

National Institute for Health and Clinical Excellence

Corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over

Response to consultee and commentator comments on the draft scope

Comments on the draft scope

Section	Consultees	Comments	Action
Background information	GlaxoSmithKline	The background on asthma as a disease is succinct and covers the necessary ground. We feel that including the BTS guidelines verbatim rather than paraphrasing would add clarity to the scope.	This would make the scope too lengthy. Added reference to the SIGN guideline number and web site URL.
	Altana Pharma UK	We are content with the accuracy and completeness of this information.	No action required
	Trinity-Chiesi Pharmaceuticals Ltd	We are content with the accuracy and completeness of this information.	No action required
	Asthma UK	it seems accurate and complete	No action required
	British Lung Foundation	Looks accurate and complete.	No action required
	Cochrane Airways Group	This seems sensible.	No action required
	General Practice Airways Group	Add the criteria for initiating inhaled corticosteroids, as recommended by SIGN/BTS Guidelines	Added

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The technology/ intervention	GlaxoSmithKline	<p>It should be noted that mometasone is only available as a dry powder inhaler (DPI), not as a pressurised metered dose inhaler (MDI). For the compound preparations, Seretide is available as both MDI and DPI and Symbicort as DPI only.</p> <p>Further consideration should also be given to the introduction of CFC-free inhalers, not only in terms of the environment but also in terms of which products will actually be available for prescribers in the future.</p>	<p>This is noted in the background information.</p> <p>All currently available CFC and non-CFC inhalers will be included.</p>
	Altana Pharma UK	We are content that the description of the technology is accurate.	No action required
The technology/ intervention	AstraZeneca UK Ltd	To follow current English/Welsh terminology, AstraZeneca suggest substitution of the phrase 'compound preparations' with 'combination inhalers' to indicate use of an inhaled corticosteroid and long acting beta agonist in the same inhaler.	Changed
	Ranbaxy (UK) Ltd	Please note that in October 2005 Easyhlaer Beclometasone 200 microgram / dose inhalation powder was launched in the UK -	Also added Easyhaler budesonide – launched 07 02 06
	Trinity-Chiesi Pharmaceuticals Ltd	We are content that the description of the technology is accurate	No action required
	VIATRIS Pharmaceuticals Ltd	<p>The description of the five inhaled corticosteroids is accurate, but the list of technologies is confusing and does not appear to be complete. Viatris would recommend reviewing this list carefully before the scope is finalised.</p> <p>Specifically the Viatris product is incorrectly named. The correct name is 'Novolizer Budesonide' please note the 'z'. Novolizer is the brand name for the inhaler device. In addition, the list of beclometasone technologies is not comprehensive.</p> <p>In order to simplify the list of technologies Viatris would recommend that the technolgy list is separated into 2 sublists, i.e i) inhaled corticosteroids and the combinations , ii) delivery systems</p>	<p>Corrected spelling</p> <p>Added one additional beclometasone product – not aware of any others (based on British National Formulary).</p>

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	Cochrane Airways Group	This is an extensive overview. I assume that the classification of HFA-BDP extrafine (QVAR) as BDP will be clarified when the analyses are undertaken. The evidence to date suggests that it has a different potency than existing formulations	Noted already in the 'Other considerations' section of the scope (Statement regarding variation in dose-equivalence).
The technology/ intervention	Cochrane Airways Group	Some people may well prefer to use one type of device over another – and there are many people with asthma who are given spacers as well to administer their medication. Retaining some sense of how these issues affect evidence would be useful. At the scoping stage this need only be acknowledged. However, the analysis/interpretation of evidence will need to be take account of some of the issues regarding concordance – cost effectiveness should incorporate some assessment of continued acceptance and ease of use of the delivery devices involved (especially as some are not available through both MDIs and dry powder forms). Issues of concordance are particularly important seeing as adolescents are also included in this analysis.	The difficulties of this appraisal are acknowledged and timelines have been extended to take this into account.
	General Practice Airways Group	Yes, although it could be mentioned that inhaled corticosteroids, delivered via a metered -dose inhaler can be administered via spacer devices.	Added
	Royal College of General Practitioners	1. Standard comparators I think they should add: inhaled corticosteroids used in combination with leukotriene antagonists	Given the complexity of this appraisal it has been decided that comparators should be kept to a minimum
Licensing issues	Altana Pharma UK	In confidence information removed	
	AstraZeneca UK Ltd	In confidence information removed	
	Ranbaxy (UK) Ltd	Ranbaxy will be launching Easyhaler Budesonide 100 mcg, 200mcg and 400mcg.	Added
	Trinity-Chiesi Pharmaceuticals Ltd	In confidence information removed Pulvinal was licensed in January 2001.	

