HOUSE OF COMMONS LIBRARY

DEBATE PACK

Number CDP 2018/0075, 16 March 2018

Debate on an e-petition relating to access to the drug Orkambi for people with cystic fibrosis

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This pack has been prepared ahead of the debate to be held in Westminster Hall on Monday 19 March 2018 at 4.30 pm on e-petition 209455, *Make Orkambi available on the NHS for people with cystic fibrosis*. The debate will be opened by Paul Scully MP.

Contents

1. Background

Orkambi is the brand name of a medicine (lumacaftor–ivacaftor) that is licenced to treat cystic fibrosis in patients who have a specific genetic mutation causing the disease (called the F508del mutation). In 2016, the National Institute for Health and Care Excellence (NICE) reviewed the use of Orkambi and concluded that it could not recommend it for routine use on the basis that it could not be considered cost-effective.[1]

Since this time, there have been discussions between the pharmaceutical company that makes Orkambi, Vertex, and NHS England regarding the funding of this medicine. It is not routinely funded anywhere in the UK at present.

There has been ongoing campaigning for patient access to Orkambi. A petition on the Government and Parliament Petitions website calls on the Government to bring the negotiations between Vertex, NHS England and NICE to a resolution.[2] At the time of writing, it has been signed by over 114,000 people. The Petitions Committee has considered the petition and tabled a debate on this subject for 19 March 2018. The debate will be led by Paul Scully MP.

2. Cystic Fibrosis

Cystic fibrosis is a genetic condition which results in an increase of mucus in the body. It is caused by a genetic mutation in the CFTR gene. This gene normally works to control the levels of salts in the cells but when this is not working, it results in a build-up of thick mucus which commonly affects the lungs and digestive system.

The build-up of mucus in the lungs of patients with cystic fibrosis, can lead to breathing problems and recurrent infections. Shortness of breath, cough and wheezing are common symptoms. The pancreas is also commonly affected in cystic fibrosis. This can affect its ability to produce the enzymes necessary to break down food and can lead to malnutrition. It can also impact on the production of insulin and cause diabetes. Other organs that can be affected include sinuses, bones and joints, the reproductive system and liver.

Babies are screened for cystic fibrosis at birth using a heel prick test as part of the NHS newborn screening programme. It is estimated that 1 in 2,500 babies will be born with cystic fibrosis in the UK and there are around 10,400 individuals living with this condition in the country.[3]

Treatment for cystic fibrosis usually seeks to manage symptoms. Medications including steroids, antibiotics, insulin and bronchodilator inhalers are often used. Nutritional advice and physiotherapy for airway

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1 NICE, Lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation, July 2016

2 UK Government and Parliament petitions, Make Orkambi available on the NHS for people with Cystic Fibrosis

3 Cystic Fibrosis Trust, Cystic Fibrosis FAQs

clearance are commonly part of management.[4] In October 2017, NICE published updated clinical guidelines on the diagnosis and management of cystic fibrosis.

Prognosis is variable but much improved in recent years. Most people with cystic fibrosis will still have a shorter than average life expectancy. The Cystic Fibrosis Trust reports that, whilst a number of factors will affect this, the median survival for an individual with cystic fibrosis is currently 47 years. It is thought that children born now with the condition will live longer.[5]

Recently, new medicines have been licenced that aim to target the genetic mutations that cause cystic fibrosis. Orkambi is licenced to treat cystic fibrosis in patients who have a specific genetic mutation causing the disease.

3. Orkambi

Orkambi is the brand name of a medicine (lumacaftor–ivacaftor) that is licenced to treat cystic fibrosis in patients who have a specific genetic mutation causing the disease (called the F508del mutation). About 50% of individuals with cystic fibrosis in the UK have this genetic mutation. The initial licence was for use only in patients aged 12 and over, but the manufacturer, Vertex, has recently announced that the EU licence for this medicine has been extended for use in children aged 6 to 11 years.[6]

The Cystic Fibrosis Trust describes how this medicine works:

> Orkambi is a combination medicine, made up of ivacaftor and lumacaftor. Lumacaftor helps get more proteins to the surface of cells in the body, and ivacaftor helps the chloride channels in the cells to operate more effectively. The combination of these two things helps to keep a healthy balance of salt and water in the organs – particularly the lungs.[7]

3.1 NICE assessment

In 2016, the National Institute for Health and Care Excellence (NICE) conducted a technology appraisal (see Box 1) on the use of Orkambi. In July 2016 NICE published its final decision[8]- that Orkambi was not recommended for use on the basis that it could not be considered cost-effective:

> Carole Longson, director of the NICE Centre for Health Technology Evaluation, acknowledged that a new treatment option for people with cystic fibrosis was important. But she added, "For the benefits it offers, the cost of Orkambi is too high. We can only recommend treatments when we are certain they are both clinically effective and represent good value for money. If the

4 NHS Choices, Cystic Fibrosis treatment, February 2018
5 Cystic Fibrosis Trust, Cystic Fibrosis FAQs
6 Vertex, Vertex Receives Expanded EU Approval for ORKAMBI® (lumacaftor/ivacaftor) in Children Ages 6-11 Years, January 2018
7 Cystic Fibrosis Trust, Orkambi
8 NICE, Lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation, July 2016

> company is able to put forward a proposal that provides Orkambi at a cost effective price, we would welcome it."[9]

NICE guidance on Orkambi is scheduled to be reviewed in 2019.

