NIHR | Innovation Observatory

HEALTH TECHNOLOGY BRIEFING
OCTOBER 2019

Fevipiprant maintenance therapy for uncontrolled asthma – add on therapy

NIHRIO ID	5871	**NICE ID**	9813
Developer/Company	Novartis Pharmaceuticals UK Ltd	**UKPS ID**	641186

Licensing and market availability plans	Currently in phase III clinical trials.

SUMMARY

Fevipiprant is in clinical development for the treatment of patients aged 12 years and older with uncontrolled asthma who remain symptomatic despite treatment with inhaled corticosteroids (ICS) with or without at least one additional controller. Whilst there is no cure for asthma, most patients are able to control their symptoms by taking daily preventative medication and additional controllers when required. However, a small subset of asthma patients are resistant to the current standard of care for asthma and are unable to control their symptoms. This can have severe implications on their quality of life as uncontrolled asthma can result in decreased physical fitness, decreased sleep quality and decreased productivity at work or school.

Fevipiprant is administered orally once daily. It works by preventing the binding of substances called prostaglandin to DP_2 receptors on inflammatory cells therefore preventing the inflammatory response to triggers that result in an asthma attack. Fevipiprant is the first asthma drug to decrease the airway smooth muscle mass that is often excessive in the airways of patients with asthma. If licensed, fevipiprant will offer a new treatment option for patients with uncontrolled asthma.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

PROPOSED INDICATION

Maintenance treatment in patients aged 12 years and older with asthma who remain symptomatic with inhaled corticosteroids (ICS) with or without at least one additional controller.[a]

TECHNOLOGY

DESCRIPTION

Fevipiprant (QAW-039) is an oral, highly selective, potent and reversible prostaglandin D_2 (PGD_2) type 2 receptor (DP_2) antagonist that blocks the effects of PGD_2 on inflammation.[1,2] DP_2 is expressed by inflammatory cells such as eosinophils, T_H2 lymphocytes and mast cells. Binding of prostaglandin to the DP_2 receptor mediates the activation and migration of T_H2 cells and eosinophils as well as the release of inflammatory cytokines, which is critical in the immunopathogenesis of allergic asthma.[3] Therefore the PGD_2/DP_2 axis has been considered a potentially effective target for asthma therapy.[4]

Fevipiprant is in clinical development as an add-on therapy for asthma that remains uncontrolled despite the patient having received ICS with or without at least one additional controller. In the phase III clinical trials (NCT02563067; EudraCT 2015-003172-67 and NCT02555683; EudraCT 2015-002553-35) participants received a 150mg dose of fevipiprant, 450mg dose of fevipiprant or placebo once daily for 52 weeks in addition to receiving Global Initiative for Asthma (GINA) standard of care asthma therapy.[5-8]

INNOVATION AND/OR ADVANTAGES

One of the important components that leads to variable airflow limitation in asthma is increased airway smooth muscle (ASM) mass. Bronchial biopsies from patients show that fevipiprant appears to be the first asthma drug that reduces ASM mass.[3] Given that it is orally administered, fevipiprant works systemically and is therefore able to reach all areas of the lungs, including the smaller, lower airways.[1]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Fevipiprant does not currently have a Marketing Authorisation in the EU/UK for any indication.

Fevipiprant is currently in phase II and III clinical development for the treatment of asthma in paediatrics, nasal polyps chronic obstructive pulmonary disease.[9]

PATIENT GROUP

DISEASE BACKGROUND

Asthma is a common, chronic inflammatory respiratory disease of the airways that can affect people at any age but most commonly starts in childhood.[10] People with asthma have inflamed airways that are sensitive to various stimuli.[11] During an asthma attack (exacerbation) the airway becomes even more inflamed, the muscles around the airway constrict and there is a

[a] Information provided by Novartis General Medicines in UK PharmaScan

build-up of sputum resulting in the airway becoming increasingly narrow. This makes it difficult for air to move in and out of the lungs causing symptoms such as coughing, wheezing, shortness of breath and chest tightness.[12] Most patients with asthma are able to control their symptoms by routinely taking ICS with or without the additional controller long-acting beta-agonists but some patients have uncontrolled symptoms that are unresponsive to standard therapy.[13,14] It is not yet fully understood why some patients do not respond to standard therapy but patients with severe, uncontrolled asthma have been shown to have increased levels of PGD_2 compared to patients without well-controlled asthma.[4,15]

