Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	A11X05		
Policy Title	Riociguat for Pulmonary Arterial Hypertension		
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Section K - Activity Impact			
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 riociguat for certain patients with pulmonary arterial hypertension (PAH). Pulmonary hypertension services reported 6,484 active patients in 2014 in the UK, of which around 45% had a diagnosis of PAH.[i] Thus, it is estimated that there were around 2,450 active patients in England with a pulmonary arterial hypertension diagnosis in 2014.[ii] The incidence of PAH is estimated at between 0.9 and 7.6 cases per million persons,[iii] which is equivalent to 50 to 410 persons in England in 2014/15.[iv] However, as noted in the policy proposition, general	

		incidence and prevalence rates may be underestimated as a result of mis- and/or undiagnosed patients.[v]
	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 Eligible patients are persons with PAH with World Health Organisation (WHO) functional class (FC) II and III.[vi] The target population that could be eligible for riociguat can be classed under three clinical scenarios, (each scenario here refers to patients accessing treatment at a specific point in the pathway): The **first clinical scenario** is constituted of patients first starting targeted medical therapy, where monotherapy with PDE5 inhibitor (PDE5i) drugs is contraindicated (either because patients are intolerant or suffer from adverse reactions). This group currently uses endothelin antagonist receptors (ERAs) as monotherapy. Under the policy, up to c. 20 - 30 patients in the prevalent population may be eligible for riociguat, but it is estimated that few patients (an estimated c.1/3 of those eligible or c. 10 patients) would use riociguat instead of an ERA within the prevalent population in 2014/15.[vii] The **second clinical scenario** is made up of WHO FC III patients who currently use a combination of PDE5i and ERAs,[viii] and would be considered for adding a prostaglandin to their existing treatments following a failure to stabilise[ix] on dual therapy. It is estimated that approximately 150-200 patients in the prevalent population may be eligible for riociguat under this scenario, but it is estimated that only around 50% (75 - 100) would move to using riociguat instead of a PDE5 in 2014/15i.[x] The **third clinical scenario** would be a small group of patients, that might use riociguat in combination with a prostaglandin or with an ERA and prostaglandin instead of a combination of ERAs, PDE5is, and prostaglandins.[xi] This group comprises ~ 5 - 15 eligible patients from the prevalent population in 2014/15.[xii] In total, approximately 175 - 245 patients from the prevalent population could be eligible for riociguat, with an estimated 90 to 125

		taking up riociguat. Note that these figures relate to prevalence – the incidence or number of new patients joining the cohort each year would be much smaller.
	K1.3 What age group is the treatment indicated for?	K1.3 The policy indicates riociguat for use in adults (over 18 years).
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 The median age of patients treated with disease targeted therapy (the drugs in the pathway covered by the present policy) is 59 years in 2013/14 (60 for women and 58 for men).[xiii] This has been stable over the past 5 years (it varied from 59 to 60).[xiv] The interquartile range is 42-71 years.[xv] In 2014 the number of female patients with pulmonary arterial hypertension was approximately twice as high as the number of male patients.[xvi]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Currently, patients under the three clinical scenarios above undergo the following treatments: The **first clinical scenario** would currently use monotherapy of endothelin antagonist receptors (ERAs). This would be used as a monotherapy after consideration for PDE5i. Bosentan (an ERA) is used approximately 69% of cases, ambrisentan (another ERA) in c. 31%.[xvii] This group comprises is estimated at fewer than 10.[xviii] The **second clinical scenario** would currently use a combination of PDE5i and ERAs.[xix] In relation to PDE5is, sildenafil is used in circa 95% of cases, tadalafil in 5% of cases.[xx] It is estimated that the split between common ERAs is as set out in relation to the first scenario.