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Licensing issues	VIATRIS Pharmaceuticals Ltd	The Novolizer® is currently licensed in the UK to deliver budesonide (Novolizer® Budesonide), for the treatment of persistent asthma in adults and children of 6 years and above. In addition, Novolizer® Salbutamol and Novolizer® Formoterol are currently undergoing review by the MHRA. Combinations are also under development for inclusion in this device. In confidence information removed..	No action required
Population	GlaxoSmithKline	The population is defined appropriately at 12 years and over	No action required
	Altana Pharma UK	In our opinion the population is defined appropriately and there is no need to consider other populations separately.	No action required
	AstraZeneca UK Ltd	AstraZeneca would suggest clarification at this stage that the relevant population are those adults and children aged 12 years or over with chronic asthma.	The word 'chronic' has been added.
	Trinity-Chiesi Pharmaceuticals Ltd	In our opinion the population is defined appropriately and there is no need to consider other populations separately.	No action required
	Asthma UK	This is a relevant topic for both asthma and COPD but in this context it would be helpful to assess the groups separately which will require a clearer definition of asthma (or exclusion criteria for COPD)	Assume asthma has been diagnosed – diagnostic criteria are beyond the scope
	British Lung Foundation	Well defined and clear - but can a 12 year old be fairly compared to a 22, 32, 42 year old etc	This issue was discussed at the scoping workshop in December 2004. It was agreed that 12 years was an appropriate age at which to split the 2 parallel appraisals.
	Cochrane Airways Group	This is very broad (and understandably so). Will there be some attempt to classify study populations according to the BTS/SIGN guidelines? Subgroups such as those dependent on high doses of ICS will benefit more from drugs with greatest potency (e.g. HFA-BDP and FP) than those with mild intermittent asthma.	Examples of potential subgroups including different degrees of severity of asthma added under 'other considerations'.

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Population	General Practice Airways Group	Generally yes, but smokers respond differently to ICS than non-smokers.	Examples of potential subgroups including smokers added under 'other considerations'.
	Royal College of General Practitioners	Should special groups such as older people & minority ethnic groups be considered? What about the COPD/asthma "overlap" group.	It is unclear how age and ethnicity will affect response to different drugs. (NB this is not an appraisal of devices) Examples of potential subgroups including those with an element of COPD added under 'other considerations'.
	Southampton Health Technology Assessments Centre (SHTAC) and Peninsula Technology Assessment Group (PenTAG)	The population should be defined as having 'chronic asthma' to be consistent throughout the scope	The word 'chronic' has been added.
Comparators	GlaxoSmithKline	The appraisal objective is to appraise the clinical and cost effectiveness of corticosteroids which would meet the criteria of an appraisal. The current scope appears to cover a broader remit and wider comparisons.	The number of comparators have been minimised as far as possible in order to facilitate this complex appraisal.