Uncontrolled asthma is associated with frequent and intrusive symptoms that result in major functional limitation such as wheezing, coughing and shortness of breath. These asthma symptoms may lead to other more general symptoms such as fatigue, exhaustion, decreased physical fitness and poor sleep quality.[16] Patients with severe, uncontrolled asthma report that their disease results in a decreased ability to complete daily activities, limits to leisure and lifestyle and a loss in productivity at work or school.[16]

Can please you add a brief description about the causes/risk factors of asthma?

CLINICAL NEED AND BURDEN OF DISEASE

Around 5.4 million adults and children in the UK are currently receiving treatment for asthma.[17] Whilst the exact number of these patients who have uncontrolled symptoms isn't known, a Dutch population survey of adults with asthma estimated 17% of asthma patients had uncontrolled symptoms despite standard of care.[14] Using the above estimates,[17] this would equate to about 918,000 patient in in the UK. Asthma has very high healthcare costs, estimated in the UK to be at least £1.1 billion.[18] These costs are due to medications, physician visits, hospitalisations and the costs of oral corticosteroid side effects.[14]

In England 2017/2018 there were 102,408 finished consultant episodes (FCE) and 73,877 hospital admissions with a primary diagnosis of asthma (ICD-10 code J45), resulting in 148,548 FCE bed days and 11,700 day cases.[19] In England in 2017 there were 1,156 deaths with asthma (ICD-10 codes J45-J46) recorded as the underlying cause.[20]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

There is no cure for asthma, therefore treatment aims to control symptoms so that asthma patients are able to have normal functionality whilst minimising adverse reactions to the treatment. Patients normally complete a personal action plan with their doctor or specialist asthma nurse. The personal action plan focusses on which medicines to take and adherence to regime, how to identify if asthma symptoms are getting worse and what to do if an acute asthma exacerbation occurs.[21]

Current guidelines from the British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) recommend a stepwise approach to treatment aligned with the pathway of GINA.[22] If asthma symptoms are not under control then the treatment should be increased to the next step. If asthma symptoms are under control then treatment should be stepped down until the patient reaches a point where their asthma is under control at the lowest possible controlling therapy.[14]

CURRENT TREATMENT OPTIONS

According to existing BTS/SIGN guidelines for the treatment asthma, there are four types of therapies to control asthma:[22]

- Short acting bronchodilator therapy to be taken to relieve symptoms during an asthma exacerbation
  - inhaled short acting β_2 agonists
  - inhaled ipratropium bromide
  - theophyllines
- Regular preventer therapy to improve symptoms, improve lung function and prevent asthma attacks
  - ICS (first choice)
  - leukotriene receptor antagonists
  - nedocromil sodium
- Initial add-on therapy is prescribed to patients whose asthma is uncontrolled with low-dose ICS alone
  - inhaled long-acting β_2 agonist (LABA)
  - combination ICS/LABA inhalers
- Additional controller therapies
  - increased dose of inhaled corticosteroids
  - leukotriene receptor antagonists

PLACE OF TECHNOLOGY

If licensed, fevipiprant may offer an additional treatment option for asthma patients aged 12 years and older whose symptoms are currently uncontrolled on standard of care asthma treatment.

CLINICAL TRIAL INFORMATION

Trial	**LUSTER 1, NCT02555683, EudraCT 2015-002553-35, CQAW039A2307; adults and adolescents aged 12 years and older; fevipiprant vs placebo both in addition to standard of care asthma therapy; phase III**
Sponsor	Novartis Pharmaceuticals
Status	Active, not recruiting
Source of Information	Trial registry[6,8]
Location	16 EU countries (incl UK), USA and other counties
Design	Randomized, placebo-controlled, parallel assignment, double blind study
Participants	n=894; males and females aged 12 years and older; diagnosed with severe asthma, uncontrolled on GINA 4/5 medication, based on an Forced Expiratory Volume in 1 second (FEV1) of ≤90% for subjects aged 12 to 17 years and an FEV1 of ≤80% for subjects aged 18 years or older; evidence of airway reversibility or airway hyper-reactivity; history of 2 or more exacerbations with the 12 months prior to entering the study.

