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Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	A01X01		
Policy Title	Ivacaftor for children aged 2-5 years with cystic fibrosis (named mutations)		
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Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
K1 Current Patient Population & Demography / Growth	K 1.1 What is the prevalence of the disease/condition?	K1.1 This policy proposes to **routinely commission** the use of ivacaftor in children aged 2 to 5 with cystic fibrosis. Cystic fibrosis (CF) is a common life-limiting, inherited disease. It has an estimated carrier rate of 1 in 25[i] and an incidence of 1 in 2,500 live births,[ii] with 7,900 to 8,900 people in England affected.[iii] [iv] More specifically, the prevalence amongst the age group in which the treatment is intended for – those between the age of 2 and 5 – is estimated at between 910 and 1,020 in England in 2014/15.[v] [vi]
	K.1.2 What is the number of patients currently eligible for the treatment under the proposed	K1.2 The target population refers to children aged 2-5 years with cystic fibrosis that have at least one copy of the G551D mutation as well as other

	policy?	gating mutations.[vii] The G551D mutation affects roughly 5.7% of patients, while the other gating mutations affect less than 0.3% of CF patients in the UK.[viii] Currently, the CF Registry has a total of 45 patients aged 2-5 registered with these gating mutations in England.[ix] Therefore the current (2014/15) target population for ivacaftor under the policy is 45.
	K1.3 What age group is the treatment indicated for?	K1.3 The treatment is indicated for children aged 2 to 5.
	K1.4 Describe the age distribution of the patient population taking up treatment.	K1.4 The policy relates to the narrow range of those aged 2 to 5 years old. No distribution effects have been identified within the group. Cystic fibrosis is distributed evenly between the sexes and it tends to be more prevalent amongst Caucasians than other ethnicities.[x]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Currently, there are estimated to be three children aged 2-5 that are receiving **ivacaftor**.[xi] The **other current treatments** for this group include (estimated activity rates for the target population in parentheses):[xii] • Specialist dietary advice and enzyme replacement therapies (100%) • Nutritional supplements (less than 20%) • Regular chest physiotherapy (100%) • Oral antibiotics (100%) • Intravenous antibiotics (30%) • Inhaled antibiotics (30 - 40%)

		• Medicines, such as dornase alfa and azithromycin (less than 10%) to reduce inflammation in the lungs, relieve bronchospasm, and alleviate viscosity of mucus in the airways. The cost of activity for the above treatments is dependent on the severity of the symptoms for the patient population.[xiii] The majority (c. 85%) of paedeatric patients are in the lower severity bands (Band 1 - 2A[xiv]). Therefore it can be estimated that around 85% of patients would:[xv] • have up to 56 days of IV antibiotic use a year; • spend up to 14 days in hospital a year.
	K1.6 What is the projected growth of the disease/condition prevalence (prior to applying the new policy) in 2, 5, and 10 years?	K1.6 No change to the future prevalence rate is anticipated; however, the prevalent population identified in K1.1 would grow in line with population growth.[xvi] For the 2-5 year old cohort, it is estimated to be in the region of: • ~923 to 1,035 patients in 2016/17 (year 1) • ~926 to 1,039 patients in 2017/18 (year 2) • ~934 to 1,048 patients in 2020/21 (year 5) The target population in future years depends on the number of patients entering and leaving the 2-5 cohort each year. Assuming that around 11 patients enter the cohort each year[xvii] and that those aged 5 in each year leave the cohort,[xviii] the total number of patients is estimated in the region of:[xix] • ~54 patients in 2016/17 (year 1) • ~51 patients in 2017/18 (year 2) • ~46 patients in 2020/21 (year 5)
	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2,5 and 10 years	K1.7 The activity for **ivacaftor** for this age group would be close to zero in the absence of a policy, as the few patients currently receiving the drug following clinical trials would move into the policy for those six and older in the coming years.