		The **third clinical scenario** currently uses a combination of PDE5is, and ERAs and prostaglandins.[xxi] This group comprises ~5 - 15 patients.[xxii] Prostaglandins, iloprost; treprostinil and epoprostenol are used in an estimated 54%; 16% and 30% of cases.[xxiii] Relative use of specific ERAs and PDE5is is estimated to be as set out in relation to scenario 2. One individual funding request for **riocioguat** for patients with PAH was submitted for the period 2013/14 to September 2015/16. The current activity for riociguat may therefore be very low, if not nil.[xxiv]
	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 The growth of the number of patients who access pulmonary hypertension services is estimated at 5% per annum, whilst the number of patients who receive disease targeted drugs is estimated to grow at 7%.[xxv]
	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 target population would currently receive treatments outlined in K1.5. Based on patient numbers in K1.5 and the growth rate set out in K1.6, the **total number of patients from the prevalent population within the first clinical scenario** (receiving an **ERA**) **that are estimated to use riociguat under the policy** is estimated at around: [xxvi] • Under 10 total persons in 2016/17 • Approx. 8-10 total persons in 2017/18 • Approx. 10-15 total persons in 2020/21. In **clinical scenario 2**, the total number of prevalent patients (**receiving an ERA and PDE5i**) **that would be estimated to use riociguat under the policy** is estimated at around: [xxvii] • Approx. 85 - 115 total persons in 2016/17

- Approx. 90 - 125 total persons in 2017/18
- Approx. 115 - 150 total persons in 2020/21.

In the **third clinical scenario**, the total number of patients (**receiving an ERA and a prostaglandin) that would be estimated to use riociguat under the policy** is estimated at approximately 5 - 15 in future years.[xxviii]

K1.8 How is the population currently distributed geographically?

K1.8 Patients are distributed across England.

For the number of patients active by specialised centre, see the table below:

Specialised pulmonary hypertension centre	Patients active and alive, 31/03/2014
Sheffield Teaching Hospitals NHS Foundation Trust	823
Royal Free London NHS Foundation Trust	331
Imperial College Healthcare NHS Trust	430
Royal Brompton and Harefield NHS Foundation Trust	428
Papworth Hospital NHS Foundation Trust	291
The Newcastle upon Tyne Hospitals NHS Foundation Trust	252

Based on the National Audit of Pulmonary Hypertension 2014. Note that patients at these centres may not reside in England, and could reside elsewhere in the UK.

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 The new policy proposes to add riociguat as a routinely commissioned drug as part of the existing policy for PAH.
	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 growth of the target population is likely to be affected by the following two factors: (a) an increase in prevalence; (b) an increase in the ratio of patients with pulmonary hypertension who receive disease targeted drugs. See K1.6.
	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 Given there may currently be very few patients who receive riociguat, if any, most of the future activity would represent a **net increase as compared to the 'do nothing' scenario**[xxix] in the number of patients who access riociguat. The **total number accessing** the treatment could be (see K1.7 – note that this is not the year on year increase):[xxx] • Approx. 50 - 70 persons in 2016/17 • Approx. 110 -150 persons in 2017/18 • Approx. 130 - 180 persons in 2020/21[xxxi] This relates to the total patients from the prevalent population – this is not the year on year increase.

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 The current activity is set out in K1.5; patients would be using ERAs, PDE5i, and/or prostaglandins. K3.2 The total number of patients receiving **riociguat** is estimated to be:[xxxii] • Approx. 50 - 70 persons in 2016/17 • Approx. 110 -150 persons in 2017/18 • Approx. 130 - 180 persons in 2020/21 Compared to K1.5, the number of patients on **ERAs could be lower by:**[xxxiii] • Under. 10 persons in 2016/17 • Approx. 10 persons in 2017/18 • Approx. 10 - 15 persons in 2020/21 The number of patients on **PDE5is could be lower by:**[xxxiv] • Approx. 45 - 65 persons in 2016/17 • Approx. 95 - 140 persons in 2017/18 • Approx. 120 - 165 persons in 2020/21 It is estimated that the number of patients on **prostaglandins** would not be reduced by the use of riociguat.[xxxv] No patients would be using a **PDE5i** as this is not taken in combination with riociguat.[xxxvi] .