Schedule	Participants were randomised to receive dose 1 of fevipiprant, dose 2 of fevipiprant or placebo administered orally once daily for 52 weeks.
Follow-up	n/a
Primary Outcomes	Number of moderate to severe asthma exacerbations [Time frame: 52 weeks]
Secondary Outcomes	• Change in baseline in Asthma Quality of Life Questionnaire+12 [Time frame: 52 weeks] • Change from baseline in Asthma Control Questionnaire-5 score [Time frame: 52 weeks] • Change in baseline in pre-dose FEV1 (litres) [Time frame: 52 weeks] • Assess safety by monitoring of adverse events [Time frame: 52 weeks]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Estimated primary completion date in October 2019.

Trial	**LUSTER 2, NCT02563067, EudraCT-2015-003172-67, CQAW039A2314; adults and adolescents aged 12 years and older; fevipiprant vs placebo both in addition to standard of care asthma therapy; phase III**
Sponsor	Novartis Pharmaceuticals
Status	Completed
Source of Information	Trial registry[5,7]
Location	6 EU countries (not incl UK), USA, Canada and other counties
Design	Randomized, placebo-controlled, parallel assignment, double blind study
Participants	n= 877 participants; males and females; aged 12 years and older; severe asthma; uncontrolled on GINA 4/5 asthma medication; FEV1 ⩽80% of the predicted normal value for patients aged ⩾18 years; FEV1 of ⩽90% for patients aged 12 to <18 years; asthma control questionnaire (ACQ) score of >1.5; a history of at least 2 asthma exacerbations within the 12 months prior to entering the study.
Schedule	Patients received dose 1 of fevipiprant, dose 2 of fevipiprant or placebo administered orally once daily for 52 weeks in addition to standard care for asthma.
Follow-up	Active treatment for 52 weeks, overall follow-up not reported.
Primary Outcomes	• Moderate-to-severe asthma exacerbations [Time frame: 52 weeks]
Secondary Outcomes	• Change from baseline in asthma quality of life questionnaire+12 score [Time frame: 52 weeks] • Change from baseline in asthma control questionnaire-5 [Time frame: 52 weeks] • Change from baseline in FEV1 (litres) – [Time frame: 52 weeks] • Safety as assessed by monitoring adverse events [Time frame: 52 weeks]
Key Results	Not reported
Adverse effects (AEs)	Not reported

Expected reporting date	Study completion date reported as August 2019.

Trial	**SPIRIT, NCT03052517, EudraCT-2016-001560-11, CQAW039A2315; adults and adolescents aged 12 years and older; bevipiprant vs placebo both in addition to standard of care asthma therapy; phase III**
Sponsor	Novartis Pharmaceuticals
Status	Ongoing
Source of Information	Trial registry[23,24]
Location	18 EU countries (including UK), USA, Canada and other countries
Design	Randomized, placebo-controlled, double blind, parallel assignment study
Participants	n=1,570; males and females; aged at least 12 years or older; Patients completing a prior phase 3 study of QAW039: a diagnosis of asthma uncontrolled on GINA 3/4/5 asthma medication; an FEV1 of ≤85% of the predicted normal value; evidence of airway reversibility or hyper-reactivity; an ACQ score ≥1.5 prior to entering the study; patients completing a prior phase 3 study of QAW039
Schedule	Patients received either dose 1 of fevipiprant, dose 2 of fevipiprant or placebo administered orally once daily for 52 weeks in combination with standard of care for asthma.
Follow-up	Active treatment period 52 weeks, overall follow-up not reported
Primary Outcomes	• Safety demonstrated by the incidence of adverse events [Time frame: up to 160 weeks]
Secondary Outcomes	• Rate of patients with at least 1 treatment emergent adverse events by primary system organ class [Time frame: 52 weeks] • Rate of treatment emergent patient deaths and patient hospitalizations due to an asthma exacerbation [Time frame: 52 weeks] • Rate of patients with at least 1 treatment emergent adverse effects by primary system organ class [Time frame: 160 weeks] • Rate of treatment emergent patient deaths and patient hospitalizations due to an asthma exacerbation [Time frame: 160 weeks]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	The estimated primary completion date reported as November 2022.