		Activity rates for **other treatments** would remain the same as set out in K1.5, and the level of activity would grow in line with the growth rates set out in K1.6.
	K1.8 How is the population currently distributed geographically?	K1.8 Across England – based on the evidence reviewed, no significant geographical differences in the disease have been identified.
K2 Future Patient Population & Demography	K2.1 Does the new policy: move to a non-routine commissioning position / substitute a currently routinely commissioned treatment / expand or restrict an existing treatment threshold / add an additional line / stage of treatment / other?	K2.1 This policy expands an existing treatment threshold from those aged six years and older to those aged 2 to 5.
	K2.2 Please describe any factors likely to affect growth in the patient population for this intervention. (e.g. increased disease prevalence, increased survival)	K2.2 The age at which children are diagnosed with the specific mutation that ivacaftor targets could affect the growth in the eligible patient population. However, CF is typically diagnosed at an early age.[xx]
	K 2.3 Are there likely to be changes in geography/demography of the patient population and would this impact on activity/outcomes? If yes, provide details.	K2.3 None identified.
	K2.4 What is the resulting expected net increase or decrease in the number of patients who will access the treatment per year in year 2, 5 and 10?	K2.4. Under the policy, there is expected to be an increase in the number of patients taking up the treatment (ivacaftor). Currently, the number of patients accessing the treatment each year is expected to be close to nil as set out in K1.7. As compared to the do nothing case, every year the number of patients on ivacaftor is estimated to be in the region of 50 patients.[xxi] Under the policy, in the first year that the policy has effect, almost all patients

		that are in the age group are expected to begin treatment, with 75% of full year effect to allow for policy implementation in 2016/17.[xxii] After the first year of the policy, the number of patients accessing the treatment each year is estimated to be, as set out in K1.6: • ~54 patients in 2016/17 (year 1) • ~51 patients in 2017/18 (year 2) • ~46 patients in 2020/21 (year 5) Approximately 11 patients are estimated to enter the cohort each year,[xxiii] and approximately the same number is estimated to leave the cohort each year (because they would turn 6 and fall under the policy for those aged 6 and over, which is already routine commissioning).
K3 Activity	K3.1 What is the current annual activity for the target population covered under the new policy? Please provide details in accompanying excel sheet. K3.2 What will be the new activity should the new / revised policy be implemented in the target population? Please provide details in accompanying excel sheet.	K3.1 Current annual activity is identified in K1.5; patients are treated using existing treatments, with only a few patients using ivacaftor. K3.2 Ivacaftor is the first drug that aims to treat the cause of CF rather than the symptoms. The medicine works differently to other medicines as it targets the production of the thick sticky mucus that causes the majority of the problems in CF.[xxiv] Under the policy, it is estimated that 100% of the eligible population would receive **ivacaftor**.[xxv] The dosage for ivacaftor for ages 2-5 is: 100 mg/day for those less than 14kg and 150mg/day for those over 14kg.[xxvi, xxvii] Seventy-five percent of full year effect is estimated in 2016/17 (full year effect from 2017/18) to allow for policy adoption. In addition to ivacaftor, patients may continue to receive **other treatments** and medications outlined in K1.7 and K1.5, as ivacaftor has been considered as an 'additive therapy to usual care.'[xxviii]

		Based on the evidence from studies on other age groups[xxix] and discussions with clinicians, a reduction in the use of antibiotics to treat chest infections or the amount of enzymes required for those on ivacaftor could be inferred. [xxx] However, at present, direct evidence of the benefit of ivacaftor's use for those aged 2 to 5 is not available. Physiotherapy requirements are estimated to remain the same under the policy.[xxxi]
	K3.3 What will be the comparative activity for the 'Next Best Alternative' or 'Do Nothing' comparator if policy is not adopted? Please details in accompanying excel sheet.	K3.3 Under the 'do nothing' scenario, activity would be as set out in K1.5 and K1.7, with few patients on ivacaftor and most on the other conventional treatments. Once these patients reach the age of 6, they would be eligible to receive ivacaftor.
K4 Existing Patient Pathway	K4.1 If there is a relevant currently routinely commissioned treatment, what is the current patient pathway? Describe or include a figure to outline associated activity.	K4.1 Cystic fibrosis can be diagnosed through the sweat test, new born screening or genetic testing. New born screening tests have been introduced in many countries, and have been routine throughout the UK since October 2007. There is no routine commissioning of disease-modifying drugs in cystic fibrosis in the 2-5 year old population. Current existing standard treatments target the complications rather than cause of the disease and include nutritional repletion (e.g. pancreatic enzyme supplementation and nutritional supplementation), relief of airway obstruction (e.g. physiotherapy, drugs to improve sputum clearance, bronchodilators), treatment of airway infection (e.g. antibiotics), suppression of inflammation (e.g. steroids, high dose ibuprofen) and lung transplantation.
	K4.2. What are the current treatment access criteria?	K4.2 Access to standard treatments above depends on the patient developing CF-associated complications.
	K4.3 What are the current treatment stopping points?	K4.3 Stopping points for the standard treatments above depend on the response to the treatment of the complications.