	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 The 'do nothing' scenario refers to current activity, assumed to be the 'steady state' rolled forward in future years. The future activity levels are therefore set out in K1.7; patients would be using ERAs, PDE5i, and/or prostaglandins.
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 Current PAH commissioning policy in use which commissions disease targeted therapies for adults in **WHO functional class II or III only** as follows: First-line therapy – PDE5i (sildenafil or tadalafil) as monotherapy. If contraindicated or not appropriate an ERA (bosentan, ambrisentan, macitentan) is currently commissioned as alternative first line therapy Second-line therapy – Patients who (within 8-12 weeks) failed to tolerate or had an unsatisfactory response to first-line therapy may now progress to dual therapy of PDE5i and an ERA. Third-line therapy – As second line therapies and a prostaglandin. Some patients may receive PDE5i and a prostaglandin.
	K4.2. What are the current treatment access criteria?	K4.2 See K4.1.
	K4.3 What are the current treatment stopping points?	K4.3 Patient Stopping Criteria: The continued use of targeted therapies will be reviewed on a regular basis. The key factors influencing the cessation of treatment will be:- • Successful transplant surgery (few patients) • Clinically relevant side-effects

		• Poor/no response to treatment Drug therapies may also be withdrawn “at the end of life” phase.
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 As K4.1-K4.3 K5.2 As K4.1-K4.3
K6 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy.	K6.1 See pathway diagram at end of this document. This policy will include riociguat for adults in **WHO functional class II or III (as well)**, follows: *Clinical scenario 1* Monotherapy – PDE5i (sildenafil or tadalafil) as monotherapy. If contraindicated or not appropriate **riociguat** will be commissioned as an alternative monotherapy therapy. *Clinical scenario 2*

		Option as a second-line therapy will remain unchanged. Patients who (within 8-12 weeks) failed to tolerate or had an unsatisfactory response to first-line therapy may now progress to dual therapy of PDE5i and an ERA. Patients in functional class III who have not achieved stasis of disease progression with a PDE5 inhibitor and an ERA will be switched to riociguat and an ERA. Patients in functional class II who have not achieved stasis of disease progression with a PDE5 inhibitor and an ERA will have a prostaglandin added to this combination. *Clinical scenario 3* Patients in functional class III receiving a PDE5 inhibitor in combination with a prostaglandin who fail to stabilise, will receive riociguat in combination with a prostaglandin or in combination with an ERA and a prostaglandin. Patients in functional class II receiving a PDE5 inhibitor in combination with a prostaglandin who fail to stabilise, will have an ERA added to this combination.
	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.	K6.2 Patient Stopping Criteria: The continued use of target therapies will be reviewed on a regular basis. The key factors influencing the cessation of treatment will be:- • Successful transplant surgery • Clinically relevant side-effects • Poor/no response to treatment Drug therapies may also be withdrawn "at the end of life" phase.
K7 Treatment Setting	K7.1 How is this treatment delivered to the patient?	K7.1 The treatment would usually be for homecare delivery.[xxxvii] Only prescribable by designated centres.

	○ Acute Trust: 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 anticipated change.
K8 Coding	K8.1 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 As riociguat is a high cost drug, activity may be recorded in the high cost drug dataset. K8.2 The existing pulmonary hypertension audit would capture information on activity for riociguat.
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?	K9.1 No new requirements. K9. Currently Riociguat is a Black Triangle drug – product is subject to additional monitoring and any suspected adverse drug reactions should be reported vis Yellow Card Scheme.

		Additionally, each centre will need to provide commissioners with a monthly monitoring statement covering the following fields: • ID number • Patient Initials • NHS number • PCT/SCG codes • Drug and dose • Notification of changes to drugs and dosage • Discontinuation date • Reason for discontinuation • Monthly cost • Annual cost • Survival • Quality of Life estimate (emphasis 10) • Absolute 6 minute walk The above data will need to be submitted to the National Pulmonary Hypertension Audit.
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Routine monitoring only.
	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	
	K9.5 Is there inked information required to complete quality dashboards and if so	K9.5 No

	is it being incorporated into routine performance monitoring?	
	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 Anticipated that Blueteq system will be used.
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 There are six tertiary PAH centres that provide diagnosis, intervention and support to patients with PAH. Only these centres are able to initiate disease targeted treatments as described in K4.1 - K6.3. Current centres: Imperial college Healthcare NHS Trust Royal Brompton & Harefield NHS Foundation Trust Royal Free Hampstead NHS Trust Papworth Hospital NHS Foundation Trust Sheffield Teaching Hospitals NHS Foundation Trust The Newcastle upon Tyne NHS Foundation Trust