Trial	**ZEAL-1, NCT03215758, Eudra-CT-2017-001273-16, CQAW039A2316; adults and adolescents aged 12 years and older; fevipiprant vs placebo both in addition to standard of care asthma therapy; phase III**
Sponsor	Novartis Pharmaceuticals
Status	Completed
Source of Information	Trial registry[25,26]
Location	4 EU countries (not incl UK), USA and other countries

Design	Randomized, placebo-controlled, parallel assignment, double-blind study
Participants	n=675; males and females; aged 12 years and older; patients with an asthma diagnosis according to GINA 2016 guidelines for at least 6 months; have been treated with ICS with or without an additional controller.
Schedule	Subjects received a dose of fevipiprant or placebo once daily in addition to standard of care asthma therapy for 12 weeks.
Follow-up	Active treatment for 12 weeks, overall follow-up not reported.
Primary Outcomes	• Change in FEV1 (litres) from baseline [Time frame: 12 weeks]
Secondary Outcomes	• Change from baseline in daytime asthma symptom score [Time frame: 12 weeks] • Change from baseline in the number of puffs of short-acting beta agonist taken per day [Time frame: 12 weeks] • Change from baseline in Asthma Quality of Life Questionnaires+12 [Time frame: 12 weeks]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Primary completion date reported as July 2019

Trial	**ZEAL-2, NCT03226392, EudraCT-2017-001272-40, CQAW039A2317; adults and adolescents aged 12 years and older; fevipiprant vs placebo both in addition to standard of care asthma therapy; phase III**
Sponsor	Novartis Pharmaceuticals
Status	Completed
Source of Information	Trial registry[27,28]
Location	10 EU countries (not incl UK), USA, Canada and other countries
Design	Randomized, placebo-controlled, parallel assignment, double blind study
Participants	n=702; males and females; aged 12 years and older; patients with an asthma diagnosis according to GINA 2016 guidelines; have been treated with ICS with or without an additional controller
Schedule	Subjects received a dose of fevipiprant or placebo once daily in addition to standard of care asthma therapy for 12 weeks.
Follow-up	n/a
Primary Outcomes	Change in FEV1 (litres) from baseline [Time frame: 12 weeks]
Secondary Outcomes	• Change from baseline in daytime asthma symptom score [Time frame: 12 weeks] • Change from baseline in the number of puffs of short-acting beta agonist taken per day [Time frame: 12 weeks] • Change from baseline in Asthma Quality of Life Questionnaires+12 [Time frame: 12 weeks] • To assess the safety demonstrated by incidence of adverse effects, electrocardiograms and vital signs and laboratory tests [Time frame: 12 weeks]

Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Primary completion date reported as July 2019

ESTIMATED COST

The cost of fevipiprant is not yet known.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal. Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and older. March 2008
- NICE guideline in development. Asthma: diagnosis, monitoring, and chronic asthma management (NG10143). Expected publication date: January 2020.
- NICE guideline Asthma: diagnosis, monitoring and chronic asthma management (NG80). November 2017.
- NICE quality standard. Asthma (QS25). February 2013.
- NICE diagnostic guidance. Measuring fractional exhaled nitric oxide concentration in asthma: NIOX MINO, NOIX VERO and NObreath (DG12). April 2014.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. Specialised Respiratory Services (Adult) – Severe Asthma. 170002/S. April 2017

OTHER GUIDANCE

- Scottish Intercollegiate Guidance Network 158. British guideline on the management of asthma. July 2019.[22]
- International European Respiratory Society, American Thoracic Society. Guidelines on definition, evaluation and treatment of severe asthma. April 2014.[29]

ADDITIONAL INFORMATION

REFERENCES

1 Bateman ED, Guerreros AG, Brockhaus F, Holzhauer B, Pethe A, Kay RA, et al. Fevipiprant, an oral prostaglandin DP2 receptor (CRTh2) antagonist, in allergic asthma uncontrolled on low-dose inhaled corticosteroids. *The European respiratory journal*. 2017;50(2). Available from: https://erj.ersjournals.com/content/50/2/1700670.long 10.1183/13993003.00670-2017.