K5 Comparator (next best alternative treatment) Patient Pathway	K5.1 If there is a 'next best' alternative routinely commissioned treatment what is the current patient pathway? Describe or include a figure to outline associated activity. K5.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	K5.1 Not applicable. K5.2 Not applicable.
K6 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy. K6.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	K6.1 Ivacaftor will be added to existing standard treatment. Treatment will continue unless the patient meets stopping criteria. Stopping criteria include lack of reduction in sweat chloride levels, allergy to ivacaftor (rashes are usually transient), non-adherence (for which safeguarding should be considered), and significant side effects such as liver function abnormalities (AST or ALT greater than 5 times the upper limit of normal). K6.2 Numbers that will discontinue treatment in this age group are difficult to estimate as there is no long term data. Data from the CF registry shows that 7 out of 329 CF patients on Ivacaftor in the UK have discontinued (all reasons), therefore an estimate of c.2% drop out will be used.
K7 Treatment Setting	K7.1How is this treatment delivered to the patient? ○ Acute Trust:	K7.1 Ivacaftor would be delivered through homecare arrangements.[xxxii]

	Inpatient/Daycase/Outpatient ○ Mental Health Provider: Inpatient /Outpatient ○ Community setting ○ Homecare delivery K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what? e.g. service capacity	K7.2 No
K8 Coding	K.8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded? K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.1 It is proposed that all patients treated with ivacaftor for CF have their usage entered into the CF registry and included within the minimum dataset for excluded drugs.[xxxiii] K8.2 Activity for the new patient pathway is expected to be identified using the CF registry, which includes the treatments and procedures available and their use amongst the CF population. On the registry, there would be note of patients' progress, including if they stopped treatment and why.[xxxiv]
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule? K9.2 If this treatment is a drug, what pharmacy monitoring is required? K9.3 What analytical information /monitoring/ reporting is required?	K9.1 No K9.2 See National Service specifications for Cystic Fibrosis (Children) A01/S/b. K9.3 Outcomes must be reported in the CF registry. Specific audit reports on the use of ivacaftor and specific outcomes in this age group will be requested by the commissioner. These reports need to be designed and included in the new format of the CF registry (due Feb 2016).

	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 None.
	K9.5 Is there linked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 No
	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 No
	K9.7 Do you anticipate using Blueteq or other equivalent system to guide access to treatment? If so, please outline. *See also linked question in M1 below*	K9.7 Use of a prior approval software platform for all CF drugs is planned from 2016/17 onwards.
Section L - Service Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
L1 Service Organisation	L1.1 How is this service currently organised? (i.e. tertiary centres, networked provision)	L1.1 All services are provided in accordance with the CF Trust document "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011). Specialist centres are responsible for providing care plans for all patients (National Service specifications for Cystic Fibrosis (Children) A01/S/b). All specialist centres need to be fully operational and in a position to take referrals. Clearly defined links must be in place with community services and hospitals. Centres serving more rural areas must be able to demonstrate an ability to provide either network care or outreach care for children where appropriate.
	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 No change.
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Patients enter the CF pathway following diagnosis, which is usually

		shortly after birth following standard new born testing.
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 The referral route will remain unchanged but there will be a change in age of referral (from over 6 year olds to 2-5 year olds), and an initial increase in referrals when the policy is implemented.
	L2.3 Is the new policy likely to improve equity of access?	L2.3 No change to equity of access anticipated.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 No change expected to equality of access or outcomes.
L3 Implementation	L3.1 Is there a lead in time required prior to implementation and if so when could implementation be achieved if the policy is agreed?	L3.1 No anticipated lead time for implementation. The drug is already licensed and available for prescription.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 No change required.
	L3.3 Is there a change in provider staffing required?	L3.3 No change required.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 No change required.
	L3.5 Are there changes in the support services that need to be in place?	L3.5 No change required.
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 No change required.
	L3.7 Is there likely to be either an increase or	L3.7 No change anticipated.