	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 No anticipated change.
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Current referrals come from consultant physicians, typically cardiology and respiratory consultants in secondary care. Occasionally referrals come from other specialities including haematology, rheumatology and infectious diseases.
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 No anticipated change.
	L2.3 Is the new policy likely to improve equity of access?	L2.3 No anticipated change.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 No anticipated change.
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 lead time. Riociguat is licenced and currently commissioned for use in the UK for another indication (PH secondary to CTEPH)
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 No anticipated change

	L3.3 Is there a change in provider staffing required?	L3.3 No anticipated change
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 No anticipated change
	L3.5 Are there changes in the support services that need to be in place?	L3.5 No anticipated change
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 No anticipated change
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 No anticipated change
	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 Publication of new commissioning policy

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?	M1.1 No, see M1.2.
	M1.2 Is this treatment excluded from national prices?	M1.2 Riociguat is a high cost drug excluded from tariff.
	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?	M1.3 As an excluded drug, the price is subject to local negotiations. The list price is £997.36 (excl. VAT) for 42 tablets of 0.5mg; 1.0mg; 1.5mg; 2.0mg or 2.5mg (same price).[xxxviii] The annual costs are noted in M2.1.
	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?	M1.4 Not applicable.
	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 VAT may be recoverable where the drug is delivered via homecare. The price of riociguat does not include VAT for the

		calculations in sections M2 and M3 where this is the case.[xxxix]
	M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new policy?	M1.6 A prior approval software platform could be used to ensure riociguat is used at the correct point in the pathway, and trend analysis could be used to assess whether the correct questions are being asked to ensure proper use within the policy.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 The **cost of riociguat** is estimated at c. £26,000 per patient per year. This is calculated based on 3 daily tablets at £23.75 each.[xl] Where homecare is not used, the cost per patient is estimated at around £31,000 (incl. 20% VAT).[xli] Note that the cost per patient per year (without homecare) of the drugs which riociguat may replace is estimated at:[xlii] For patients in the **first clinical scenario**, riociguat would replace an ERA, with estimated savings of: [xliii] • c. £23,500 for bosentan; or • c. £23,500 for ambrisentan For patients in the **second and third clinical scenarios**, riociguat would replace a PDE5i, with estimated savings of: [xliv] • c. £154 for sildenafil (PDE5i); or • c. £6,400 for tadalafil (PDE5i) Overall, the **net cost per patient** in year 1 is estimated at between c. **£6,000** (where riociguat replaces an ERA)[xlv] **and £26,000** (where riociguat replaces a PDE5i).
	M2.2 What is the revenue cost per patient in future years (including follow	M2.2 As there are no costs of administration, the only cost is the cost of the drug itself (and a small amount for homecare delivery where

	up)?	applicable). The cost of this drug per patient per year is the same as in M2.1; the length during which patients would pursue treatment is linked to life expectancy and also to the likelihood of developing complications.[xlvi]
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. M3.2 Where this has not been identified, set out the reasons why this cannot be measured.	M3.1 Cost pressure. The cost pressure in 2016/17 is estimated at around c. £1.2m to £1.7m in 2016/17 assuming 50% part year effect. This could increase to c. £2.5m to £3.6m in 2017/18.[xlvii] M3.2 Not applicable.
M4 Overall cost impact of this policy to the NHS as a whole	M4.1 Indicate whether this is cost saving, neutral, or cost pressure for other parts of the NHS (e.g. providers, CCGs). M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole. M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.1 Cost neutral as this is commissioned by NHS England. M4.2 Cost pressure. As set out in M3.1, the cost pressure is estimated to be c. £1.2m to £1.7m in 2016/17 and c. £2.5m to £3.6m in 2017/18. 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 To be determined by CPAG.
M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 The first financial risk concerns the number of patients in each clinical scenario. Depending on the number of patients in each clinical scenario, the cost impact could vary. The costs might also be higher if homecare was not used, as VAT would not be recoverable.
	M6.2 Can these be mitigated, if so how?	M6.2 A prior approval software platform could be used to ensure riociguat is used at the correct point in the pathway, and trend analysis could be used to assess whether the correct questions are being asked to ensure proper use within the policy.
	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	M6.3 The scenarios tested above assume a target population of c. 175 (low estimate) and c. 245 (high estimate) in 2014/15, which is estimated in future years based on a growth rate of 7%. Of this, group, not all patients would take up treatment (only approx. 50 to 70 in year 1 (with 50% part year effect); and c. 105 to 150 in year 2), and