2 Kao CC, Parulekar AD. Spotlight on fevipiprant and its potential in the treatment of asthma: evidence to date. *Journal of asthma and allergy*. 2019;12:1-5. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6324611/ 10.2147/JAA.S167973.

3 Saunders R, Kaul H, Berair R, Gonem S, Singapuri A, Sutcliffe AJ, et al. DP 2 antagonism reduces airway smooth muscle mass in asthma by decreasing eosinophilia and myofibroblast recruitment. *Science translational medicine*. 2019;11(479):eaao6451. Available from: https://stm.sciencemag.org/content/11/479/eaao6451.full 10.1126/scitranslmed.aao6451.

4 Domingo C, Palomares O, Sandham DA, Erpenbeck VJ, Altman P. The prostaglandin D2 receptor 2 pathway in asthma: a key player in airway inflammation. *Respiratory research*. 2018;19(1). Available from: https://respiratory-research.biomedcentral.com/articles/10.1186/s12931-018-0893-x 10.1186/s12931-018-0893-x.

5 EU Clinical Trials Register. *A 52-week, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of QAW039 when added to existing asthma therapy in patients with uncontrolled severe asthma. Trial ID: 2015-003172-67*. 2015. Status: Completed. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-003172-67/SK [Accessed 24 September 2019].

6 EU Clinical Trials Register. *A 52-week, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of QAW039 when added to existing asthma therapy in patients with uncontrolled severe asthma. Trial ID: 2015-002553-35*. 2018. Status: Ongoing. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-002553-35/ES/ [Accessed 24 September 2019].

7 Clinicaltrials.gov. *Study of Efficacy and Safety of QAW039 in Patients With Severe Asthma Inadequately Controlled With Standard of Care Asthma Treatment. Trial ID: NCT02563067*. 2015. Status: Completed. Available from: https://ClinicalTrials.gov/show/NCT02563067 [Accessed 25 September 2019].

8 Clinicaltrials.gov. *Study of Efficacy and Safety of QAW039 in Patients With Severe Asthma Inadequately Controlled With Standard of Care Asthma Treatment. Trial ID: NCT02555683*. 2015. Status: Active, not recruiting. Available from: https://ClinicalTrials.gov/show/NCT02555683 [Accessed 25 September 2019].

9 Clinicaltrials.gov. *Search for Fevipiprant | Phase 2, 3*. 2019. Available from: https://clinicaltrials.gov/ct2/results?cond=&term=&type=&rslt=&age_v=&gndr=&intr=Fevipiprant&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&lupd_s=&lupd_e=&sort= [Accessed 03/10/2019].

10 NICE guidance. *Asthma: diagnosis, monitoring and chronic asthma management (NG80)*. Last Update Date: Nov 2019. Available from: https://www.nice.org.uk/guidance/ng80 [Accessed 24 September 2019].

11 NICE guidance. *Bronchial thermoplasty for severe asthma (IPG635)*. Last Update Date: Dec 2018. Available from: https://www.nice.org.uk/guidance/ipg635 [Accessed 24 September 2019].

12 British Lung Foundation. *What is asthma?* Available from: https://www.blf.org.uk/support-for-you/asthma/what-is-asthma [Accessed 24 September 2019].

13 NHS inform. *Asthma*. Available from: https://www.nhsinform.scot/illnesses-and-conditions/lungs-and-airways/asthma [Accessed 24 September 2019].

14 Global Initiative For Asthma. *Difficult-to-treat and severe asthma in adolescent and adult patients* Last Update Date: April 2019. Available from: https://ginasthma.org/wp-content/uploads/2019/04/GINA-Severe-asthma-Pocket-Guide-v2.0-wms-1.pdf [Accessed 24 September 2019].