	decrease in the number of commissioned providers? L3.8 How will the revised provision be secured by NHS England as the responsible commissioner? (e.g. publication and notification of new policy, competitive selection process to secure revised provider configuration)	L3.8 The revised provision will be secured through negotiation with the sole manufacturer.
L4 Collaborative Commissioning	L4.1 Is this service currently subject to or planned for collaborative commissioning arrangements? (e.g. future CCG lead, devolved commissioning arrangements)?	L4.1 No
Section M – Finance Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
M1 Tariff	M1.1 Is this treatment paid under a national prices, and if so which? M1.2 Is this treatment excluded from national prices? M1.3 Is this covered under a local price arrangements (if so state range), and if so are you confident that the costs are not also attributable to other clinical services? M1.4 If a new price has been proposed how has this been derived / tested? How will we ensure that associated activity is not additionally / double charged through existing routes?	M1.1 The drug is excluded from national tariff as a high cost drug. M1.2 Ivacaftor is a high cost drug excluded from national tariff. It will be funded through pass through payment against invoices received from provider Trusts, subject to the terms of the Patient Access Scheme.[xxxv] M1.3 The list price for ivacaftor is noted at around £14,000 for 56 tablets, or around £183,000 per year.[xxxvi] M1.4 Not applicable.

	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 VAT would be recoverable under a homecare arrangement.[xxxvii]
	M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new policy?	M1.6 No prior authorisation has been identified. An electronic prior approval software platform system would be used.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 The first year of treatment is estimated to cost £183,000 per patient based on the list price in the first year of full year effect (2017/18).[xxxviii] The estimated cost for those aged 2-5 is thought to be similar as for older patients.[xxxix] Although the dosage size for children aged 2 to 5 is between a third and a half of the amount of the adult dosage, there is evidence that the price charged for the 50mg and 75mg packs may be the same as the 150mg pack.[xl] The other costs associated with ivacaftor may include an additional sweat test, as well as blood tests and liver function monitoring. These costs would be within the year of care tariff and not paid separately.[xli] There would also be homecare costs for quarterly delivery.[xlii] There may be benefits associated with the treatment, in terms of reduced complications and their associated treatment in the longer term.[xliii] Please see M3.1 for further details.
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 The cost per patient for ivacaftor would be the same as the cost in the first year.

		Once a patient is prescribed ivacaftor, they receive follow up appointments on a regular basis, but this would not be in addition to the existing patient pathway.[xliv] In future years, there may also be a reduction in the tariff band used (and in other activity including the use of excluded drugs such as nebulised antibiotics) as activity falling under conventional therapy for the group may reduce in future.[xlv] The patent for ivacaftor is not set to expire within the next ten years.[xlvi] Once the market is opened, there is expected to be a relatively rapid decrease in the price of the drug. [xlvii]
M3 Overall Cost Impact of this Policy to NHS England	M3.1 Indicate whether this is cost saving, neutral, or cost pressure to NHS England.	M3.1 Cost pressure. The **net cost** to NHS England in 2016/17 is estimated to be approximately £7.4m, based on 75% of full year effect. In the first year of full year effect (2017/18), the cost is estimated at around £8.9m. In year 5, the cost is estimated at around £7.8m. This cost accounts for the cost of ivacaftor as well as possible benefits based on clinician best estimates of future outcomes. The direct **cost of ivacaftor** is estimated at c. £7.4m in 2016/17, £9.2m in 2017/18, and £8.4m in 2020/21. This is based on the costs set out in M1 and the population under the policy as set out in K2 and K3. There could be **cost savings** to NHS England from the reduction in future care costs associated with this cohort of patients. These possible benefits could be estimated at a savings of c. £325k in 2017/18 and approximately £650k in 2020/21. This level of savings could be achieved if patients remained on Band 1 of the year of care tariff (c. £450k savings in year 5), [xlviii] if there was a 25% reduction in nebulised antibiotics for onging *P. aeruginosa* infections (c. £20k savings in year 5), and if use of dornase alfa reduced by 75% (c. £200k savings in year 5).[xlix] There could be greater benefits in future years if patients continue to avoid