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Comparators	GlaxoSmithKline	<p>Firstly the scope appears to be addressing alternative treatment management strategies by making comparisons between compound products and increased dose ICS and compound products with ICS and the addition of oral bronchodilators. This would appear to make the review more like a clinical guideline. (As a point of clarification, the scope should also specify whether ICS will be compared only when used alone or when used in combination with LABA).</p>	<p>Corticosteroids will be compared with each other regardless of concomitant therapy. Combinations will be compared with corticosteroids alone and the use of two separate inhalers (one corticosteroid and one LABA).</p>
		<p>Secondly, this broader approach means the review will be inordinately complex due to the extensive number of comparisons that would be necessary. At our estimation, in theory, this could reach over a thousand potential comparisons. This complexity would also lead us towards a view that this is best served either as a guideline, or alternatively as a specific appraisal of ICS within a broader clinical guideline process.</p>	<p>Would there be added value in another clinical guideline given the existence and established status of the BTS/SIGN document?</p>
		<p>In answer to the specific questions for consultation, we do not feel it is appropriate to compare the compounds with combinations of ICS and oral bronchodilators, nor to increased dose of ICS or to make broader comparisons with the use of cromones and leukotriene receptor antagonists (LTRAs). We believe this would make the review unfeasible and is beyond the stated appraisal objectives. To limit the review to comparisons of ICS alone, in combination with LABA , or the use of compound products will result in a more meaningful appraisal whilst still addressing the original remit.</p>	<p>Oral bronchodilators will not be included as comparators. Comparators will be kept to a minimum in view of the complexity of this appraisal</p>
		<p>We agree that this appraisal should follow the stepwise approach recommended in the BTS guidelines. However, further specifying which comparisons should be made at clinically relevant dose equivalents at each BTS step would clarify the appraisal.</p> <p>We also recognise that dose equivalence should be taken into account when defining appropriate comparisons. However, it is also important to retain a degree of pragmatism to take account of realistic therapeutic alternatives at each step.</p>	<p>Dose equivalence can only be established after reviewing the evidence</p>
	Altana Pharma UK	<p>In our opinion, yes.</p> <p><i>(In answer to the question "Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared?")</i></p>	No action required

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Comparators	AstraZeneca UK Ltd	<p>Inhaled corticosteroids</p> <p>For nebulised preparations, the comparator is often not an active comparator but placebo. To ensure that valuable data are not 'lost' when NICE conducts its review, where no substantial data exist the Institute should accept placebo as a valid comparator.</p>	Placebo is not a relevant comparator for the purposes of this appraisal.
	AstraZeneca UK Ltd	<p>Compound preparations (Combination preparations)</p> <p>The mainstay of asthma treatment within England and Wales constitutes use of inhaled corticosteroid and short/long acting bronchodilator. National guidelines (e.g. BTS Guidelines) endorse this approach and as such, use of other agents such as oral bronchodilators is very limited and certainly not routine. There are very limited data available to inform on effectiveness. Therefore to ensure guidance produced is the most relevant possible AstraZeneca would strongly suggest that oral bronchodilators are not included as comparators in the appraisal of combination inhalers.</p>	Oral bronchodilators will not be included as comparators.
	Ranbaxy (UK) Ltd	Ranbaxy will also be launching Easyhaler Formoterol long acting beta 2 agonist. This has received European mutual recognition approval and is going through UK approval. The launch of this should be in 2006. This launch may also affect the cost effectiveness data when comparing combination therapies to the drugs administered by individual inhalers.	Will be included in the economic evaluation of combined inhalers versus separate inhalers
	Trinity-Chiesi Pharmaceuticals Ltd	<p>In our opinion, yes.</p> <p><i>(In answer to the question "Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared?")</i></p>	No action required

