

Dr Sarah Wollaston MP  
Chair, Health & Social Care Committee  
House of Commons  
London  
SW1A 0AA

Specialised Commissioning  
Skipton House  
80 London Road  
London  
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16<sup>th</sup> January 2019

Dear Dr Wollaston

### **Health & Social Care Committee Inquiry: Vertex Pharmaceuticals**

Thank you for inviting NHS England to provide any further comments in relation to the above inquiry and for sharing, confidentially, the documents Vertex and NICE disclosed to the Committee. You also asked us to provide a memorandum explaining how ivacaftor (Kalydeco) came to be made available to English NHS patients, and what the current situation is regarding its availability. This is included at **Annex A**.

I believe the documents we provided to the Committee towards the end of last year provide a full and, I hope, clear account of NHS England's position with regards to the funding and assessment of Vertex's portfolio of medicines for the treatment of cystic fibrosis (CF). However, I thought it may be helpful to highlight the following points:

- **CF is a severe, devastating and progressive disease. That is why we have made an unprecedented offer on behalf of the NHS to fund the Vertex CF portfolio.** Importantly, our offer is intended to complement the NICE appraisal process, rather than act as a substitute for it. That is why the offer is contingent on Vertex re-submitting lumacaftor/ivacaftor (Orkambi) to NICE for re-appraisal alongside any new evidence following its unsuccessful appraisal in 2016; re-engaging with the NICE appraisal of tezacaftor/ivacaftor (Symkevi) which has been suspended as a result of non-submission by Vertex; and, fully engaging, at the appropriate point, with the NICE appraisal of future triple therapies. However, the design of our July offer would still mean immediate access for patients and reimbursement for Vertex to all existing licensed treatments and future pipeline products (once licensed), and in advance of the individual NICE appraisals concluding.
- **NICE has a world-class, robust and transparent process for evaluating health technologies in the UK.** Working together, we are resolute in our efforts to introduce health technologies which deliver clinically meaningful outcomes to NHS patients and at costs which ensure value for money for tax-payers.
- **NHS England has offered unprecedented commercial flexibility to Vertex, and NICE has clarified its methods, and the flexibilities they allow for .** This process treats patients and manufacturers equitably. There is nothing particularly unusual about Vertex as a company or their products that justifies treating them exceptionally. To do so would be fundamentally unfair in terms of opportunity cost, would result in setting an unsustainable financial precedent and represent poor value for money

through a deliberate decision not to maximise health gain for the population of England.

- **The rare disease market place has evolved significantly since the introduction of ivacaftor in 2012. Rare Disease UK estimate that 1 in 17 people, or almost 6% of the population, will be affected by a rare disease at some point in their lives.** Although patient numbers for individual rare diseases may be relatively small, taken as a totality, the budget impact is huge. Cystic Fibrosis is the most common, life-limiting, recessively inherited disease in the UK, affecting approximately 10,500 people (8,700 in England). If companies like Vertex continue to price products significantly above the value they bring, then the situation is unsustainable. Vertex is an extreme outlier in terms of both its pricing and behaviour.
- **Other pharmaceutical companies are working constructively with NHS England and NICE to manage the affordability challenges posed by certain new medicines, even when these are being offered at a cost-effective price.** In contrast, the prices being demanded by Vertex don't come close to meeting the cost effectiveness thresholds that all other companies are working towards. Even if the prices being demanded by Vertex were considered a cost-effective use of NHS resources, it would be negligent for the NHS not to try and manage the affordability challenge their introduction would pose. That is why, with NICE, we introduced a budget impact test in April 2017 to help manage the affordability challenges posed by cost-effective treatments that have a budget impact of more than £20m in any of the first three years of introduction. Nevertheless, the offer we have made to Vertex requires no further reductions to manage the affordability challenges posed.

Finally, I have enclosed at **Annex B** a letter I recently sent to Dr Leiden, Chief Executive of Vertex. This letter reaffirms that the offer we made in July last year remains on the table, but with one small, but important, modification that could potentially result in Vertex generating revenues in excess of the upfront prices we are prepared to agree ahead of the NICE appraisals.