		complications of CF that are especially common in older patients.
	M3.2 Where this has not been identified, set out the reasons why this cannot be measured.	M3.2 Not applicable.
M4 Overall cost impact of this policy to the NHS as a whole	M4.1 Indicate whether this is cost pressure, neutral, or cost saving for other parts of the NHS (e.g. providers, CCGs).	M4.1 None identified as the costs for patients with cystic fibrosis are paid under specialised services by NHS England.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 Cost pressure (see M3.1).
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 Not applicable.
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 No evidence of costs or savings beyond the NHS has been identified.
M5 Funding	M5.1 Where a cost pressure is indicated, state known source of funds for investment, where identified e.g. decommissioning less clinically or cost-effective services.	M5.1 Funded from the specialised commissioning allocation.
M6 Financial	M6.1 What are the material financial risks to implementing this policy?	M6.1 The estimates are based on a relatively tightly defined population and drug price, which limits the risk surrounding the policy.

	M6.2 Can these be mitigated, if so how?	M6.2 Not applicable.
	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	M6.3 None generated as the target population is well identified through the register.
M7 Value for Money	M7.1 What evidence is available that the treatment is cost effective? *e.g. NICE appraisal, clinical trials or peer reviewed literature*	M7.1 A systematic review (Whiting et al, 2014) showed the incremental cost effectiveness ratio (ICER) for ivacaftor varied between £335,000 and £1,274,000 per Quality Adjusted Life Year (QALY). The total additional lifetime cost for all eligible cystic fibrosis patients in England ranged from £438 million to £479 million for the lifetime cost and for standard care the lifetime cost was £72 million.
	M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.2 There is sparse evidence on the cost effectiveness of ivacaftor.
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs*	M8.1 No
	M8.2 If so, confirm the source of funds to meet these costs.	M8.2 Not applicable.

[i] Cystic Fibrosis Trust. "What is cycstic fibrosis".[Online]. Accessible at http://www.cysticfibrosis.org.uk/about-cf/what-is-cystic-fibrosis [Accessed 12/11/15]. This is also reflected internationally -- Massie, J., Petrou, V., Forbes, R., Curnow, L., Ioannou, L., Dusart, D., Bankier, A. and Dalatycki, M. (2009). Population-based carrier screening for cystic fibrosis in Victoria: The first three years' experience. Australian and New Zealand Journal of Obstetrics and Gynaecology, 49(5), pp.484-489. [Online] accessible at: http://www.ncbi.nlm.nih.gov/pubmed/19780730 [Accessed 17/11/11].

[ii] Dodge, J., Morison, S., Lewis, P., Coles, E., Geddes, D., Russell, G., Littlewood, J. and Scott, M. (1997). Incidence, population, and survival of cystic fibrosis in the UK, 1968-95. Archives of Disease in Childhood, 77(6), pp.493-496. [Online] accessible at: http://www.ncbi.nlm.nih.gov/pubmed/9496181 [Accessed 17/11/11].

[iii] UK Cystic Fibrosis Registry. (2015). Cystic Fibrosis strength in numbers. UK Cystic Fibrosis Registry.

[iv] After rebasing the number of CF patients registered on the UK CF registry to account for the proportion of the English population in the UK population (84%). In the UK as a whole there are between 9,432 and 10,583 people with CF. The lower estimate relates to the number of patients with complete data, while the upper estimate includes newly diagnosed patients that have not had their first annual review for the year.

[v] There are 1,082 patients aged 2-5 registered on the CF registry. This is assumed to be the lower bound as it does not include newly diagnosed patients. Applying the ratio of 9,432:10,583 from endnote iv, the upper estimate for this age group is estimated to be c. 1,214. UK Cystic Fibrosis Registry. (2015).

[vi] After rebasing the number of patients on the UK CF registry aged 2-5 to account for the proportion of patients in England. Cystic Fibrosis Registry. (2015). Cystic Fibrosis strength in numbers. UK Cystic Fibrosis Registry.