Box 1: NICE Technology Appraisals

NICE produces recommendations, called Technology Appraisals, on whether or not treatments should be routinely commissioned on the NHS. NICE describes the appraisal process as follows:

> We are asked to look at particular drugs and devices when availability varies across the country. This may be because of different local prescribing or funding policies, or because there is confusion or uncertainty over its value. Our advice ends the uncertainty and helps to standardise access to healthcare across the country.[10]

An appraisal can classify a treatment, drug or device as 'recommended' (to be routinely commissioned), 'optimised' (to be commissioned in certain circumstances), 'only in research' or 'not recommended.'

Under the NHS Constitution, the relevant commissioning body (NHS England in the case of specialised treatments, CCGs for most other treatments) is legally obliged to fund treatments recommended by NICE within three months of the publication of the technology appraisal (or longer, if a different time period is specified).

Where there is a NICE recommendation not to fund a treatment routinely, it should be noted that commissioners of NHS services cannot impose a "blanket ban." They must consider exceptional individual cases where funding should be provided and must have procedures in place for deciding what are known as "Individual Funding Requests." Doctors, on behalf of patients, can make an Individual Funding Request for treatment to NHS England or local commissioners for treatments that are not routinely funded. [11]

Vertex and NHS England discussions

A December 2017 Parliamentary question response highlighted that since the 2016 NICE decision, there had been a dialogue between the drug company, Vertex, and NHS England about access to Orkambi:

> In July 2016, the National Institute for Health and Care Excellence (NICE), the independent body that develops guidance on drugs and treatments for clinical and cost effectiveness for the National Health Service in England, was unable to recommend Orkambi as a cost effective use of NHS resources.
>
> Since then there has been a constructive dialogue between the company, NHS England and NICE, including discussion hosted through NICE's confidential 'Office for Market Access', although NICE is yet to receive any fresh proposals from Vertex, the company that manufactures Orkambi. Both NHS England and NICE have been consistent in advice to Vertex, that progress can only be made by working through NICE's appraisal processes and the existing commercial framework.
>
> Any funding decisions in the absence of positive NICE technology appraisal guidance should be made by NHS commissioners based on an assessment of the available evidence and on the basis of an individual patient's clinical circumstances.[12]

9 BMJ, Cystic fibrosis drug is not cost effective, says NICE, June 2016
10 NICE, Technology appraisal guidance
11 NHS England, Individual funding requests for specialised services a guide for patients, November 2017
12 HC Written Question: 119915, Orkambi, 22 December 2017

A new funding proposal

In February 2018, Vertex announced that it had proposed a new 'portfolio approach' to the Government on the funding of Orkambi. The specifics of the proposal have not been made public, but Vertex have said that it offers fair and equal access to precision medicines for cystic fibrosis:

> We share the CF community's sense of urgency on access to new Vertex medicines and we are committed to working with the NHS to find a sustainable funding solution. That is why we have proposed to the Government a bold new portfolio approach that could make our medicines available to patients as soon as possible. It provides budget certainty and value to the NHS – and offers fair and equal access for CF patients to precision medicines that are tailored to specific genetic mutations.
>
> Our proposal follows the recent announcement that two of our triple-combination next generation correctors are going forward into phase III clinical trials. At Vertex we are developing medicines to treat 90% of CF patients who will one day be eligible for treatment able to treat the underlying cause of the disease.
>
> We believe that our approach is a first for England, and a first for the UK. We have already demonstrated it works in other countries – and offers CF patients who could benefit, access to ORKAMBI® (lumacaftor/ivacaftor). The proposed portfolio approach is for England but we continue to engage in meaningful discussions with the devolved nations.[13]

It has been reported that an agreement had been reached in the Republic of Ireland on a similar basis on funding for Orkambi, and another cystic fibrosis medicine, Kalydeco. [14]

The Cystic Fibrosis Trust report that Orkambi is also available in Austria, Denmark, France, Germany, Luxembourg, the Netherlands, Italy, Greece, and the United States.[15]

3.2 Devolved Nations

Scotland

The Scottish Medicines Consortium (SMC) reviews all licensed medicines and makes recommendations on funding to NHS Scotland.[16] The SMC reviewed Orkambi in 2016, and concluded that it could not be recommended for routine use in Scotland. It said that:

> The submitting company's justification of the treatment's cost in relation to its health benefits was not sufficient and in addition the company did not present a sufficiently robust clinical and economic analysis to gain acceptance by SMC.[17]

Vertex, the pharmaceutical company, provide the following information about the ongoing discussions with the SMC in Scotland:

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13 Vertex, Update on access to Vertex CF medicines in England, 15 February 2018
14 Pharmaphorum, Vertex negotiating with NHS England on cystic fibrosis drug access, 20 February 2018
15 Cystic Fibrosis Trust briefing: Your voice: Orkambi and new medicines for cystic fibrosis, 16 February 2018
16 Scottish Medicines Consortium website
17 SMC, lumacaftor-ivacaftor (Orkambi), May 2016

