

Drug allergy: diagnosis and management

Clinical guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline is the basis of QS97.

Overview

This guideline covers diagnosing and managing drug allergy in all age groups. It aims to make it easier for professionals to tell when someone is having an allergic reaction, by specifying the key signs and patterns to look out for. It also makes recommendations on improving people's understanding of their drug allergies, and ensuring these are recorded properly in their medical records.

Who is it for?

- Healthcare professionals
- Commissioners and providers
- People with a suspected or diagnosed drug allergy and their families and carers

Introduction

All drugs have the potential to cause side effects, also known as 'adverse drug reactions', but not all of these are allergic in nature. Other reactions are idiosyncratic, pseudo-allergic or caused by drug intolerance. The British Society for Allergy and Clinical Immunology (BSACI) defines drug allergy as an adverse drug reaction with an established immunological mechanism. The mechanism at presentation may not be apparent from the clinical history and it cannot always be established whether a drug reaction is allergic or non-allergic without investigation. Therefore, this guideline has defined drug allergy as any reaction caused by a drug with clinical features compatible with an immunological mechanism.

Hospital Episode Statistics from 1996 to 2000 reported that drug allergies and adverse drug reactions accounted for approximately 62,000 hospital admissions in England each year. There is also evidence that these reactions are increasing: between 1998 and 2005, serious adverse drug reactions rose 2.6-fold. Up to 15% of inpatients have their hospital stay prolonged as a result of an adverse drug reaction.

About half a million people admitted to NHS hospitals each year have a diagnostic 'label' of drug allergy, with the most common being penicillin allergy. About 10% of the general population claim to have a penicillin allergy; this has often been because of a skin rash that occurred during a course of penicillin in childhood. Fewer than 10% of people who think they are allergic to penicillin are truly allergic. Therefore, penicillin allergy can potentially be excluded in 9% of the population. Studies have shown that people with a label of penicillin allergy are more likely to be treated with broad-spectrum, non-penicillin antibiotics, such as quinolones, vancomycin and third-generation cephalosporins. However, use of these antibiotics in people with an unsubstantiated label of penicillin allergy may lead to antibiotic resistance and, in some cases, sub-optimal therapy.

Allergic reactions to non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, diclofenac, naproxen and aspirin, are common. In particular, 5–10% of people with asthma are affected. About one-third of people with chronic urticaria have severe reactions to NSAIDs, involving angioedema and anaphylaxis.

Anaphylaxis-type reactions occur in approximately 1 in 1000 of the general population. Anaphylaxis during general anaesthesia occurs in 1 in 10,000–20,000 anaesthetics. These patients may be denied general anaesthesia in the future unless a safe combination of drugs can be identified.

Major issues identified by this guideline include poor clinical documentation of drug allergy and a lack of patient information. Computerised primary care record systems are often unable to distinguish between intolerance and drug allergy and this can lead to a false label of drug allergy, particularly if the person's reaction took place many years previously and details about their reaction have been lost. Furthermore, there is no routine system in place for people to keep a record of their own drug allergies. This can lead to confusion over which drugs can be taken safely and can result in people inadvertently taking a drug they are allergic to, particularly when buying over-the-counter preparations from a pharmacy.

Analysis of patient safety incidents reported to the National Reporting and Learning System between 2005 and 2013 identified 18,079 incidents involving drug allergy. These included 6 deaths, 19 'severe harms', 4980 'other harms' and 13,071 'near-misses'. The majority of these incidents involved a drug that was prescribed, dispensed or administered to a patient with a previously known allergy to that drug or drug class.

Diagnosing drug allergy can be challenging and there is considerable variation both in how drug allergy is managed and in access to specialist drug allergy services. This can lead to under diagnosis, misdiagnosis and self-diagnosis. This variation may be caused by insufficient awareness of available services or by a lack of local provision of drug allergy centres. Some people are never offered referral to specialist services and instead stay in primary care while others have their drug allergy managed in other disciplines. Therefore, only a small proportion of people are treated in specialist allergy centres.

In view of the variation in provision of care for people with drug allergy, the scope of this guideline identified a need for guidance to improve clinical management for people affected by drug allergy. This guideline has been developed for use by healthcare professionals at all levels of healthcare and offers best practice advice on the diagnosis, documentation and communication of drug allergy in adults, children and young people.

Safeguarding children

Remember that child maltreatment:

- is common
- can present anywhere, such as emergency departments and primary care or on home visits.

Be aware of or suspect abuse as a contributory factor to or cause of the symptoms or signs of drug allergy in children. Abuse may also coexist with drug allergy. See the NICE guideline on [child](#)

maltreatment for clinical features that may be associated with maltreatment.