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Comparators	VIATRIS Pharmaceuticals Ltd	<p>What is meant by the term 'agent'? Does this mean the "pharmacologically active agent" or 'the pharmacologically active agent and the delivery system'?</p> <p>It will not be possible to compare the corticosteroids given via different dry-powder inhalers because there is no DPI that incorporates more than one of the corticosteroids to be compared.</p> <p>Alternatively, the different corticosteroid treatments could be compared using pMDIs to establish the pharmacological effectiveness and relevance of the molecules for the treatment of asthma.</p> <p>Following this a comparison of different inhalers with the same corticosteroid e.g. budesonide which can be delivered by the Turbohaler® and the Novolizer® and beclometasone which can be delivered by a variety of inhaler devices. This could help to establish the comparative, efficacy and cost-effectiveness of the different products.</p> <p>If analysed in this way the guidance may make one level of conclusions regarding the choice of corticosteroid and a second level of conclusions regarding the choice of delivery systems.</p> <p>The combinations could be compared in the same way.</p> <p>This is perhaps long-winded, but is reflective of the complexity of the comparisons needed.</p>	<p>'Agent' changed to 'drug'</p> <p>Indirect comparisons may be used to compare DPIs – cannot assume that PMDIs are all the same between different drugs either.</p> <p>Methods of analysis will be determined by the Assessment Group.</p>
	Asthma and Allergy research Group, University of Dundee	Should be comparison of ICS +LABA vs ICS +LTRA or ICS +Theophylline	It has been decided to limit comparators to a minimum to facilitate this complex appraisal. Leukotriene antagonists and theophyllines will not be comparators.
	Asthma UK	From a patient perspective, I am sure some parents use oral bronchodilators for ease of administration to their children nevertheless these are not usually necessary for children age 12 and above as they can normally master inhaler technique if an appropriate device and training is given. I expect that anything which clarifies usefulness of oral bronchodilators would be helpful as they are currently not deemed the most effective therapy, nevertheless some people with asthma prefer this route.	Oral bronchodilators will not be included as comparators.

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Comparators	Cochrane Airways Group	<p>Comparing the steroids with each other is the best way to ascertain some kind of dose response and idea of relative efficacy. How common are oral bronchodilators used? I thought that they had been supplanted by inhaled LABAs.</p> <p>The inclusion of compound preparations (whilst relevant) also introduces some issues regarding additional comparators. Anti-leukotriene agents are natural competitors to inhaled LABAs</p>	<p>Oral bronchodilators will not be included as comparators.</p> <p>It has been decided to limit comparators to a minimum to facilitate this complex appraisal. Leukotriene antagonists will not be comparators</p>
	British Lung Foundation	Comparators proposed are comprehensive.	No action required
	General Practice Airways Group	<p>Yes except oral bronchodilators are seldom used, are considered as "Step 4 " therapy and therefore not as a comparator to inhaled steroids/combinations.</p> <p>Comparison with leukotriene receptor antagonists is strongly recommended.</p>	<p>Oral bronchodilators will not be included as comparators.</p> <p>It has been decided to limit comparators to a minimum to facilitate this complex appraisal. Leukotriene antagonists will not be comparators</p>