> Vertex met with representatives of the NHS National Procurement Scotland (NPS) and the Scottish Medicines Consortium (SMC) to discuss whether they would be agreeable, in principle, to assessing a portfolio approach. Their feedback to us has been that there are challenges to this as the current policy framework cannot support a portfolio assessment, despite recent changes to access to medicines policy in Scotland designed to make the system more flexible.
>
> Vertex will continue to work with the SMC, to explore all options. As part of this, at the earliest opportunity we will put in a financial proposal for the whole portfolio through these processes.[18]

Wales

In Wales, there is a statutory obligation for local health boards to make medicines available when they have been recommended in NICE technology appraisal guidance.[19]

An October 2017 Welsh Assembly Question response from the Cabinet Secretary for Health, Well-being and Sport, Vaughan Gething AM, set out that there was ongoing discussion with Vertex on Orkambi:

> Orkambi® (lumacaftor/ivacaftor) is indicated for the treatment of cystic fibrosis in patients aged 12 years or older with the F508del gene mutation.
> In 2016, the National Institute for Health and Care Excellence (NICE) re-issued their Technology Appraisal guidance under their "Do Not Do" guidance, emphasising that Orkambi® should not be made routinely available.
> The All-Wales Medicines Strategy Group (AWMSG) has contacted the pharmaceutical company, Vertex Pharmaceuticals, and has strongly encouraged them to make a submission to the AWMSG for appraisal. Whilst Vertex has agreed in principle to submit clinical data for appraisal by AWMSG, they have not committed to any firm date for doing so. However, discussions have commenced with Vertex on the most effective approaches to appraisal for the additional license extensions due to come on stream over the next few years. My officials will ensure the future appraisal of lumacaftor/ivacaftor (Orkambi®) is covered.
> In the interim, the Welsh Health Specialised Services Committee (WHSSC) has agreed a patient access scheme with Vertex Pharmaceuticals and it is available in the Welsh NHS, where clinically appropriate.[20]

Northern Ireland

In Northern Ireland, the Department of Health reviews all NICE technology appraisals for applicability in Northern Ireland before deciding whether to implement them.[21]

In a letter to MLAs in December 2017, Richard Pengelly, the Permanent Secretary of the Department of Health set out that the department had endorsed the NICE technology appraisal on Orkambi and the medicine would not be routinely commissioned in Northern Ireland:

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18 Cystic Fibrosis Trust, Orkambi
19 NHS Wales, Governance e-manual: NICE guidance,
20 Welsh Assembly, Written Question: WAQ74323, October 2017
21 Department of Health, Social Service and Public Safety, Circular HSC (SQSD) 3/13, December 2013

> The Department has a formal link with the National Institute for Health and Care Excellence (NICE) under which NICE Technology Appraisals are reviewed locally for their applicability in Northern Ireland. Where found to be applicable they are endorsed by the Department for implementation within Health and Social Care (HSC). NICE can only recommend that treatments be routinely funded within the NHS when there is clear evidence that they are both clinically effective and represent value for money.
>
> NICE does not recommend the use of lumacaftor and ivacaftor (Orkambi) for treating cystic fibrosis and has published guidance to this effect (TA398). In August 2016 the Department endorsed TA398 as applicable in Northern Ireland. Therefore, Orkambi is not offered as a routinely commissioned treatment for cystic fibrosis in any of the UK jurisdictions.[22]

The letter went on to state that the Health and Social Care Board had met with Vertex to discuss Orkambi, and there may be further meetings in the future.

3.3 Stopping the clock campaign

The Cystic Fibrosis Trust have an ongoing campaign on access to precision medicines for cystic fibrosis patients (such as Orkambi) - Stopping the clock.

The Cystic Fibrosis Trust provides updates on the campaign on its website. The Chief Executive, David Ramsden, has said that the new proposal from Vertex was an important step, and called on the Government to consider the offer:

> The manufacturer claims this approach will help provide equitable access to new Vertex medicines for people with CF in a way that could enable the NHS to budget for the longer-term.
>
> David Ramsden, Chief Executive of the Cystic Fibrosis Trust, said: "After over a year of waiting, this proposal from Vertex is an important step in gaining access to Orkambi for people with CF in the UK. We recognise the hard work required ahead and we appeal to Vertex to be open to discussion and negotiation.
>
> "We also urge the Government to consider this offer seriously and to recognise its significance not just for Orkambi, but for other new, innovative treatments in the CF development pipeline. We will keep pushing to see progress across the whole of the UK and will not stop fighting until all who are eligible have access as soon as possible.
>
> "We call on everyone affected by CF to help us ensure these discussions are robust and ask those willing to help to continue to tell their stories to their MPs, MSPs, AMs, MLAs and ensure that UK governments take responsibility for making progress in negotiations." Visit our campaigning pages to learn how you can help.[23]

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22 Cystic Fibrosis Trust, Vertex proposal for access to Orkambi and other treatments, 15 February 2018 (Hyperlink provided to Vertex statement)

23 Cystic Fibrosis Trust, Vertex proposal for access to Orkambi and other treatments, 15 February 2018

4. The petition

A petition on the Parliament and Government website calls on the Government to bring the negotiations between Vertex, NHS England and NICE to a resolution:

> Conventional CF treatments target the symptoms of CF, precision medicines like Orkambi tackle the cause of the condition. Though Orkambi is not a cure, it has been found to slow decline in lung function, the most common cause of death for people with CF, by 42%
>
> In July 2016, the National Institute of Clinical Excellence (NICE) recognised Orkambi as an 'important treatment.' They were, however, unable to recommend the drug for use within the NHS on grounds of cost effectiveness and a lack of long-term data. We are calling on the British Government to call for a resolution to ongoing negotiations between Vertex Pharmaceuticals, NHS England and NICE as a matter of the utmost urgency. It is essential that a fair and sustainable agreement is found.[24]

The Department of Health and Social Care has responded to the petition. It has said that Ministers are continuing to engage with Vertex, NHS England, NICE and the Cystic Fibrosis Trust to encourage the parties to reach a deal:

> We want patients to benefit from clinically and cost effective treatments. We welcome the dialogue between Vertex and NHS England to agree a deal that would make Orkambi available to NHS patients.
>
> The National Institute for Health and Care Excellence (NICE) is the independent body that provides guidance on the prevention and treatment of ill health and the promotion of good health and social care. NICE produces a range of guidance products, including technology appraisals, clinical guidelines and quality standards. NICE's guidance is based on a thorough assessment of the available evidence and is developed through wide consultation with stakeholders. NHS commissioners are required to fund drugs and treatments recommended by NICE technology appraisals.
>
> NICE published its final guidance on the use of Orkambi in July 2016 and did not recommend it for use in treating Cystic Fibrosis. NICE's appraisal committee concluded that while Orkambi was clinically effective and important for managing cystic fibrosis, the benefits were not sufficient to justify its considerable cost. Officials from NHS England engaged with Vertex (the manufacturer) to explore proposals to secure a pricing structure that would enable a positive recommendation from NICE – however, Vertex was unable to come forward with a viable model that would enable the drug to be funded.
>
> NICE periodically reviews its guidance to determine whether there is significant new evidence that might affect its recommendations. NICE's guidance on Orkambi is scheduled to be reviewed in July 2019. If significant new evidence comes to light before the scheduled date to review the drug, NICE has processes in place to bring forward a review. NICE remains open to a further approach

[24] UK Government and Parliament petitions, Make Orkambi available on the NHS for people with Cystic Fibrosis

from the company, with new evidence or a revised price. Although there has been recent correspondence between NHS England and the company, NICE has not yet received any fresh proposals from the company.

A number of meetings have been held with Vertex, and the Department welcomes any further negotiations between NICE, NHS England and Vertex. Ministers are continuing to engage with Vertex, NHS England, NICE and the Cystic Fibrosis Trust to encourage the responsible parties to reach a deal.

Department of Health and Social Care

5. News items

PharmaTimes.com

Vertex offers 'portfolio approach' to secure access to CF meds

19 February 2018

http://www.pharmatimes.com/news/vertex_offers_portfolio_approach_to_secure_access_to_cf_meds_1222691

The Times [Subscription]

Cystic fibrosis sufferers denied life-prolonging drug by NHS

14 January 2018

https://www.thetimes.co.uk/article/cystic-fibrosis-sufferers-denied-life-prolonging-drug-by-nhs-w062qc5z3

New Scientist

Cystic fibrosis drug halts lung damage in young children

9 June 2017

https://www.newscientist.com/article/2134112-cystic-fibrosis-drug-halts-lung-damage-in-young-children/

BMJ

Cystic fibrosis drug is not cost effective, says NICE

BMJ 2016; 353 doi: https://doi.org/10.1136/bmj.i3409 Cite this as: BMJ 2016;353:i3409

20 June 2016

http://www.bmj.com/content/353/bmj.i3409

6. Press releases

Cystic Fibrosis Trust

Vertex proposal for access to Orkambi and other treatments

15 February 2018

Drug manufacturer Vertex has submitted a proposal to NHS England for access to its current and future CF treatments. The offer, described by Vertex as a 'portfolio approach', is similar to that adopted in the Republic of Ireland, and covers not just Orkambi but also future drugs in the pipeline – including new combination therapy Symdeko (tezacaftor/ivacaftor).

The manufacturer claims this approach will help provide equitable access to new Vertex medicines for people with CF in a way that could enable the NHS to budget for the longer-term.

David Ramsden, Chief Executive of the Cystic Fibrosis Trust, said:

> After over a year of waiting, this proposal from Vertex is an important step in gaining access to Orkambi for people with CF in the UK. We recognise the hard work required ahead and we appeal to Vertex to be open to discussion and negotiation.
>
> We also urge the Government to consider this offer seriously and to recognise its significance not just for Orkambi, but for other new, innovative treatments in the CF development pipeline. We will keep pushing to see progress across the whole of the UK and will not stop fighting until all who are eligible have access as soon as possible.
>
> We call on everyone affected by CF to help us ensure these discussions are robust and ask those willing to help to continue to tell their stories to their MPs, MSPs, AMs, MLAs and ensure that UK governments take responsibility for making progress in negotiations.

Visit our campaigning pages to learn how you can help.

Read the full Vertex statement.

Cystic Fibrosis Trust

Update: Trust demands action over access to medicine

23 January 2018

Following a meeting with Orkambi manufacturer Vertex on Monday, David Ramsden, the Cystic Fibrosis Trust's Chief Executive, has issued a statement demanding action and backing a community-led petition to the Government.