This section has been agreed with the Royal College of Paediatrics and Child Health.

Drug recommendations

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation. The full list of recommendations is in [section 1](#).

Assessment

- When assessing a person presenting with possible drug allergy, take a history and undertake a clinical examination. Use the following boxes as a guide when deciding whether to suspect drug allergy.

Boxes 1–3 Signs and allergic patterns of suspected drug allergy with timing of onset^[1]

Box 1 Immediate, rapidly evolving reactions

<p>Anaphylaxis – a severe multi-system reaction characterised by:</p> <ul style="list-style-type: none"> • erythema, urticaria or angioedema and • hypotension and/or bronchospasm 	<p>Onset usually less than 1 hour after drug exposure (previous exposure not always confirmed)</p>
<p>Urticaria or angioedema without systemic features</p>	
<p>Exacerbation of asthma (for example, with non-steroidal anti-inflammatory drugs [NSAIDs])</p>	

Box 2 Non-immediate reactions without systemic involvement

<p>Widespread red macules or papules (exanthema-like)</p>	<p>Onset usually 6–10 days after first drug exposure or within 3 days of second exposure</p>
<p>Fixed drug eruption (localised inflamed skin)</p>	

Box 3 Non-immediate reactions with systemic involvement

<p>Drug reaction with eosinophilia and systemic symptoms (DRESS) or drug hypersensitivity syndrome (DHS) characterised by:</p> <ul style="list-style-type: none"> • widespread red macules, papules or erythroderma • fever • lymphadenopathy • liver dysfunction • eosinophilia 	<p>Onset usually 2–6 weeks after first drug exposure or within 3 days of second exposure</p>
<p>Toxic epidermal necrolysis or Stevens–Johnson syndrome characterised by:</p> <ul style="list-style-type: none"> • painful rash and fever (often early signs) • mucosal or cutaneous erosions • vesicles, blistering or epidermal detachment • red purpuric macules or erythema multiforme 	<p>Onset usually 7–14 days after first drug exposure or within 3 days of second exposure</p>
<p>Acute generalised exanthematous pustulosis (AGEP) characterised by:</p> <ul style="list-style-type: none"> • widespread pustules • fever • neutrophilia 	<p>Onset usually 3–5 days after first drug exposure</p>

Common disorders caused, rarely, by drug allergy: <ul style="list-style-type: none">• eczema• hepatitis• nephritis• photosensitivity• vasculitis	Time of onset variable
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Documenting and sharing information with other healthcare professionals

Documenting new suspected drug allergic reactions

- When a person presents with suspected drug allergy, document their reaction in a structured approach that includes:
 - the generic and proprietary name of the drug or drugs suspected to have caused the reaction, including the strength and formulation
 - a description of the reaction (see [recommendation 1.1.1](#))
 - the indication for the drug being taken (if there is no clinical diagnosis, describe the illness)
 - the date and time of the reaction
 - the number of doses taken or number of days on the drug before onset of the reaction
 - the route of administration
 - which drugs or drug classes to avoid in future.

Maintaining and sharing drug allergy information

- Prescriptions (paper or electronic) issued in any healthcare setting should be standardised and redesigned to record information on which drugs or drug classes to avoid to reduce the risk of drug allergy.

- Check a person's drug allergy status and confirm it with them (or their family members or carers as appropriate) before prescribing, dispensing or administering any drug (see also [recommendation 1.3.4](#)). Update the person's medical records or inform their GP if there is a change in drug allergy status.

Providing information and support to patients

- Discuss the person's suspected drug allergy with them (and their family members or carers as appropriate) and provide structured written information (see [recommendation 1.2.3](#)). Record who provided the information and when.
- Ensure that the person (and their family members or carers as appropriate) is aware of the drugs or drug classes that they need to avoid, and advise them to check with a pharmacist before taking any over-the-counter preparations.

Providing information and support to people who have had specialist drug allergy investigations

- Allergy specialists should give the following written information to people who have undergone specialist drug allergy investigation:
 - the diagnosis – whether they had an allergic or non-allergic reaction
 - the drug name and a description of their reaction (see [recommendation 1.1.1](#))
 - the investigations used to confirm or exclude the diagnosis
 - drugs or drug classes to avoid in future
 - any safe alternative drugs that may be used.

Non-specialist management and referral to specialist services

General

- Refer people to a specialist drug allergy service if they have had:
 - a suspected anaphylactic reaction (also see the NICE guideline on [anaphylaxis](#)) or
 - a severe non-immediate cutaneous reaction (for example, drug reaction with eosinophilia and systemic symptoms [DRESS], Stevens–Johnson Syndrome, toxic epidermal necrolysis).

