National Institute for Health and Clinical Excellence

Anaphylaxis
Pre publication check
11 – 25 October 2011

Type	Stakeholder	Order No	Section	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Royal College of Nursing	1.00			There are no comments to submit at this stage on behalf of the Royal College of Nursing.	Thank you for your comment.
SH	British Society for Allergy and Clinical Immunology	2.00	1 Recommendations	8-10	The explanation that the term 'severe allergic reaction is commonly used rather than 'anaphylaxis' as described on para 2 page 3, does not appear in the Recommendations, which **must** read as stand alone as this is the only section many users will read. Suggest incorporate into recommendations 1.1.1	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.01	1.1.5	8	Tryptase should be measured in all cases of suspected anaphylaxis. Food-induced anaphylaxis in children should not be a reason for not measuring acute tryptase because: a. Although data is scanty in food allergy in children and tryptase is thought not always to be raised, it has been shown to be raised in some cases. b. It is often not measured and therefore little data to support exclusion of this group from testing. c. The cause is commonly not known at time of the acute event – and assumptions about aetiology are often incorrect. Foods are therefore often	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

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					wrongly implicated. Tryptase **must** therefore be measured in all patients.	
SH	British Society for Allergy and Clinical Immunology	2.02	Care pathway 2	11	As above – tryptase in food induced anaphylaxis in children	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.03	Table 2	14	Suggest title should be 'suspected anaphylaxis' rather than anaphylaxis. For example, in anaesthetic studies, some of the reactions suspected to be anaphylaxis turn out to be other events (technical or surgical problems or physiological responses to drugs), as correctly mentioned in 3.1.3.2, page 21	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.04		25	Tryptase – as item 2.03 above	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.05	3.3.4	45	Model assumptions. We are not aware of data showing 20% of patients undergoing venom immunotherapy drop out. BSACI have recently produced a guideline on venom allergy (Krishna MT et al Clin Exp Allergy 2011;41:1201-20). Hardly any patients drop out by choice; and only a small % discontinue due to severe side effects. Ie although the proportion suffering side effects is higher, only a minority of these discontinue immunotherapy.	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.06	3.3.4 Model assumptions	45	Assumptions in the model. Drug treatment (oral antihistamines) of idiopathic anaphylaxis is often used for longer periods and sometimes long-term. The data which has been used is from older papers from one USA group and not in current use or recommended in UK. Perhaps	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

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					considered by NICE as making little difference to costings – however still incorrect	
SH	British Society for Allergy and Clinical Immunology	2.07	Table 11	47	Model assumptions. Under specialist care the recurrent rate of idiopathic anaphylaxis is less because expert knowledge makes a difference in diagnosis and management of these difficult cases. The reduction occurs in 3 ways: 1. prevention (by drug control, usually with daily antihistamines) of further attacks; or reduction in their severity. 2. early patient self treatment of acute attack, gaining control and preventing A&E attendance or hospital admission. 3. Causes for 'idiopathic anaphylaxis' are gradually being discovered and specialist care allows investigation which can lead to determination of cause, thus avoidance and prevention of further episodes. This issue is addressed on page 59, para 4, but not fully covered and still leaving doubt as to the value of a specialist service. This should be clarified	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.08	Table 12	48	Model assumptions. The cost of an adult follow up allergy out-patient appointment is less than first attendance, whereas it is given as more (£450 follow up cf £321 new). Eg in non-mandatory national tariffs for Allergy the cost of follow-up allergy appt is about half the first attendance eg approx £155 cf £305).	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.09		48	After venom immunotherapy there should be fewer further reactions than stated (2.5 reactions per lifetime) eg efficacy for wasp venom IT is approx 95%; and for bee venom IT	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