		treatment would be delivered via homecare.[xlviii] Two scenarios were tested in relation to the base case. In a first scenario, if all patients in the target population of 245 in 2014/15are prescribed riociguat, then an estimated: • 140 patients would take riociguat in year one (with a 50% phasing assumption) • 300 patients would take riociguat in year two (with full year effects) • An estimated cost impact of up to c. £3.2m in 2016/17, and up to c. £6.9m in 2017/18.[xlix] A second scenario concerns the share of patients receiving homecare. Currently an estimated c. 10% of patients may not receive PAH medications via homecare.[l] For these patients 20% VAT applies on the cost of drugs. Adjusting the cost impact figures stated in M3.1 to account for these patients would yield a cost impact of c. £1.2m to £1.7m in 2016/17, and c. £2.6m to £3.7m in 2017/18. If these patients were moved to homecare, there would be savings of £55,000 to £78,000 in 2017/18 (with full year effects).[li] If patients could avoid or delay using prostaglandin following the treatment, there could be savings to NHS England.
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*	M7.1 No evidence on cost effectiveness. One study (Burudpakdee et al, 2014) reported an incremental per capita cost of £0.18 ($0.27) for

	literature M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	riociguat coverage in a US Medicare insured population. M7.2 This was a hypothetical exercise carried out in relation to a US population and some caution should be exercised in extrapolating this study to England. This was also low level evidence.
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs* M8.2 If so, confirm the source of funds to meet these costs.	M8.1 Not identified. M8.2 Not applicable.

[i] National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014.

[ii] This is calculated as 84% (share of English population in UK population, ONS) multiplied by 45% of 6,484, see National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014, p.8. Figures for England were estimated based on UK figures and using the ratio of the population in England as a percentage of the UK population, based on ONS data: http://www.ons.gov.uk/ons/dcp171778_420462.pdf, last accessed: 10/12/2015.

[iii] NHS England/A11/P/b, Publications Gateway Reference 01720, "Pulmonary Hypertension Policy, National policy for targeted therapies for the treatment of pulmonary hypertension in adults", May 2014, Pulmonary Hypertension CRG.

[iv] This is based on the incidence rate multiplied by the Office of National Statistics population estimate for England in 2014.

[v] Frost et al., 2013, quoted in: NHS England/A11/P/b, Publications Gateway Reference 01720, "Pulmonary Hypertension Policy, National policy for targeted therapies for the treatment of pulmonary hypertension in adults", May 2014, Pulmonary Hypertension CRG.

[vi] See Policy Proposition.

[vii] Policy Proposition, discussions with the policy working group.

[viii] There may be some patients within this group that were contraindicated to PDE5is, and may therefore be on monotherapy with an ERA at this point.

[ix] See Policy Proposition. Failure to stabilise refers to the lack of clinical worsening based on a number of measures, including 6 minute walking distance, haemodynamic markers, adverse events and toxicity, Borg dyspnoea scale, NT Pro-BMP level, WHO functional class, quality of life, and time to clinical worsening.

[x] Policy proposition, discussions with the policy working group.

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

[xii] Policy proposition; discussions with the policy working group.

[xiii] National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014.

[xiv] National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014.

[xv] [xv] National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014.

[xvi] This range is for 2012/13, based on National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014.

[xvii] Analysis of data in National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014, p. 22.

[xviii] Policy proposition; discussions with the working group.

[xix] See Policy Proposition.

[xx] See information for first group for the split of ERAs. Analysis of data in National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014, p. 22.