> Yesterday we met with Vertex Pharmaceuticals, the manufacturers of Kalydeco and Orkambi, to demand that they act now and present a bold deal to make their medicines available across the

whole of the UK. It has now been over two years since Orkambi was licensed for use. It is still not available on the NHS and Vertex last submitted an offer over a year ago.

We have met with Vertex a number of times over the last few months and, despite reassurances over progress, we seem to be no closer to a deal being done. Every further day of delay means that damage is being done and lives are being lost that could be prevented.

The government has a vital role to play in making these medicines more widely available. We are pleased that there is a new debate being arranged in the Scottish Parliament, engagement from the Welsh Health Minister and that Ian Austin, MP for Dudley North, is chairing a roundtable meeting for England with supportive MPs and Vertex on 28th February. We will use all of these opportunities to demand that a solution is found.

The voice of people with cystic fibrosis is vital to ensure that Ministers and decision makers around the UK recognise the fundamental importance of addressing this issue. That is why we support a community-led petition to the UK Government that today stands at over 50,000 signatures. Ensuring access to existing medicines and future treatment innovations is our number one priority and we will not stop until that goal has been achieved.

We will continue to share updates on Facebook and on our website over the coming weeks. For information and to join our campaigning efforts, please visit cysticfibrosis.org.uk/joinacampaign.

Vertex

Vertex Receives EU Approval for ORKAMBI® (lumacaftor/ivacaftor) in Children with Cystic Fibrosis Ages 6-11 with Two Copies of the F508del Mutation

10 January 2018

- In Europe, there are approximately 3,400 children ages 6-11 who have two copies of the F508del mutation -

- Existing reimbursement agreements in countries like Ireland will enable rapid access to ORKAMBI; country-by-country reimbursement processes will now begin in other countries-

LONDON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the European Commission has granted extension of the Marketing Authorization for ORKAMBI® (lumacaftor/ivacaftor), the first medicine to treat the underlying cause of cystic fibrosis (CF) in people with two copies of the *F508del* mutation, to include children ages 6 through 11. In Europe, there are approximately 3,400 children ages 6 through 11 with two copies of this mutation. Existing reimbursement agreements in countries such as Ireland will enable rapid access to ORKAMBI for these children.

In other countries across the European Union, Vertex will now begin the country-by-country reimbursement process.

> The innovative long-term agreements we have reached in countries like Ireland will enable eligible children to have rapid access to ORKAMBI, said Simon Bedson, Senior Vice President and International General Manager at Vertex. Where these agreements are not in place, Vertex is committed to working with local authorities so those who could benefit from this medicine are able to do so as quickly as possible.

The European Commission's decision is based on data from two Phase 3 studies of ORKAMBI in children with CF ages 6 through 11 who have two copies of the *F508del* mutation. In 2017, *The Lancet Respiratory* published 24-week data from one of these studies, which demonstrated statistically significant improvements in lung function (as assessed by the absolute change in lung clearance index, or $LCI_{2.5}$,and predicted forced expiratory volume in one second, or $ppFEV_1$) among children treated with ORKAMBI compared to placebo. Improvements in body mass index (BMI) and the Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score were also observed, although they were not statistically significant. Safety data were similar to those observed in an earlier Phase 3 open-label safety study in children ages 6 through 11. The most common adverse events that occurred more frequently among those receiving ORKAMBI compared to placebo were infective pulmonary exacerbation, productive cough, nasal congestion, oropharyngeal pain, abdominal pain upper, headache, upper respiratory tract infection and sputum increased.

> A principal goal of treating CF is slowing the progressive lung damage caused by this life-shortening genetic disease while improving health in the short term, said Professor Marcus Mall, M.D., Director of the Division of Pediatric Pulmonology & Allergology and the Cystic Fibrosis Center at the Heidelberg University Hospital, Germany. Studies of ORKAMBI in children ages 6 through 11 have shown improvements in clinically relevant outcomes, like lung function and weight gain.

About Cystic Fibrosis (CF)

CF is a rare, life-shortening genetic disease affecting approximately 75,000 people across North America, Europe and Australia.

CF is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene. Children must inherit two defective *CFTR*genes — one from each parent — to have CF. There are approximately 2,000 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working or too few CFTR protein at the cell surface. The defective function or absence of CFTR protein results in poor flow of salt and water into and out of the cell in a number of organs. In the lungs, this leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death. The median age of death is in the mid-to-late 20s.

About ORKAMBI® (lumacaftor/ivacaftor)

In people with two copies of the *F508del* mutation, the CFTR protein is not processed and trafficked normally within the cell, resulting in little-to-no CFTR protein at the cell surface. Patients with two copies of the *F508del* mutation are easily identified by a simple genetic test.

ORKAMBI is a combination of lumacaftor, which is designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the F508del-CFTR protein, and ivacaftor, which is designed to enhance the function of the CFTR protein once it reaches the cell surface. ORKAMBI is available as tablets and is typically taken twice per day.

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious and life-threatening diseases. In addition to clinical development programs in CF, Vertex has more than a dozen ongoing research programs focused on the underlying mechanisms of other serious diseases.