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					approx 80-85%. In UK ratio of wasp: bee IT is 4: 1 ie approx 80% of treatments are for wasp anaphylaxis. Further stings cause no reaction in patients where venom IT is effective. There is lack of data to predict efficacy of venom IT over a lifetime, but this therapy is know to be effective for a least 10 years.	
SH	British Society for Allergy and Clinical Immunology	2.10	General Economic model		The comments (8, 9 and 10 above) on assumptions in the economic model would all tend to further improve the cost-benefit of a specialist service. Even if this did not alter ICERs, the factual statements should be correct Point 8 was partly taken into account in discussion on page 59 Further discussion, to factually correct these points (8,9 and10), should be added (eg under Limitations pages 56-59).	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.11		62	Table, box on trade off, para 3. The effect on those with cardiac problems is extremely rare. Thus suggest accurate to add the word 'rarely' as follows: "…for example those with cardiac problems, could *rarely* have adverse events as a result of using an adrenaline injector".	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	British Society for Allergy and Clinical Immunology	2.12	3.5.2 Table And 3.5.3.1	68-71	There is evidence which is not included on reduction of further anaphylaxis in nut allergy. In a large prospective study of further reactions in nut allergy in patients receiving specialist allergy care, specialist allergy care reduced the incidence of severe reactions 60-fold. Patients were classified by the severity of their reactions,	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

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					thus those with anaphylaxis were identified separately. The rate of further reactions overall (all severities combined) in this study was 3% annual incidence, compared to 50%, 33% and 14% in other studies. Nuts are the most common food cause fatal and near fatal reactions. (Clark & Ewan. Good prognosis, clinical features and circumstances of peanut and tree nut reactions in children managed by a specialist allergy center. J Allergy Clin Immunol 2008; 122(2): 286-9).	
SH	British Society for Allergy and Clinical Immunology	2.13	1.1.2	72	This should be referral pathway *to a specialist allergy service*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Meda	3.00	3:Table 12 Additional key parameters in economic model	48	**The cost of auto injectors is at £26.45 within the table.** The average cost of auto-injectors is not £26.45.This is the reference price for EpiPen® Auto-Injector. All brands are different and the EpiPen® Auto-Injector is the least expensive by approximately 14% **Number of adrenaline injectors provided per year (assumes two devices to be available at any one time with a shelf-life of 6 months each)** The assumption of a six-month expiry date is wildly inaccurate and refers to an unusual period in supply where the previous distributor was winding down distribution in preparation for	Thank you for your comment. A shelf-life of 12 months was used in the model and stated in the main body of the document. This estimate has now been corrected within the table.

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					the launch of their own device. A 12 month shelf life would be more realistic.	
SH	MHRA	4.00			This organisation responded and said they had no comments.	Thank you for your comment.
SH	Department of Health	5.00			Department of Health has no substantive comments to make regarding this consultation	Thank you for your comment.
SH	Royal College of Paediatrics and Child Health	6.00	4th and 5th paragraphs	4	*In the last sentence, 4th paragraph no evidence has been provided to support the statement 'substantial underestimate' and in the first sentence 5th paragraph to support the statement 'many' people' do not receive optimal management of their condition.*	Thank you for your comment. The word 'substantial' has been removed from the sentence referred to in the fourth paragraph. The sentence in the fifth paragraph has been amended so it reads '...it is believed that many people do not receive optimal management.'
SH	Royal College of Paediatrics and Child Health	6.01	1.1.8	9	*There will not be inpatient paediatric units at every hospital with a receiving A&E department and observation and assessment units may be the appropriate facility with initial discharge to the GP or to the children's community nursing team including what to do if a further episode occurs, and with appropriate referral for further assessment and treatment.*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.02	1.1.9	9	*It is unrealistic for all patients to be referred to specialist centres and general paediatric senior staff working in a clinical network arrangement with specialist allergists could manage these patients – the key is to refer the children to the professional with the right skills and competencies. Children should be seen in a paediatric facility where staff not only have the necessary skills but also have additional skills*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