[xxi] See information for second group for the split of prostaglandins.

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

[xxiii] Analysis of data in National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014, p. 22.

[xxiv] Based on the national IFR database.

[xxv] Growth rates calculated based on historic audit data suggested growth rates over 10%. However, clinician experience indicated that recent growth has tapered, and an estimate of 5% and 7% has been used to estimate future increases in the population with PAH under treatment, and in the number of patients within the target population (a subset of those using medical therapy). These rates are applied to the population under treatment and the target population as set out in K1.1 and K1.2. Figures are rounded.

[xxvi] Figures are rounded.

[xxvii] Figures are rounded.

[xxviii] Figures are rounded. This population is not estimated to grow.

[xxix] 'Do nothing' scenario assumes that current activity rolls forward.

[xxx] Figures are rounded.

[xxxi] Note: this assumes that the number of patients in the third clinical scenario does not grow over time, as discussed with policy working group.

[xxxii] Figures are rounded.

[xxxiii] Patients under clinical scenario 1 would discontinue use – figures rounded.

[xxxiv] Patients under clinical scenario 2 and 3 would discontinue use – figures rounded.

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

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

[xxxvii] As discussed with the policy working group.

[xxxviii] British National Forumulary. Adempas (bayer): https://www.evidence.nhs.uk/formulary/bnf/current/2-cardiovascular-system/25-hypertension-and-heart-failure/251-vasodilator-antihypertensive-drugs/riociguat/adempas, last accessed 11/02/2016.

[xxxix] See Gov.UK website: https://www.gov.uk/government/publications/vat-notice-70157-health-professionals-and-pharmaceutical-products/vat-notice-70157-health-professionals-and-pharmaceutical-products, last accessed: 20/01/2017.

[xl] See M2.1.

[xli] This includes 20% VAT.

[xlii] All the costs listed below are based on NHS England/A11/P/b, Publications Gateway Reference 01720, "Pulmonary Hypertension Policy , National policy for targeted therapies for the treatment of pulmonary hypertension in adults", May 2014, Pulmonary Hypertension CRG.

[xliii] All the costs listed below are based on NHS England/A11/P/b, Publications Gateway Reference 01720, "Pulmonary Hypertension Policy , National policy for targeted therapies for the treatment of pulmonary hypertension in adults", May 2014, Pulmonary Hypertension CRG.

[xliv] All the costs listed below are based on NHS England/A11/P/b, Publications Gateway Reference 01720, "Pulmonary Hypertension Policy , National policy for targeted therapies for the treatment of pulmonary hypertension in adults", May 2014, Pulmonary Hypertension CRG.

[xlv] This takes the difference of £26,000 for riociguat and £19,600 for ERAs, where £19,600 is the estimated price without VAT.

[xlvi] For life expectancy of patients with pulmonary hypertension, see National Audit of Pulmonary Hypertension, Report for the audit period April 2013 to March 2014, Fifth Annual Report: Key findings from the National Audit of Pulmonary Hypertension for the United Kingdom, Channel Islands, Gibraltar and the Isle of Man, 2014, p. 25-29.

[xlvii] To compute these estimates, the following yearly drug costs were used (for comparator drugs):c. £19,600 for Bosentan (excl. VAT), c. £19,600 for Ambrisentan (excl. VAT); c. £130 for Sildenafil (excl. VAT); c. £5,300 for Tadalafil (excl. VAT), based on the Clinical Commissioning Policy: National Policy for targeted therapies for the treatment of pulmonary hypertension in adults, May 2014, https://www.england.nhs.uk/wp-content/uploads/2014/06/a11-ps-b.pdf, last accessed: 19/01/2016. No cost of administering the drugs is included: they can be taken orally, at home.

[xlviii] ERAs and PDE5is are assumed to be delivered via homecare, thus VAT is removed from the relevant drug prices stated in M2.1.

[xlix] This uses the upper figures of the target population in each group stated in K1.2.

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

[li] A saving of £5,200 of VAT (20% of £26,000) for c. 10% of the target population of the 105to 150 patients who would take riociguat in 2017/18..