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Comparators	Royal College of General Practitioners	<p>Regarding the questions for consultation:</p> <p>a. I am not sure of the worth of comparing treatment with oral bronchodilators as it is an extremely uncommon practice apart from in severe asthma.</p> <p>b. I agree it is worth comparing with leukotriene antagonists but not worthwhile with cromones as they are now rarely used.</p> <p>Would also recommend including:</p> <ol style="list-style-type: none"> 1) primary care consultation rate, secondary care hospitalisation and A+E attendance and other psychosocial outcomes as well. 2) encompass 'real-world' issues such as compliance and inhaler technique in the evaluations and to recognise that generalisability from RCTs may be an issue. Observational studies should be included in the analysis of evidence 3) How does the potency of inhaled steroids compare? 4) What effect does delivery system make? 5) How do the relative side effect profiles compare? 6) What are the clinical and cost implications of using combination products? 7) Are there quality issues with generic pMDIs? 	<p>Oral bronchodilators will not be included as comparators</p> <p>Potency and device related issues will have to be taken into account as far as the evidence allows.</p> <p>Quality issues with licensed products are not within the remit of the Institute</p>
	SHTAC and PenTAG	<p>In relation to compound preparations containing a corticosteroid and a long-acting beta2 agonist for inhalation compared to inhaled corticosteroids and long-acting beta2 agonists administered by separate inhalers - the advantage of compound preparations appears to be convenience for the patient who only has to use (and carry with them) one inhaler instead of two. However, there may be little difference in clinical and cost effectiveness between these two modes of delivery, assuming little or no difference in cost or efficacy. This may not, therefore, be a useful comparison.</p>	<p>Have now limited this comparison to the economic analysis only – i.e. a comparison of the costs of the different means of administration assuming equivalence in effectiveness.</p>
Outcomes	GlaxoSmithKline	<p>The appraisal does need to cover a range of outcomes, as it is now well recognised that patient reported outcome measures are as important as objective lung function measures and they enable a consideration of the total impact of asthma on the patient. In addition, due to the length of time over which ICS have been researched, the outcome measures can vary significantly between trials.</p>	<p>Patient reported outcomes will be measured in the assessment of health-related quality of life.</p>

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Outcomes	GlaxoSmithKline	<p>Therefore, when making comparisons, the outcome measures must not only be meaningful clinical measures of asthma but also standard so that cross trial comparisons are valid.</p> <p>From our experience in the asthma research field, we would suggest that as a minimum, the most appropriate measures of lung function are: FEV1 and change in morning PEF.</p>	FEV ₁ and PEF included already
		<p>In terms of symptoms, the variation in the ways in which 'wheeze' and 'shortness of breath' can be measured will be hugely variable across studies, if measured at all. We would suggest that symptom free days and symptom free nights would be more meaningful, comparable and universal measures for symptoms, in addition to use of relief medication.</p>	Symptom free days/nights added
		<p>Exacerbations need to be clearly defined, as these can range from a small change in medication to hospitalisation.</p> <p>For HR QOL, due to the age of most of the trials it is unlikely that EQ5D will have been measured in many. In this case, having HR QOL that can be mapped to utility scores is probably the most likely available outcome.</p>	Added acute mild versus acute severe definitions as suggested below
		Altana Pharma UK	<p>In our opinion, yes.</p> <p><i>(In answer to the question "Will these outcome measures capture the most important health related benefits of the technology?")</i></p>
	AstraZeneca UK Ltd	<p>AstraZeneca believe it is important that the term 'acute exacerbations' is defined within the scope. We believe it should be split into 'acute mild' and 'acute severe' exacerbations and that the definitions of these are as follows:</p> <ul style="list-style-type: none"> • Acute mild = contact with healthcare professional required • Acute severe = hospitalisation, course of oral steroids or visit to A+E required <p>AstraZeneca also believe that there should be a separate outcome based on reliever use only. This is because reliever use is a standard outcome that is measured in the majority of clinical trials conducted in asthma.</p>	<p>Added</p> <p>Not added – it is difficult to relate the use of as required medication to clinical outcome</p>
	Trinity-Chiesi Pharmaceuticals Ltd	<p>In our opinion, yes.</p> <p><i>(In answer to the question "Will these outcome measures capture the most important health related benefits of the technology?")</i></p>	No action required

