Dear Health and Social Care Committee,

We write to you as parents, our young child has Cystic Fibrosis. They have the genetic mutation that Vertex’s drug, Orkambi, targets and would improve their quality and length of life.

We cannot explain myself, let alone expect you to understand, the sheer dread and helplessness it is to know that we are likely to outlive our child. The anguish in knowing that a drug exists that can change that, and spare them from unnecessary suffering and decline in health, but that they are denied it, is unbearable. To refuse them and many others, a drug, that is made in the UK and sold worldwide from the UK, is inhumane.

The Department of Health and Social Care, NHS England, NICE and Vertex have all had a part to play in this inexcusable situation, and we are very grateful that you have opened this inquiry.

Issues with NICE

We appreciate that all new drugs need to be appraised for clinical and cost effectiveness, however there are issues with the current system that NICE use.

1. Rare, but not rare enough

NICE have two main appraisal pathways, the Technical Appraisal (TA) for the vast majority of drugs for common diseases and conditions, and the Highly Specialised Technology (HST) for very rare conditions.

Cystic Fibrosis is a rare disease, affecting approximately 10,500 people in the UK. However, as CF is caused by many different genetic mutations, drugs such as Orkambi only work in a subset of patients. Orkambi could be affective for around 4,000 patients.

The Highly Specialised Technology can recommend drugs up to £300,000 per QALY, whereas the standard Technical Appraisal pathway can only recommend drugs up to £30,000 per QALY. These thresholds are arbitrary and haven’t been reviewed or increased inline with inflation or the increased cost of drug development.

Use of the HST is only allowed for very rare conditions which affect less than 1,000 people in the UK, and only at the direction of DoHSC.

This means that Orkambi has to be assessed through the standard Technology Appraisal, in the same way as a drug that is effective for all 66 million people in the UK. Research and Development costs for new drugs are the same no matter how many potential patients will benefit from it. Therefore it is obvious that the per patient treatment cost will be far greater for a drug for 4,000, than a drug for 66 million people.
Why is there such a sharp cliff between allowing drug costs up to £300,000 for up to 1,000 patients, to £30,000 for up to 66 million patients? Cystic Fibrosis is a rare disease, but not rare enough, so it is unfairly included in the common TA pathway. There should be a middle pathway for rare diseases, to reflect the increased per patient R&D costs. Why isn’t the allowed cost graduated between very rare and common?

2. CF diverse severity and symptoms are not reflected in the Technical Appraisal

The severity of Cystic Fibrosis is very diverse, even within age groups. Orkambi’s effectiveness is also varied, with patients responding to treatment in a range of success. The NICE Technical Appraisal process reduces the diversity of severity and response to treatment into a single ‘base-case’ fictional patient. This base-case is used to determine clinical and cost effectiveness.

This disregard for the diversity of severity of disease and response to treatment masks the true value of Orkambi to some patients. For example, when the study groups are split by age you can see that Orkambi has a greater effect on younger patients. 2-5 year olds sweat chloride levels dropped further with treatment and benefited from a greater increase of years of life than those 12 years or older. This leads to a lower cost per QALY for younger patients, but this is disregarded due to the simplification to the base-case patient.

This leads to the NICE process discriminating on the basis of age.

3. Narrow focus of NICE appraisal

The NICE appraisal of Orkambi focused on an uplift in FEV1 as a marker of clinical effectiveness. There was disappointment that Orkambi didn’t achieve a similar uplift in FEV1 as Kalydeco, which led to Orkambi’s refusal.

We now know that FEV1 isn’t the most significant marker of clinical effectiveness. Reductions in pulmonary exacerbations and reduction in lung decline are far more important to both quality and length of life. Orkambi has since been proven to achieve a similar rate in reducing both exacerbations and the rate of lung decline as Kalydeco. This reduction in exacerbations and lung decline are not linked to the initial uplift in FEV1.

The ‘Cystic Fibrosis Questionnaire-Revised’ (CFQ-R) is a health related quality of life measure used in clinical trials and the NICE appraisals. It is designed to measure the patient reported change in their quality of life and is used to determine the clinical effectiveness of treatments. However, it is known that people with long term conditions underestimate their true rate of progression of their disability. Therefore it is an ineffective measure of clinical effectiveness, especially when reported by young children.

4. Wider socioeconomic impact

The NICE appraisal only takes into consideration the reduction in existing costs of current standard of care. Long term disabilities involve a wider socioeconomic impact due to patients, parents and carers are often unable to work due to the burden of treatment. This wider economic impact should be included in the cost effectiveness calculations, as Orkambi has enabled patients to work themselves, and their family to return to work and contribute to the UK economy.
5. Discrimination against chronic genetic diseases

As CF is a genetic disease, the patient population is fixed. It is a chronic disease, meaning treatments have to be taken for life. The cost effectiveness calculation is unfairly applied to chronic genetic diseases. As the patient population is static, the lifetime cost of treatment is high and therefore the cost per QALY gained is high. If the patient population changes every year, and a new cohort of 4,000 people are treated each year, the lifetime cost of treatment and cost per QALY gained is much lower. Even though the overall budget impact is the same.