15 Asthma UK. *What is severe asthma?* Available from: https://www.asthma.org.uk/advice/severe-asthma/what-is-severe-asthma/ [Accessed 24 September 2019].

16 McDonald VM, Hiles SA, Jones KA, Clark VL, Yorke J. Health-related quality of life burden in severe asthma. *The Medical journal of Australia*. 2018;209(S2):S28-S33. Available from: https://www.mja.com.au/journal/2018/209/2/health-related-quality-life-burden-severe-asthma.

17 Asthma UK. *Asthma facts and statistics*. Available from: https://www.asthma.org.uk/about/media/facts-and-statistics/ [Accessed 18 October 2019].

18 Mukherjee M, Stoddart A, Gupta RP, Nwaru BI, Farr A, Heaven M, et al. The epidemiology, healthcare and societal burden and costs of asthma in the UK and its member nations: analyses of standalone and linked national databases. *BMC Medicine*. 2016 2016/08/29;14(1):113. Available from: https://doi.org/10.1186/s12916-016-0657-8 10.1186/s12916-016-0657-8.

19 NHS Digital. *Hospital Admitted Patient Care Activity, 2017-18: Diagnosis.* . Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2017-18 [Downloaded 27 November 2018].

20 Office for National Statistics. *Deaths from asthma and COPD, England and Wales, 2001 to 2017 by occurrence*. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/adhocs/009602deathsfromasthmaandcopdenglandandwales2001to2017byoccurrence [Downloaded 12 February 2019].

21 NHS. *Asthma Treatment*. Available from: https://www.nhs.uk/conditions/asthma/treatment/ [Accessed 24 September 2019].

22 British Thoracic Society SIGN. *British Guideline on the Management of Asthma* Last Update Date: 24 Jul 2019. Available from: https://www.brit-thoracic.org.uk/quality-improvement/guidelines/asthma/ [Accessed 24 September 2019].

23 Clinicaltrials.gov. *Study of Safety of QAW039 in Patients With Asthma Inadequately Controlled on Standard-of-care Asthma Treatment. Trial ID: NCT03052517*. 2017. Status: Recruiting. Available from: https://ClinicalTrials.gov/show/NCT03052517 [Accessed 25 September 2019].

24 EU Clinical Trials Register. *A 2-treatment period, randomized, placebo-controlled, multicenter parallel-group study to assess the safety of QAW039 when added to existing asthma therapy in GINA steps 3, 4 and 5 patients with uncontrolled asthma. Trial ID: 2016-001560-11*. 2017. Status: Ongoing. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-001560-11/SK/ [Accessed

25 Clinicaltrials.gov. *Study of Efficacy and Safety of QAW039 When Added to Standard-of-care Asthma Therapy in Patients With Uncontrolled Asthma. Trial ID: NCT03215758*. 2017. Status: Active, not recruiting. Available from: https://ClinicalTrials.gov/show/NCT03215758 [Accessed 25 September 2019].

26 Register ECT. *A 12-week, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of QAW039 when added to standard-of-care asthma therapy in patients with uncontrolled asthma. Trial ID: 2017-001273-16*. 2017. Status: completed. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-001273-16/SK [Accessed 24 September 2019].

27 Clinicaltrials.gov. *Study of Efficacy and Safety of QAW039 When Added to Standard-of-care Asthma Therapy in Patients With Uncontrolled Asthma. Trial ID: NCT03226392*. 2017. Status: Active, not recruiting. Available from: https://ClinicalTrials.gov/show/NCT03226392 [Accessed 25 September 2019].

28 EU Clinical Trials Register. *A 12-week, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of QAW039 when added to standard-of-care asthma therapy in patients with uncontrolled asthma. Trial ID: 2017-001272-40*. 2017. Status: Completed. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-001272-40/SE/ [Accessed 24 September 2019].

29 International European Respiratory Society ATS. *International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma* Last Update Date: 2014. Available from: https://erj.ersjournals.com/content/43/2/343 [Accessed 24 September 2019].

NB: This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.