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Outcomes	VIATRIS Pharmaceuticals Ltd	<p>Additional outcomes that could be considered:</p> <ul style="list-style-type: none"> - waking at night, - interference with daily physical activity. - hospitalisations. Unless the use of systemic corticosteroids is a marker for hospitalisations, we would recommend the 'number of non-routine hospitalisations' as an outcome measure as this will dramatically affect the cost-effectiveness of a treatment. - compliance. This is particularly important in ensuring asthma control with corticosteroids. The BTS/SIGN guidelines recommend the checking of compliance before escalating to step 3. 	<p>Added symptom-free nights and hospital admissions now forms part of the definition of severe exacerbation. Treatment adherence is always an issue with appraisals of drug treatments, but good data are often lacking.</p>
	Asthma and Allergy research Group, University of Dundee	<p>Should include surrogate inflammatory markers such as airway hyperreactivity, exhaled nitric oxide ,sputum eosinophils , serum ECP, markers of airway remodelling -e.g. biopsy basement membrane thickness</p> <p>Mortality is a key outcome here -especially wrt recent GSK SMART study</p> <p>Need to evaluate exacerbations not just in terms of % reduction but also in terms of NNT from meta-analysis</p>	<p>It is not usual to use surrogate outcomes where clinical outcomes are available.</p> <p>Mortality has been added as an outcome</p>
	Asthma UK	<p>From a patient perspective, reduced days off sick and reduced frequency / severity of attacks would be important outcomes. Some thought will be needed to clarify what constitutes an attack as often worsening is gradual in onset. How about looking at the number of unclaimed prescriptions for each device? Confounding variables will also need to be identified eg. triggers, smoking status.</p>	<p>It is unlikely that there are data on unclaimed prescriptions. Other outcomes should be covered by health-related quality of life. Confounding should be eliminated by randomisation.</p>
	Cochrane Airways Group	<p>Definition of outcome is always a tricky process and I suspect that transparency will be the key here.</p> <p>Separating 'acute exacerbations' from 'systemic steroids' is eminently sensible - but there are many instances when exacerbations are defined by doubling of inhaled steroid. Do acute exacerbations mean unscheduled contact with GP/acute services? Or does it refer to hospital admission? Some sense of how these may reflecty different severities of exacerbations would be useful.</p>	<p>Have clarified definition of exacerbations as suggested above</p>

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Outcomes	General Practice Airways Group	<p>Recommend adding patient -reported measures of asthma control such as the Asthma Control Questionnaire (ACQ-Juniper)</p> <p>Measures of airways inflammation (e.g exhaled nitric oxide) and airways hyperactivity (PC20) might help.</p> <p>The definition of acute exacerbations needs to be clarified. Separate outcome measures of oral steroid use, hospitalisations could be used or combined (as in many studies) as "severe exacerbations".</p> <p>The incidence of side effects might vary according to the inhaler device by which the drug is delivered.</p>	<p>Do not usually specify the scales on which outcomes should be measured (may limit the evidence which can be included)</p> <p>The definition of exacerbations has been clarified</p> <p>Device issue noted – will also apply to other outcomes</p>
	Royal College of General Practitioners	Outcomes I think they should add patient reported asthma control e.g asthma control questionnaire	This should be covered by health-related quality of life
Economic analysis	GlaxoSmithKline	<p>Due to the large number of potential comparisons, the economic analysis will be necessarily complex and extensive. In addition to the number of clinical comparisons to be made, the pricing structure of these medications means that a further number of comparisons would be needed when costs of medications are taken into account.</p> <p>There are a number of technical issues where a more detailed discussion between the assessment groups and manufacturers may reduce uncertainty.</p> <p>For example, as most ICS come in a variety of preparations, they can be used in many combinations to reach a required dose. If comparing Seretide to its components: fluticasone comes in 17 different preparations at 17 different price points and salmeterol in four. This means there are potentially 68 prices that could be chosen for this one comparator.</p> <p>A potential approach of price per 100mcg (per BDP equivalent) for each product weighted by its use in practice could be followed to allow for simpler comparisons.</p> <p>Whilst issues such as this may not strictly be a scoping issue, an agreed approach may allow more meaningful submissions to be made.</p>	<p>Noted. The timelines for this appraisal have been extended to take this into account.</p> <p>Noted</p>
	Asthma UK	Would the measure you are suggesting be sufficiently sensitive to allow distinction between modes of therapy?	This section reflects the reference case recommendations