Issues with DoHSC

6. Unwilling to incentivise precision medicine and orphan disease treatments

Many of the issues with the NICE appraisal can only be addressed by the Department of Health and Social Care.

The DoHSC could have instructed NICE to use the Highly Specialised Technology pathway for Orkambi, due to its orphan status and limited 4,000 potential patients.

The arbitrary price per QALY gained used by NICE are set by the DoHSC. DoHSC could put graduated cost thresholds in place to cover rare and orphan diseases. This would allow costs between the £300,000 and £30,000 cliff.

Issues with NHS England

7. Genetic discrimination

Kalydeco is another drug from Vertex that treats CF for around 500 patients with specific genetic mutations. Kalydeco was appraised by a Health Technology Assessment, conducted by the NHS National Institute for Health Research.

The HTA concluded that Kalydeco had a cost effectiveness of between £335,000 and £1,274,000 per QALY gained. They also concluded that Kalydeco reduced the number of exacerbations by 55%, exacerbations requiring hospitalisation by 36%, and reduced lung decline by 47%.

Kalydeco is available to patients and funded by NHS England.

Since then, Orkambi’s appraisal concluded a cost effectiveness of around £272,265 per QALY gained. It also concluded that Orkambi reduced the number of exacerbations by 40%, exacerbations requiring hospitalisation by 61%, and reduced lung decline by 42%.

Considering the similar clinical effectiveness between Orkambi and Kalydeco, and the similar cost per QALY gained, how can some patients receive treatment and other patients be denied treatment? They are two treatments for the same disease, with the same cost effectiveness. The only difference is the genetic mutation that they treat. The decision to fund treatment is purely on the basis of the patients genes.

NHS England claims to provide ‘Health and high quality care for all’, yet they are applying genetic discrimination.
Issues with Vertex

8. Disengagement with NICE process

Since Vertex's initial application to NICE in 2016, Vertex has not submitted any more evidence or cost effectiveness models for re-appraisal by NICE. This is despite the large amount of clinical research, evidence and understanding of the effects of Orkambi since 2016.

NHS England are unable to negotiate without an understanding of the cost effectiveness of a drug. NICE cannot reevaluate their appraisal without new data and submission from Vertex. So until Vertex reengage with NICE and submit a new application to the NICE committee, we are at a stalemate.

Only Vertex can break this stalemate.

We fear that Vertex are looking to protect their eventual price for their future triple combination therapies. Therefore they may be unwilling to accept a lower price for Orkambi. However in the three years that Orkambi has been licensed by the EMA, over 200 patients that could have potentially benefited from Orkambi have died. Vertex’s triple combination therapy is still in development and it will be years until it could be available for young children, due to trials and licensing starting at 12+ years. In that time, young children could be treated with Orkambi as a bridging treatment until the triple combination treatments are available to them.

Vertex must reengage with NICE, and provide a new cost effectiveness model that includes all the new data since the original 2016 appraisal.

Negotiations on the price of Orkambi must be kept separate from the renegotiations around the price of Kalydeco. Kalydeco’s ongoing price should not hinder the Orkambi negotiations. Vertex should put forward a new case for Orkambi’s cost effectiveness that can be looked at in isolation from Kalydeco or the future triple combination therapies.

9. Reasonable pricing

At Orkambi’s list price, Vertex is asking for almost twice the cost of all current CF standard of care, for 50% of the CF population. That is 2.5% of the total NHS drugs budget for 4,000 patients.

Vertex has to realise the unique situation of CF in the UK. Due to genetic inheritance, the UK has 12% of the global CF population. The UK has 1% of the global population. For common conditions and disease with the same global prevalence, the UK would typically contribute 1% of the global revenue of the available treatment. Asking the UK to contribute 12% of the global revenue for CF treatments places an unfeasible burden on the UK. As the UK branch of Vertex handles the global sales of it Cystic Fibrosis drugs, we are sure that you will be requesting papers that detail the prices and deals they have reached with other countries.

There must be a middle ground that Vertex and NHS England can reach.

10. Tax avoidance

Vertex run their global sales from their UK branch. Last year Vertex took £1.8 billion in turnover in the UK, yet they claimed a £1.8 million tax credit, due to an “operating loss”.

Despite taking £4.1 billion in the last 3 years, they have effectively paid zero UK corporation tax in the last 10 years.

Vertex has been allowed to avoid paying potentially over £600 million to the UK treasury, by transferring profits overseas through ‘licensing fees’ to other Vertex group companies.
11. HMRC Research and Development Credits

Vertex has received over £10 million in research and development credits from HMRC in the last ten years. These credits have been used in the research and development of Orkambi.

How can a company be allowed to receive over £10 million and allowed to avoid over £600 million in corporation tax, but still deny patients access to their drugs through unfeasibly high prices?

Yours sincerely,

Name and address withheld.