[vii] The other gating mutations include: G178R, S549N, S549R, G551S, G970R, G1244E, S1251N, S1255P and G1349D CFTR. Yu, H., Burton, B., Huang, C., Worley, J., Cao, D., Johnson, J., Urrutia, A., Joubran, J., Seepersaud, S., Sussky, K., Hoffman, B. and Van Goor, F. (2012). Ivacaftor potentiation of multiple CFTR channels with gating mutations. Journal of Cystic Fibrosis, 11(3), pp.237-245. [Online] accessible at: http://www.ncbi.nlm.nih.gov/pubmed/22293084 [Accessed 17/11/11].

[viii] Policy proposition; NHS Commissioning Board. (2012). Clinical Commissioning Policy: Ivacaftor for Cystic Fibrosis. A01/P/b. [Online] accessible at: https://www.england.nhs.uk/wp-content/uploads/2013/04/a01-p-b.pdf [Accessed 17/11/11]. Other gating mutations include G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, and G1349D.

[ix] Based on Cystic Fibrosis Registry data 2014 supplied to the policy working group.

[x] NHS Commissioning Board. (2012). Clinical Commissioning Policy: Ivacaftor for Cystic Fibrosis. [Online] accessible at: https://www.england.nhs.uk/wp-content/uploads/2013/04/a01-p-b.pdf [Accessed 17/11/11].

[xi] Based on discussions with the policy working group. These children had been included in an earlier trial for the drug, and receive the drug in the absence of a policy. It is estimated that these children would be treated in the same way as children not currently receiving the drug under the policy.

[xii] Based on discussions with the policy working group, and information from the CF registry.

[xiii] Due to variation in the severity of symptoms across CF patients, the NHS has created a year of care tariff. These bands relate to the length of treatment and whether there are complications.

[xiv] The bands increase with the use of CF related services. Figure based on correspondence with the policy working group. Based on 2014/15 national tariff.

[xv] Based on the banding definitions.

[xvi] The demographic specific growth rate is estimated using the cohorts 0-4 and 5-9 from the ONS population projections. These are then adjusted to account for the age group 2-5. Discussions with the policy working group indicated that higher apparent growth rates for prevalence noted in the CF registry reflected better data collection rather than a growing population.

[xvii] The number of patients entering the cohort is calculated by dividing the total number of patients (45) by the number of age groups (4), which equals 11.25.

[xviii] As there is sufficient granularity in the CF registry dataset, the number of patients in each age group is known in 2014/15. Therefore, up to 2019/20 the number of patients leaving the cohort each year is known. From 2019/20, however, the number of patients leaving the cohort is estimated to equal 11.25 and a steady state is reached.

[xix] Based on the target population set out in K1.2 and using the growth rate used for the overall CF population. Note that actual number of patients by age has been used in this calculation, leading to a non-linear trend in the initial years.

[xx] Based on discussions with the policy working group. Around 88% of CF patients are diagnosed before the age of two, while 8% are diagnosed between the age of two and six (Cystic Fibrosis Registry Annual Data Report 2014). The mutations affected by this policy are typically diagnosed in the first three to four weeks from birth.

[xxi] Growth in the population would be minimal as set out in K1.6. This assumes no patients would stop treatment. In clinical evidence from the older cohort, the drop-out rate was around 2 - 3%.

[xxii] Based on discussions with the policy working group.

[xxiii] Growth in the population would be minimal as set out in K1.6. This assumes no patients would stop treatment. In clinical evidence from the older cohort, the drop-out rate was around 2 - 3%.

[xxiv] NHS Commissioning Board. (2012). Clinical Commissioning Policy: Ivacaftor for Cystic Fibrosis. [Online] accessible at: https://www.england.nhs.uk/wp-content/uploads/2013/04/a01-p-b.pdf [Accessed 17/11/11]. The number of patients exiting and entering in a particular may vary.

[xxv] Based on discussions with the policy working group.

[xxvi] Please refer the Summary of Product Characteristics. Note that the weight has not been estimated here as the evidence indicates that the price may be similar across dosages. It is assumed that cost would also be similar across formulations (see endnote xxxix).