Founded in 1989 in Cambridge, Mass., Vertex's headquarters is now located in Boston's Innovation District. Today, the company has research and development sites and commercial offices in the United States, Europe, Canada and Australia. Vertex is consistently recognized as one of the industry's top places to work, including being named to *Science* magazine's Top Employers in the life sciences ranking for eight years in a row. For additional information and the latest updates from the company, please visit www.vrtx.com.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)

Vertex initiated its CF research program in 2000 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. KALYDECO® (ivacaftor), ORKAMBI® (lumacaftor/ivacaftor), tezacaftor, VX-440, VX-152, VX-659 and VX-445 were discovered by Vertex as part of this collaboration.

Special Note Regarding Forward-looking Statements

This press release contains forward-looking statements, as defined in the Private Securities Litigation Reform Act of 1995, as amended, including the quotes in the second and fourth paragraphs of this press release and statements regarding the timing of access to ORKAMBI for patients 6 through 11 and the country-by-country reimbursement approval process. While the company believes the forward-looking statements contained in this press release are accurate, there are a number of factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, risks related to commercializing ORKAMBI for patients 6 through 11 in Europe and the other risks listed under Risk Factors in Vertex's annual report and

quarterly reports filed with the Securities and Exchange Commission and available through Vertex's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

Vertex

Vertex Announces Long-Term Reimbursement Agreement with the Republic of Ireland for ORKAMBI® (lumacaftor/ivacaftor), KALYDECO® (ivacaftor) and Future Cystic Fibrosis Medicines

1 June 2017

-Agreement provides access to ORKAMBI for people who have two copies of the F508del mutation and expands access to KALYDECO for all eligible patients-

LONDON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq:VRTX) today announced it has reached an agreement with the Health Service Executive (HSE) in the Republic of Ireland to fund ORKAMBI® (lumacaftor/ivacaftor) for all of the approximately 500 people in Ireland with cystic fibrosis (CF) ages 12 and older who have two copies of the *F508del* mutation. The agreement also expands access to KALYDECO® (ivacaftor) for children ages 2 to 5 with any approved gating mutation (*G551D*, *G178R*, *S549N*, *S549R*, *G551S*, *G1244E*, *S1251N*, *S1255P* and *G1349D*) and to people ages 18 and older who have an *R117H* mutation. These reimbursements are effective immediately. This innovative long-term agreement also enables rapid access for people with these mutations if the labels of the existing medicines are expanded to cover additional age groups and if new Vertex medicines are approved for these populations.

> We are pleased that these additional Irish CF patients will finally join the thousands of others around the world who are already benefitting from ORKAMBI and KALYDECO, said Simon Bedson, Senior Vice President and International General Manager at Vertex. We thank the leaders in Ireland for working with us toward an innovative reimbursement agreement that provides access to these important medicines and also recognizes the need for Vertex's continued investment in the research and development of new medicines for those people with CF, many of whom are still waiting for a treatment for the underlying cause of the disease.

CF is a rare and life-shortening genetic disease caused by a defective or missing cystic fibrosis transmembrane conductance regulator (CFTR) protein resulting from a mutation in the *CFTR* gene. ORKAMBI and KALYDECO are the first two medicines that treat the underlying cause of CF. Ireland has the highest rate of CF in the world, with approximately one in 19 Irish people carrying a disease-causing mutation in one copy of the *CFTR* gene.

In addition to Ireland, ORKAMBI is available to all eligible patients in Austria, Denmark, France, Germany, Luxembourg and the United States.

People in 27 countries are benefitting from KALYDECO. Vertex remains actively involved in additional reimbursement discussions globally, with the goal of making these transformative medicines available to all eligible patients as soon as possible.

About ORKAMBI® (lumacaftor/ivacaftor) and the F508del mutation

In people with two copies of the *F508del* mutation, the CFTR protein is not processed and trafficked normally within the cell, resulting in little-to-no CFTR protein at the cell surface. Patients with two copies of the *F508del* mutation are easily identified by a simple genetic test.

ORKAMBI is a combination of lumacaftor, which is designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the F508del-CFTR protein, and ivacaftor, which is designed to enhance the function of the CFTR protein once it reaches the cell surface. ORKAMBI is available as tablets and is typically taken twice per day.

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

About KALYDECO® (ivacaftor)

KALYDECO® (ivacaftor) is the first medicine to treat the underlying cause of CF in people with specific mutations in the *CFTR* gene. Known as a CFTR potentiator, ivacaftor is an oral medicine that aims to help the CFTR protein function more normally once it reaches the cell surface, to help hydrate and clear mucus from the airways.

For complete product information, please see the Summary of Product Characteristics that can be found at www.ema.europa.eu.

About CF

CF is a rare, life-shortening genetic disease affecting approximately 75,000 people in North America, Europe and Australia.

CF is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. There are approximately 2,000 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working or too few CFTR proteins at the cell surface. The defective function or absence of CFTR protein results in poor flow of salt and water into and out of the cell in a number of organs. In the lungs, this leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death. The median age of death is in the mid-to-late 20s.

About Vertex

Vertex is a global biotechnology company that aims to discover, develop and commercialize innovative medicines so people with serious diseases can lead better lives. In addition to our clinical development programs

focused on cystic fibrosis, Vertex has more than a dozen ongoing research programs aimed at other serious and life-threatening diseases.

Founded in 1989 in Cambridge, Mass., Vertex today has research and development sites and commercial offices in the United States, Europe, Canada and Australia. For seven years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences. For additional information and the latest updates from the company, please visit www.vrtx.com.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)

Vertex initiated its CF research program in 2000 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. KALYDECO® (ivacaftor) and ORKAMBI® (lumacaftor/ivacaftor) were discovered by Vertex as part of this collaboration.