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					such as safeguarding.	
SH	Royal College of Paediatrics and Child Health	6.03	1.1.10	9	*It should be the decision of the specialist as to whether an adrenaline auto-injector is prescribed, with a safe care pathway to call 999 immediately in the interim period until the patient is seen by the specialist. Otherwise there will be a number of inappropriately prescribed auto-injectors and there are significant training implications for emergency staff*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.04	3.1.3.1	21	**Use of mast cell tryptase testing in the diagnosis of anaphylaxis** *No evidence on the clinical utility of mast cell tryptase testing in the diagnosis of anaphylaxis in children was identified.* *These 2 points therefore do not support the listed recommendation on* **page 8: 1.1.5** *with respect to children under 16 years of age as to when and how mast cell tryptase testing should be performed.*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.05	3.1.3.4	22	**Timing of mast cell tryptase testing in the diagnosis of anaphylaxis** *No evidence on the timing of mast cell tryptase testing in the diagnosis of anaphylaxis in children was identified.* *These 2 points therefore do not support the listed recommendation on* **page 8: 1.1.5** *with respect to children under 16 years of age as to when and how mast cell tryptase testing should*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

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					be performed.	
SH	Royal College of Paediatrics and Child Health	6.06	3.2.1	26	**Review question** Should people be observed after an anaphylactic reaction? And if so, for how long?	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.07	3.2.2	26	**Evidence review** A total of 1096 articles were found by systematic searches. Full text was ordered for 73 articles based on the title and abstract. Of these, no studies assessed the effectiveness of observation or the length of time that any observation period should last (for the full review protocol and inclusion and exclusion criteria, see appendix D). *The recommendations were therefore based on the expertise, knowledge and experience of the GDG.*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.08	3.2.3	33	**Evidence statements** For details of how the evidence is graded, see 'The guidelines manual'. **3.2.3.1** *No evidence on the effectiveness of observing people after a suspected anaphylactic reaction was identified.* **3.2.3.2** *No evidence on for how long people should be observed after a suspected anaphylactic reaction was identified.*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.09	3.3.3.8	42	**Who should be given an emergency treatment plan and when should that include an adrenaline injector?** *No evidence was found that answered this*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

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					review question. *The recommendations were therefore based on the expertise, knowledge and experience of the GDG.*	
SH	Royal College of Paediatrics and Child Health	6.10	3.3.4	42	**Health Economic modelling** *Also the model assumptions on page 45 for example offering food related anaphylaxis follow up appointments every 2 years would be inappropriate for children who may grow out of their food allergy and required the food reintroduced into the diet*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.11	3.3.5	60	*Evidence to recommendations is, in a number of these questions based on the expertise, knowledge and experience alone of the GDG.*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.
SH	Royal College of Paediatrics and Child Health	6.12	3.5.3	72	**Evidence statements** For details of how the evidence is graded, see 'The guidelines manual'. **3.5.3.1** *No evidence on the effectiveness of different models of care in the diagnosis of suspected anaphylaxis was identified.*	Thank you for your comment. We do not consider this to be a comment on the factual accuracy of the guideline.

These organisations were approached but did not respond:

Addensbrookes Hospital
Airedale NHS Foundation Trust
Alder Hey Children's NHS Foundation Trust
ALK Abello
Allergy UK
Anaphylaxis Campaign, The
Association of Anaesthetists of Great Britain & Ireland
Association of Clinical Pathologists