[xxvii] For comparison, the recommended dosage for ages 6 years and older is 300mg/day.

[xxviii] Policy proposition; NHS Wales. (2014). Specialised Services Clinical Access Policy [Online] accessible at http://www.whssc.wales.nhs.uk/sitesplus/documents/1119/CP46%20Ivacaftor%20%28Kalydeco%29%20for%20G551D%20Cystic%20Fibrosis%20v1.0.pdf. [Accessed 17/11/11].

[xxix] Whiting P, Al M, Burgers L, Westwood ME, Ryder S, Hoogendoorn M, Armstrong N, Allen A, Severens J, Kleijnen J. (2014). Ivacaftor for the Treatment of Patients with Cystic Fibrosis and the G551D Mutation: A Health technology Assessment Report. . Kleijnen Systematic Reviews Ltd. [Online] accessible at http://www.ncbi.nlm.nih.gov/books/NBK261768/ [Accessed 17/11/11].

[xxx] Clinical trials and post-marketing US and UK registry data note that ivacaftor reduces hospitalisations, the rate and duration of infective pulmonary exacerbations and Pseudomonal infection. It also improves lung function and nutritional status. Based on discussions with the policy working group.

[xxxi] Based on discussions with the policy working group.

[xxxii] Based on discussions with the policy working group.

[xxxiii] Based on discussions with the policy working group.

[xxxiv] Based on discussions with the policy working group in relation to the features of the CF registry and how it would be used to record ivacaftor.

[xxxv] In line with arrangements for older cohorts receiving the drug. NHS Commissioning Board. (2012). Clinical Commissioning Policy: Ivacaftor for Cystic Fibrosis. A01/P/b.

[xxxvi] Based on a dose regimen of 150mg every 12 hours. Scottish Medicines Consortium (2012). No. (827/12). [Online] accessible at https://www.scottishmedicines.org.uk/files/advice/ivacaftor_Kalydeco_FINAL_December_2012_amended_11_01_13_for_website.pdf [Accessed 17/11/11]. See endnote xl to note the possible cost for lower doses.

[xxxvii] Based on discussions with NHS pharmacists and finance leads. Section 3.2, When can goods being provided on prescription be zero-rated for VAT purposes? https://www.gov.uk/government/publications/vat-notice-70157-health-professionals-and-pharmaceutical-products/vat-notice-70157-health-professionals-and-pharmaceutical-products. [Accessed 16/12/11].

[xxxviii] Based on a dosage of 150mg every 12 hours, assuming no discount from the adult dosage cost. [Online] accessible at http://www.ukmi.nhs.uk/applications/ndo/record_view_open.asp?newDrugID=5084 [Accessed 17/11/11].

[xxxix] Based on discussions with the policy working group. It is uncertain if the cost of the drug would be lower although the dosage would be lower.

[xl] For the state of Vermont the price per pack is $28k across the three dosage sizes. [Online] accessible at http://www.vrtx.com/vermont-prescribers-information-kalydeco [Accessed 17/11/11].

[xli] Based on discussions with the policy working group.

[xlii] Based on discussions with the policy working group. Might be more frequent (monthly) when the drug is first given.

[xliii] Based on discussions with the policy working group.

[xliv] Based on discussions with the policy working group.

[xlv] Based on discussions with the policy working group.

[xlvi] The supplementary protection certificate is not set to expire until after 2025/26 (UKMi data), which is beyond the time period considered in this document.

[xlvii] Based on discussions with the policy working group.

[xlviii] Designated CF Centres receive an annual Payment by Results tariff to provide care for patients. The tariff is a complexity-adjusted yearly banding system with seven 'bands' of increasing complexity linked to disease severity, complications and treatment requirements. The lowest tariff is £5K p.a. and the highest £40K pa. The range of costs for individuals in each band, however, is wide. Based on discussions with the policy working group. Bands based on area team data for the age group covered under the policy.

[xlix] Figures rounded. Calculations assume that benefits begin in year 2 based on discussions with the policy working group. Calculations based on drug usage and chronic infection rates data from CF Registry (2015), costs from the dictionary of medicines, and discussions with the policy working group.