Special Note Regarding Forward-looking Statements

This press release contains forward-looking statements, as defined in the Private Securities Litigation Reform Act of 1995, as amended, including the quote in the second paragraph of this press release and statements regarding the country-by-country reimbursement approval process. While the company believes the forward-looking statements contained in this press release are accurate, there are a number of factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, risks related to commercializing ORKAMBI and the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through Vertex's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

(VRTX-GEN)

7. Parliamentary material

Orkambi

Asked by: Linden, David

To ask the Secretary of State for Health and Social Care, with reference to the Government's response to e-petition 209455, on making Orkambi available on the NHS for people with cystic fibrosis, if he will place copies of the correspondence between NHS England and Vertex in the Library.

Answering member: Steve Brine | Department: Department of Health and Social Care

NHS England has advised that the correspondence requested is commercially sensitive and therefore it would not be appropriate to release this information.

HC Deb 27 February 2018 | PQ 128238

Orkambi: Republic of Ireland

Asked by: Linden, David

To ask the Secretary of State for Health and Social Care, pursuant to the Answer of 19 January 2018 to Question 122358, on Orkambi: Republic of Ireland, if he will place copies of that correspondence in the Library.

Answering member: Steve Brine | Department: Department of Health and Social Care

Copies of correspondence from the Government of the Republic of Ireland dated 28 November and 7 December 2016 and from my Rt. hon. Friend the Secretary of State to the Government of the Republic of Ireland dated 13 January 2017, on Orkambi are attached.

PQ 128237 attached document 1

PQ 128237 attached document 2

PQ 128237 attached document 3

HC Deb 27 February 2018 | PQ 128237

Orkambi

Asked by: Field, Frank

To ask the Secretary of State for Health and Social Care, what recent assessment his Department has made of the potential effect on patients with cystic fibrosis of making Orkambi available on the NHS; and if he will make a statement.

Answering member: Steve Brine | Department: Department of Health and Social Care

The National Institute for Health and Care Excellence (NICE) is responsible for making decisions on the clinical and cost effectiveness of treatments. These can be very difficult decisions, and are made on the basis of very careful consideration of the evidence and public consultation. After considering the feedback from its consultation, NICE issued guidance in July 2016 which did not recommend Orkambi to treat cystic fibrosis. The decision was based on the evidence and price proposal provided by Vertex at the time of the appraisal.

The guidance will be reviewed again in 2019. This review can be brought forward where there is new evidence that is likely to impact on the current recommendations, or if the company puts forward a proposal that demonstrates their drug is cost-effective.

HC Deb 22 February 2018 | PQ 128042

Orkambi

Asked by: Blunt, Crispin

To ask the Secretary of State for Health and Social Care, with reference to the extension of Orkambi's licence to treat patients aged six and over, what support his Department is giving to further negotiations among NICE, NHS England and the drug manufacturer, Vertex, on access to that medicine for people with cystic fibrosis.

Answering member: Steve Brine | Department: Department of Health and Social Care

The Department wants patients with cystic fibrosis to benefit from clinically and cost effective treatments, and we welcome the on-going dialogue between Vertex and NHS England to pursue a deal that would make Orkambi available to National Health Service patients.

HC Deb 24 January 2018 | PQ 122992

Orkambi

Asked by: Linden, David

To ask the Secretary of State for Health and Social Care, if he will make an estimate of the potential savings accruing to the public purse from reduced hospital admissions in the event that Orkambi were to be made available on the NHS.

Answering member: Steve Brine | Department: Department of Health and Social Care

The Department has made no estimate. Through its technology appraisal programme, the National Institute for Health and Care Excellence (NICE) provides authoritative, evidence-based guidance for the National Health Service on whether drugs and other treatments represent a clinically and cost effective use of resources. In developing

its guidance, NICE takes into account all the costs and savings associated with the treatment.

HC Deb 19 January 2018 | PQ 122336

Orkambi

Asked by: Linden, David

To ask the Secretary of State for Health and Social Care, what estimate he has made of the number of people with cystic fibrosis who would be eligible for treatment with the drug Orkambi if it were available on the NHS.

Answering member: Steve Brine | Department: Department of Health and Social Care

The number of patients aged 12 and over with cystic fibrosis homozygous for the F508del mutation, in the National Institute for Health and Care Excellence's (NICE) guidance, that might be eligible for treatment with Orkambi (lumacaftor-ivacaftor) under its marketing authorisation was estimated to be approximately 4,000 during the topic selection considerations that led to the referral of Orkambi to NICE.

HC Deb 19 January 2018 | PQ 122316

Orkambi

Asked by: Penning, Sir Mike

To ask the Secretary of State for Health, what steps he is taking to help patients with cystic fibrosis to access the drug Orkambi; and if he will make a statement.

Answering member: Steve Brine | Department: Department of Health

In July 2016, the National Institute for Health and Care Excellence (NICE), the independent body that develops guidance on drugs and treatments for clinical and cost effectiveness for the National Health Service in England, was unable to recommend Orkambi as a cost effective use of NHS resources.