Association of Paediatric Anaesthetists of Great Britain and Ireland
Association of Paediatric Emergency Medicine
Barchester Healthcare
BMJ
BOC Healthcare
Bradford District Care Trust
British Medical Association (BMA)
British National Formulary (BNF)
British Paediatric Allergy, Immunity & Infection Group
British Psychological Society, The
British Society of Immunology
British Society of Interventional Radiology
British Society of Paediatric Gastroenterology, Hepatology & Nutrition (BSPGHAN)
Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)
Camden Link
Care Quality Commission (CQC)
Central London Community Healthcare
Citizens Commission on Human Rights
College of Emergency Medicine
Commission for Social Care Inspection DO NOT USE - Replace by CQC
Connecting for Health
Dental Practitioners Association
Department for Communities and Local Government
Department for Education
Department of Health
Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)
Department of Health, Social Services & Public Safety, Northern Ireland (DHSSPSNI)
Dorset Cancer Network
Dorset PCT
Education for Health
Faculty of Dental Surgery
Faculty of General Dental Practice
Faculty of Intensive Care Medicine
George Elliott Hospital Trust
Gloucestershire Hospitals NHS Trust
Gloucestershire LINk
Great Western Hospitals NHS Foundation Trust
Greater Manchester and Cheshire Cancer Network
Greater Manchester West Mental Health NHS Foundation Trust
Hammersmith and Fulham PCT
Healthcare Improvement Scotland
Healthcare Inspectorate Wales
Healthcare Quality Improvement Partnership

Humber NHS Foundation Trust
Intensive Care Society
Interhealth Canada
JBOL Ltd
Lambeth Community Health
Lancashire Care NHS Trust
Latex Allergy Support Group
Leeds PCT
Lincoln Medical Ltd
Liverpool Community Health
Liverpool PCT
Lothian University Hospitals Trust
Luton & Dunstable Hospital NHS Foundation Trust
Ministry of Defence (MoD)
National Allergy Strategy Group
National Day Nurseries Association
National Patient Safety Agency (NPSA)
National Treatment Agency for Substance Misuse
NDR - UK
NETSCC, Health Technology Assessment
NHS Clinical Knowledge Summaries Service (SCHIN)
NHS Direct
NHS Pathways
NHS Plus
NHS Sheffield
NHS Warwickshire
NHS Western Cheshire
North Essex Partnership Foundation Trust
North Tees & Hartlepool NHS Foundation Trust
North West Allergy and Clinical Immunology Network
Northampton Primary Care NHS Trust
Northumberland Hills Hospital, Ontario
Nottingham Support Group for Carers of Children with Eczema
Paediatric Intensive Care Society
PERIGON Healthcare Ltd
Phadia Ltd
Pharmacosmos
Poole and Bournemouth PCT
Public Health Wales
Queen Anne St Medical Centre
Resuscitation Council (UK)
Rotherham NHS Foundation Trust
Royal Berkshire NHS Foundation Trust

Royal Brompton & Harefield NHS Foundation Trust
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Midwives
Royal College of Obstetricians and Gynaecologists
Royal College of Pathologists
Royal College of Physicians London
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Free Hospital NHS Trust
Royal Pharmaceutical Society of Great Britain
Royal Society of Medicine
Royal United Hospital
Royal Victoria Infirmary
Salford Royal Hospitals Foundation NHS Trust
Scarborough and North Yorkshire Healthcare NHS Trust
Scottish Intercollegiate Guidelines Network (SIGN)
Sheffield Children's NHS Foundation Trust
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence (SCIE)
Social Exclusion Task Force
Society for Acute Medicine
Society of Chiropodists & Podiatrists
Solent Healthcare
South Asian Health Foundation
South East Coast Ambulance Service
South London Cardiac and Stroke Network
South Tees Hospitals NHS Trust
South Western Ambulance Service NHS Foundation Trust
Swansea University
Trafford Primary Care Trust
UK NEQAS for Immunology and Immunochemistry
UK Ophthalmic Pharmacy Group
UNISON
United Kingdom Clinical Pharmacy Association (UKCPA)
United Lincolnshire Hospitals NHS Trust
Welsh Government
Welsh Scientific Advisory Committee (WSAC)
West Midlands Ambulance Service NHS Trust
Western Health and Social Care Trust
Wirral University Teaching Hospital NHS Foundation Trust

Wirrall Community NHS Trust
Wye Valley NHS Trust
York Teaching Hospital NHS Foundation Trust