. It is possible that collaboration in the area of HTA will be considered in the future. The Ministers for Health in Ireland and Romania subscribed to the Valetta declaration on the 9th May 2017.

Germany remains the front runner in Europe in terms of availability of newly authorized medicines following market authorization. Free pricing is available for the first year followed by a price negotiation. Failure to agree on pricing may result in referral to the Institute for Quality and Efficiency in Health Care (IQWiG). Incorporating such a system in the Irish context would have budgetary implications.

In contrast to Germany, the reimbursement of medicines in many European countries (including Ireland) and other developed countries (e.g. Australia and Canada) only occurs following post marketing evaluation.

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