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Economic analysis	British Lung Foundation	Good analysis - the aim is to identify the treatment(s) that will yield the best control of symptoms for the lowest cost to the NHS and the patient.	No action required
	General Practice Airways Group	The literature often quotes cost per asthma-free or symptom -free day.	A NICE appraisal requires preference-based utilities where possible.
Other considerations	GlaxoSmithKline	The initial searches within GSK indicate that from GSK sponsored studies alone we have in excess of a thousand studies that may be relevant. Obviously, broader literature searches will generate even more studies for consideration.	Noted – no action for scope
		The quality and relevance of all these studies will be variable, and there is a tendency for asthma studies to be unblinded. Thus when combining trial data, particular consideration should be given to the evidence hierarchy.	The Assessment group will determine the inclusion criteria, quality assessment, and the methods for combining data
	Trinity-Chiesi Pharmaceuticals Ltd	Will consideration be made of CFC-formulations and if so will they be compared to non-CFC-free agents?	This is not a comparison of formulations – non-equivalence of devices will be taken into account as far as possible.
	VIATRIS Pharmaceuticals Ltd	This review does not cover delivery systems specifically. However, as stated below recently there have been technological advances in dry powder inhalers. There is no NICE guidance on the use of delivery technology in the treatment of adult asthma. Therefore, it could be of use to compare some of the basic properties of the inhalers in this review perhaps covering lung deposition, inhaler internal resistance, ease-of-use, patient compliance etc.	Effectiveness is determined both by the pharmacological agent and by the delivery system. General advice on inhalers is outside the remit.
	Asthma and Allergy research Group, University of Dundee	Allergic rhinitis and its impact on asthma -eg adding LTRA may treat upper and lower airway inflammation in allergic asthma and concomitant rhinitis .Effect of intranasal steroid on asthma exacerbations	LTRAs are outside the remit of this appraisal.

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Other considerations	Asthma UK	The timeframes for stepping up and stepping down treatment would be useful to know. Some people with asthma tell us that they find combined inhalers easier to adjust whereas others prefer a combined inhaler for this. There has been a number of complaints from patients finding generic inhalers do not perform as well as a named brand. Whilst there has been research which did not support this, the complaints are still coming in and any insight into why this might be would be gratefully received by the users of these inhalers.	Outside the remit of a technology appraisal which is to determine clinical and cost effectiveness. Quality of licensed products is not within the Institute's remit.
	Cochrane Airways Group	Will there be an attempt to describe the methods to be used in how evidence will be assessed? What use will be made of existing reviews of evidence? How will it be graded/scrutinised? How will unpublished evidence be used?	The Assessment Group's protocol will address these issues.
	General Practice Airways Group	It is important not just to include randomised controlled trials, but to consider "real world" trials e.g observational studies where issues such as compliance, inhaler preference are included. Dose -response considerations are important for each ICS.	The Assessment Group's protocol will address these issues.
	Royal College of General Practitioners	I think for cost-effectiveness they should add what has been often used in the literature cost per symptom or asthma free day and cost per net improvement in health related quality of life.	A NICE appraisal requires preference-based utilities where possible.
Additional comments on the draft scope	GlaxoSmithKline	We strongly believe that the breadth of this review as outlined in the current scope indicates that it should be a guideline and not an health technology appraisal. We believe the potential number of comparisons needed to be made with the scope as it currently stands, make it inordinately complex as a health technology appraisal. We believe that the scope needs to be clarified to focus on the differences between inhaled corticosteroids, as stated in the original remit, rather than considering management strategies. Even this more targeted approach will still involve a large number of comparisons and volume of data.	Would there be added value in another clinical guideline given the existence and established status of the BTS/SIGN document?