Since then there has been a constructive dialogue between the company, NHS England and NICE, including discussion hosted through NICE's confidential 'Office for Market Access', although NICE is yet to receive any fresh proposals from Vertex, the company that manufactures Orkambi. Both NHS England and NICE have been consistent in advice to Vertex, that progress can only be made by working through NICE's appraisal processes and the existing commercial framework.

Any funding decisions in the absence of positive NICE technology appraisal guidance should be made by NHS commissioners based on an assessment of the available evidence and on the basis of an individual patient's clinical circumstances.

HC Deb 22 December 2017 | PQ 119915

Orkambi

Asked by: Penning, Sir Mike

To ask the Secretary of State for Health, what assessment he has made of the effect on young people with cystic fibrosis of making the drug Orkambi available on the NHS.

Answering member: Steve Brine

Through its technology appraisal programme, the National Institute for Health and Care Excellence (NICE) provides authoritative, evidence-based guidance for the National Health Service on whether drugs and other treatments represent a clinically and cost effective use of resources. NHS organisations are legally required to make funding available for drugs and treatments recommended in NICE technology appraisal guidance.

NICE published technology appraisal guidance in July 2016 that does not recommend Orkambi as a clinically and cost effective use of NHS resources. NICE concluded that, although clinically significant for managing cystic fibrosis, the longer term outcomes and benefits were not sufficient to justify its considerable costs. Orkambi is not therefore routinely available to NHS patients with cystic fibrosis.

HC Deb 22 December 2017 | PQ 119914

Orkambi

Asked by: Lake, Ben

To ask the Secretary of State for Health, what discussions he has had with cystic fibrosis charities on the effectiveness of Orkambi.

Answering member: Steve Brine | Department: Department of Health

The Parliamentary Under Secretary of State (Lord O'Shaughnessy) met with the Cystic Fibrosis Trust on 7 March 2017 following on from an adjournment debate in December 2016 on "Implications of the Accelerated Access Review for Cystic Fibrosis and other Conditions" to discuss Orkambi. However, it is for the National Institute for Health and Care Excellence as the independent body that provides guidance on the prevention and treatment of ill health and the promotion of good health and social care to make decisions on the clinical and cost effectiveness of treatments.

HC Deb 22 December 2017 | PQ 119828

Orkambi

Asked by: Lake, Ben

To ask the Secretary of State for Health, how many people with cystic fibrosis have been prescribed Orkambi in (a) England and (b) Wales in each of the last five years.

Answering member: Steve Brine | Department: Department of Health

No prescriptions for Orkambi have been submitted to the NHS Business Services Authority and NHS Digital in each of the last five years in England. We do not hold any data for Wales.

HC Deb 22 December 2017 | PQ 119827

Orkambi

Asked by: Penning, Sir Mike

To ask the Secretary of State for Health, what steps the Government is taking to ensure that the drug Orkambi is made available on the NHS to people in England with Cystic Fibrosis who have been waiting two years for that prescription; and will he make a statement.

Answering member: Steve Brine | Department: Department of Health

In July 2016, the National Institute for Health and Care Excellence (NICE), the independent body that develops guidance on drugs and treatments for clinical and cost effectiveness for the National Health Service in England, was unable to recommend Orkambi as a cost effective use of NHS resources. NICE concluded that, although clinically significant for managing cystic fibrosis, the longer term outcomes and benefits were not sufficient to justify its considerable costs. Orkambi is not therefore routinely available to NHS patients with cystic fibrosis.

Since then there has been a constructive dialogue underway between the company, NHS England and NICE, including discussion hosted through NICE's confidential 'Office for Market Access', although NICE is yet to receive any fresh proposals from Vertex, the company that manufactures Orkambi. Both NHS England and NICE have been consistent in advice to Vertex, that progress can only be made by working through NICE's appraisal processes and the existing commercial framework.

Any funding decisions in the absence of positive NICE technology appraisal guidance should be made by NHS commissioners based on an assessment of the available evidence and on the basis of an individual patient's clinical circumstances.

HC Deb 21 December 2017 | PQ 119618

Orkambi

Asked by: Lord Wigley

Her Majesty's Government whether they plan to allow the prescription of the drug Orkambi for cystic fibrosis sufferers under the age of 12; and if not, why not.

Answering member: Lord O'Shaughnessy | Department: Department of Health

Orkambi does not have a marketing authorisation in the United Kingdom for use in the treatment of children aged under 12 with cystic fibrosis. Where clinically appropriate and subject to the relevant commissioner making funding available, Orkambi may be prescribed as an off-label drug. Off-label prescribing is supported in guidance given to prescribers by both the General Medical Council and by the Medicines and Healthcare Products Regulatory Agency.

HC Deb 11 July 2017 | PQ HL251

8. Useful links and further reading

NHS Choices: Cystic fibrosis

https://www.nhs.uk/conditions/cystic-fibrosis/

National Institute for Health & Care Excellence (NICE) Technology Appraisal Guidance *Lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation* 27 July 2016

https://www.nice.org.uk/Guidance/TA398

Cystic Fibrosis Trust *Stopping the Clock* campaign

https://www.cysticfibrosis.org.uk/the-work-we-do/campaigning-hard/stopping-the-clock

NICE Guideline *Cystic fibrosis: diagnosis and management* October 2017

https://www.nice.org.uk/guidance/ng78

DEBATE PACK
CDP 2018/0075
16 March 2018

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