If you have any further questions or queries in advance of the oral evidence session, please do not hesitate to contact me.

Yours sincerely



**John Stewart**

**National Director, Specialised Commissioning**

**NHS England**

## COMMERCIAL IN CONFIDENCE

### ANNEX A

#### MEMORANDUM

#### Commissioning & Funding of Ivacaftor (Kalydeco) for the Treatment of Cystic Fibrosis (CF)

1. This memorandum responds to a request from the Health & Social Care Committee of the House of Commons to NHS England to explain how ivacaftor (Kalydeco) came to be made available to English NHS patients, and what the current situation is regarding its availability.

#### Context

2. The original decision and commercial arrangements underpinning the commissioning of ivacaftor pre-date the full establishment of NHS England from 1<sup>st</sup> April 2013. Although the clinical benefit for indicated patients is well documented, the commercial arrangements put in place at the time are unlikely to represent good value for money – particularly when viewed under a more sophisticated commercial lens and a greater knowledge of the orphan disease market.
3. Whilst the offer NHS England made in July 2018 does not seek to recover any overpayment the NHS may have made since 2013, it does seek to ensure that the entire Vertex portfolio is commissioned at a cost-effective price going forward. This includes ivacaftor, given that it is a key component of all subsequent treatments (indicated for much larger population groups), including the triple therapy.

#### NHS England's Current Commissioning Position

4. Tables 1 and 2 below summarise NHS England's current commissioning policies with respect to ivacaftor and the timelines for when these came into effect.

**Table 1: NHS England's current commissioning policies relating to ivacaftor**

Product	CF Mutation	NHS Policy Criteria
Ivacaftor	9 named CF "gating" mutations	Routinely Commissioned - as per marketing authorisations at least one copy of the named mutations for people aged 2 years and above
Ivacaftor	CF R117H mutation	Not Routinely Commissioned pending policy decision

**Table 2: Timelines for NHS England’s commissioning of ivacaftor for named mutations since 2013**

Product	CF Mutation	%of CF population	NHS Policy Criteria	Date Commissioned
Ivacaftor	Single CF G551D mutation	4%	As per marketing authorisation at least one copy of the named “gating” mutation for people aged 6 years and over	1.1.2013 Free supply 1.4.2013 Funded supply
Ivacaftor	G551D mutation plus 8 named mutations	5%	As per marketing authorisation at least one copy of the 9 named “gating” mutations G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, G1349D, for people aged 6 years and over	July 2015 Funded supply
Ivacaftor	Extension of age range across same 9 mutations	6%	As per marketing authorisations at least one copy of the 9 named “gating” mutations for people from aged 2 to 5 years in addition to 6 years and over	December 2016 Funded supply
Ivacaftor	CF R117H mutation	3%	Proposed as per marketing authorisation: two copies of the R117H mutation for people aged 18 years and over	Policy in draft and paused pending wider discussions on Vertex drug portfolio

**The NHS commissioning context when ivacaftor received its first marketing authorisation**

5. During 2012, Vertex was granted a marketing authorisation for a new drug called ivacaftor for use in patients with CF for the G551D gene mutation. During the development of ivacaftor, the manufacturer, Vertex, requested that it be evaluated by the National Institute for Health and Clinical Excellence (NICE) to achieve Technology Appraisal Guidance on the funding of the drug in the NHS, but the product did not meet its criteria for evaluation. The company then requested that the Advisory Group for National Specialised Services (AGNSS) evaluate the drug. However, the CF service, and hence the drug, did not meet the AGNSS criteria for a service that required national or highly specialised commissioning arrangements. Whilst the drug had been granted ‘orphan’ status, at that time, NICE was not responsible for evaluation of such drugs, though this is now the case.
6. Prior to April 2013, the commissioning of individual specialised services was not consistent across England, with statutory responsibility resting with individual Primary Care Trusts (PCTs). By 2012, PCTs were supported in discharging this function by ten Specialised Commissioning Groups (SCGs). These groups, which advised on (or commissioned) specialised services, were not legal entities and for this reason were hosted by and operated through PCTs according to local arrangements. The 2012 Health and Social Care Act reforms led to changes in NHS commissioning structures which resulted in SCGs being dissolved. From 1<sup>st</sup> April 2013, a new national

commissioning organisation, the NHS Commissioning Board (now referred to as NHS England), became responsible for the direct commissioning of prescribed specialised services, which included CF.