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Additional comments on the draft scope.	AstraZeneca UK Ltd	<p>As individual inhaled corticosteroids are, by definition, associated with different devices, running double blind studies in the respiratory area is extremely difficult. As such, the majority of clinical trials have been conducted in an open fashion. Additionally, for older inhaled corticosteroids placebo was accepted as a valid comparator. AstraZeneca suggest that restricting inclusion of trials to only those conducted as double blind, active comparator RCTs would result in the bulk of the data on inhaled corticosteroids being excluded, perhaps resulting in inappropriate findings.</p> <p>AstraZeneca suggest that in this instance the Institute takes a pragmatic approach and includes open / placebo controlled studies with an appreciation of the bias that is inherent to these studies compared with double blind active comparator RCTs.</p> <p>We would ask for notice regarding the approach that the Institute envisages taking to ensure that we can prepare the most appropriate submission possible.</p>	Inclusion criteria will be determined by the assessment group's protocol.
	Ranbaxy (UK) Ltd	<p>Much of the data carried out on inhaled steroid have used pMDI and spacer. Often that spacer device will have been the Volumatic. As the volumatic is no longer available in the UK market does this mean that the data using the Volumatic will be used or not?</p>	The Volumatic spacer has been reintroduced.

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Additional comments on the draft scope.	VIATRIS Pharmaceuticals Ltd	<p>It is noted that this Comments Form does not allow comments on the objective of this appraisal. The objective covers the clinical and cost-effectiveness of corticosteroids in the treatment of asthma. However, recently there have been technological advances in dry powder inhalers resulting in improved lung deposition, compliance and 'ease of use' to the extent that dry powder inhalers may now provide clinical advantage and cost effectiveness over the use of pMDIs. Lung deposition and compliance are key to controlling inflammation and therefore minimising acute episodes and the need for add-on therapy, further intervention such as systemic corticosteroids, or expensive hospitalisations, for example. The delivery system (which may be a dry-powder inhaler) is key in the effectiveness of these corticosteroids. Therefore, it is no longer possible to compare the active agent without the delivery system. Indeed, the NICE draft scope of this review mentions the inhaler technologies (Appendix A; page 3).</p> <p>As the effectiveness and cost effectiveness of the corticosteroids will be influenced by the delivery system Viatris would recommend that the objective of this review should also cover a review of the delivery system i.e "To appraise the clinical cost effectiveness of corticosteroids and the delivery systems,"</p>	<p>The objective for this appraisal is set by the Department of Health and Welsh Assembly Government remit.</p> <p>This is not specifically an appraisal of devices – it is acknowledged that effectiveness is determined both by the drug and the delivery system.</p>
		<p>Comments on the questions for consultation:</p> <p>Would it be appropriate to make broader comparisons with other drugs such as cromones and leukotriene receptor antagonists?</p> <p>Such comparisons would require broadening this already complex review. It would no longer be a review of corticosteroids, but instead a review of the treatment of chronic asthma.</p>	<p>It has been decided to limit comparators to a minimum to facilitate this complex appraisal. Leukotriene antagonists will not be comparators</p>

Section	Consultees	Comments	Action
Additional comments on the draft scope.	British Lung Foundation	The draft scope looks very thorough, logical and well thought-out. I think it is important to compare the compound preparations with combinations of inhaled corticosteroids and oral bronchodilators and/or inhaled corticosteroids. This work must be done thoroughly and must provide hard evidence to allow the most successful and cost-effective treatment strategies to be identified. Comparisons to broader drugs i.e. cromones or leukotriene antagonists might be worthwhile at a later stage but this work should not compromise the important work described. It seems logical to investigate those treatments that are already known to work well, with the aim of identifying ways to optimise their use.	No action required
	Royal College of General Practitioners	A technology assessment should also include spacer devices small and large and look at different administration devices as these contribute to efficacy of use and side effect (not just as a separate appraisal). It is important dissimilar devices are not used in comparators between drugs.	This is not specifically an appraisal of devices – it is acknowledged that effectiveness is determined both by the drug and the delivery system.

The following consultees/commentators indicated that they had no comments on the draft scope

3M Health Care Ltd.
Welsh Assembly Government