7. 2012/13 represented a transitional year, during which time specialised services, including the work of the ten SCGs, began to be overseen by four shadow NHS regions which, from 1st April 2013, would become the four NHS England regional teams we have today. During this transitional period, there were no formal or established mechanisms for developing national policy for specialised services.

### **The NHS decision-making processes that delivered commissioning of ivacaftor in 2012/13**

8. Following confirmation that neither NICE or AGNSS would provide guidance on the commissioning of ivacaftor, Vertex were directed to the specialised commissioner who provided national advice on CF, based in the Yorkshire and Humber SCG team, to determine potential routes for commissioning during 2012.
9. As approximately 300 of the total CF patient population in England were expected to be eligible for ivacaftor, a nationally co-ordinated approach was considered necessary to ensure consistency of decision making across England in advance of the new commissioning structures being fully in place. Therefore, the Yorkshire and the Humber Office of the North of England SCG, offered to lead on developing the commissioning approach for ivacaftor and to coordinate this across the other SCGs.
10. The CF commissioner secured agreement across the 10 SCG teams to commission an independent Health Technology Appraisal (HTA), similar to those employed by NICE, to evaluate the clinical and cost effectiveness of ivacaftor for the G551D mutation in people over 6 years of age.
11. To support consideration of the HTA output, a Clinical Priorities Advisory Group (CPAG) was established in mid-2012 (this group has evolved in function and purpose but remains in the current NHS England Specialised Services governance structure). The group met twice, and although a full health-economics assessment had been commissioned (and was considered), the decision-making framework from the former "AGNSS" Board was used to inform the SCG's recommendations to the four shadow NHS Commissioning Board Regional Boards in December 2012. A newly formed national Clinical Reference Group for CF was also asked to contribute to the CPAG process as a new body with a remit to provide national clinical advice to commissioners of specialised services which included patient members.
12. The recommendation was that ivacaftor be commissioned provided an agreement was reached with Vertex which discounted the list price of £182,625 per patient per year. The conclusion highlighted the commissioner concerns about the extremely high cumulative costs given the lifetime nature of the treatment. Further work to limit financial risk to the NHS was an absolute requirement prior to approval of the policy by the shadow NHS Regional Boards. An agreement was reached, and the drug became available from 1<sup>st</sup> January 2013.

## The decision-making process for commissioning of ivacaftor after 1<sup>st</sup> April 2013

13. The 1<sup>st</sup> January 2013 policy position covered a single CF gating mutation, G551D, affecting 4% of the population. In 2014, NHS England's CPAG reviewed the legacy CF policy agreed prior to NHS England's inception. No changes were made to the clinical content, but the NHS England version of the policy was published.
14. Vertex then secured further marketing authorisations for an additional 8 gated CF mutations and an extension of the age range to include 2 to 5-year olds which provided coverage to an additional 2% of the CF population. NHS England's Specialised Commissioning Team was asked to consider these 2 separate proposals through its policy programme and the NHS England CPAG processes applicable at the time, which included consideration of clinical effectiveness, patient benefit and affordability against the other developments being considered within specialised services.
15. In 2017, NHS England also agreed to develop a policy proposal for ivacaftor for patients aged 18 years and above with the R117H CF mutation in line with the recent license extension. NHS England now directly commissions NICE to support the policy development for licensed products commissioned as part of specialised services (but which aren't the subject of a full NICE Technology Appraisal). This proposal is paused pending the wider discussions about the Vertex drug portfolio as ivacaftor for this cohort was part of the portfolio deal that Vertex proposed, and NHS England included in its offer.

## NHS Commercial Agreements with Vertex for ivacaftor

16. The original 2012 commercial in confidence agreement with Vertex included free supply of ivacaftor between 1<sup>st</sup> January 2013 and 31<sup>st</sup> March 2013 after which point it became NHS funded with a [REDACTED]<sup>1</sup> discount per patient giving a discounted price of [REDACTED]<sup>2</sup> per patient per year. This scheme was agreed until 31<sup>st</sup> March 2016 with a review in autumn 2015, and with any change in the EU marketing authorisation for ivacaftor prior to the review date triggering an immediate review.
17. When NHS England reviewed the 2013 policy at CPAG in September 2014, it was noted the agreement had been referred to as a "Patient Access Scheme" and this was changed to accurately describe it as a "Commercial in Confidence" agreement.
18. The policy for ivacaftor was reviewed in July 2015 following extension of the marketing authorisation for ivacaftor for a total of 9 mutations. At this time, a new price deal was agreed to maintain the same discounted pack price, but to cap total expenditure for ivacaftor at [REDACTED]<sup>3</sup> for three years to 31<sup>st</sup> March 2018. Although Vertex did not sign a new agreement following approval of the new policy by NHS England in July 2015, this was the pricing and invoicing model applied.
19. Vertex did not agree that ivacaftor treatments for children aged 2 to 5 years would be incorporated into the same capped agreement, but did agree to the same discounted price. Once again, Vertex did not sign a new agreement to cover this arrangement following approval of the new policy by NHS England in December 2016, but this was the pricing and invoicing model applied.

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<sup>1</sup> Figure supplied to the Committee – not published

<sup>2</sup> Figure supplied to the Committee – not published

<sup>3</sup> Figure supplied to the Committee – not published

COMMERCIAL IN CONFIDENCE



ANNEX B

SUBJECT TO CONTRACT

Specialised Commissioning  
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14th January 2019

Dear Dr Leiden

I am writing to reaffirm that the commercial offer NHS England proposed in July 2018 for reimbursement of Vertex's portfolio of cystic fibrosis treatments remains on the table. However, we would like to propose one modification in light of recent clarifications provided to you by NICE around their methods and what flexibilities are available to NICE appraisal committees.

As you know, the commercial offer we made in July is intended to complement the NICE appraisal process rather than act as a substitute for it. Nevertheless, its design would mean immediate access for patients to all existing licensed treatments and future pipeline products once licensed, and in advance of the individual NICE appraisals concluding.

Part of the proposed contractual terms of the July offer was that the same contractual prices would be used in the NICE value assessment of each product. In the event that NICE concluded these prices resulted in an ICER above £30,000/QALY, the contract prices would be reduced prospectively to reflect an ICER at this level which represents the upper end of the standard cost-effectiveness range used by NICE to determine cost-effectiveness.

We have noted that, in certain exceptional circumstances, NICE committees may recommend a treatment above the upper limit of the standard threshold as set out in the NICE Methods Guide (6.3.3). Furthermore, we have noted that in certain exceptional circumstances, NICE committees may apply a discount rate of 1.5% for both costs and benefits, again set out in the NICE Methods Guide (6.2.19).

In light of these clarifications, we think it would be reasonable to adjust our offer such that Vertex could submit to NICE for consideration alternative prices to those agreed upfront with NHS England. The contractual prices would then be modified prospectively either upwards or downwards depending on the level at which the NICE Committee would recommend each treatment as a cost-effective use of NHS resources. As stated in the July deal, the agreement would reflect a single price per medicine and any pricing flexibility is contingent on full engagement with the NICE process.

I am sharing a copy of this letter with Dr Sarah Wollaston, Chair of the Health & Social Care Committee of the House of Commons and Sir Andrew Dillon, Chief Executive of NICE.

Yours sincerely

A handwritten signature in black ink, appearing to read 'John Stewart', written in a cursive style.

**John Stewart**

**National Director, Specialised Commissioning**

**NHS England**