Non-steroidal anti-inflammatory drugs (including selective cyclooxygenase 2 inhibitors)

- For people who have had a mild allergic reaction to a non-selective NSAID but need an anti-inflammatory:
 - discuss the benefits and risks of selective cyclooxygenase 2 (COX-2) inhibitors (including the low risk of drug allergy)
 - consider introducing a selective COX-2 inhibitor at the lowest starting dose with only a single dose on the first day.

Beta-lactam antibiotics

- Refer people with a suspected allergy to beta-lactam antibiotics to a specialist drug allergy service if they:
 - need treatment for a disease or condition that can only be treated by a beta-lactam antibiotic or
 - are likely to need beta-lactam antibiotics frequently in the future (for example, people with recurrent bacterial infections or immune deficiency).

General anaesthesia

- Refer people to a specialist drug allergy service if they have had anaphylaxis or another suspected allergic reaction during or immediately after general anaesthesia.

^[1] Note that these boxes describe common and important presenting features of drug allergy but other presentations are also recognised

1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

All recommendations apply to adults, children and young people.

People have the right to be involved in discussions and make informed decisions about their care, as described in [your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Assessment

1.1.1 When assessing a person presenting with possible drug allergy, take a history and undertake a clinical examination. Use the following boxes as a guide when deciding whether to suspect drug allergy.

Boxes 1–3 Signs and allergic patterns of suspected drug allergy with timing of onset^[2]

Box 1 Immediate, rapidly evolving reactions

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Box 2 Non-immediate reactions without systemic involvement

Widespread red macules or papules (exanthema-like)	Onset usually 6–10 days after first drug exposure or within 3 days of second exposure
Fixed drug eruption (localised inflamed skin)	

Box 3 Non-immediate reactions with systemic involvement

<p>Drug reaction with eosinophilia and systemic symptoms (DRESS) or drug hypersensitivity syndrome (DHS) characterised by:</p> <ul style="list-style-type: none"> • widespread red macules, papules or erythroderma • fever • lymphadenopathy • liver dysfunction • eosinophilia 	Onset usually 2–6 weeks after first drug exposure or within 3 days of second exposure
<p>Toxic epidermal necrolysis or Stevens–Johnson syndrome characterised by:</p> <ul style="list-style-type: none"> • painful rash and fever (often early signs) • mucosal or cutaneous erosions • vesicles, blistering or epidermal detachment • red purpuric macules or erythema multiforme 	Onset usually 7–14 days after first drug exposure or within 3 days of second exposure

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<p>Common disorders caused, rarely, by drug allergy:</p> <ul style="list-style-type: none"> • eczema • hepatitis • nephritis • photosensitivity • vasculitis 	<p>Time of onset variable</p>

1.1.2 Be aware that the reaction is more likely to be caused by drug allergy if it occurred during or after use of the drug and:

- the drug is known to cause that type of reaction or
- the person has previously had a similar reaction to that drug or drug class.

1.1.3 Be aware that the reaction is less likely to be caused by drug allergy if:

- there is a possible non-drug cause for the person's symptoms (for example, they have had similar symptoms when not taking the drug) or
- the person has gastrointestinal symptoms only.

Measuring serum tryptase after suspected anaphylaxis

1.1.4 After a suspected drug-related anaphylactic reaction, take 2 blood samples for mast cell tryptase in line with recommendations in the NICE guideline on [anaphylaxis](#).

1.1.5 Record the exact timing of both blood samples taken for mast cell tryptase:

- in the person's medical records and
- on the pathology request form.

1.1.6 Ensure that tryptase sampling tubes are included in emergency anaphylaxis kits.

Measuring serum specific immunoglobulin E

1.1.7 Do not use blood testing for serum specific immunoglobulin E (IgE) to diagnose drug allergy in a non-specialist setting.

1.2 Documenting and sharing information with other healthcare professionals

Recording drug allergy status

1.2.1 Document people's drug allergy status in their medical records using 1 of the following:

- 'drug allergy'
- 'none known'
- 'unable to ascertain' (document it as soon as the information is available).

1.2.2 If drug allergy status has been documented, record all of the following at a minimum:

- the drug name
- the signs, symptoms and severity of the reaction (see recommendation 1.1.1)
- the date when the reaction occurred.

Documenting new suspected drug allergic reactions

1.2.3 When a person presents with suspected drug allergy, document their reaction in a structured approach that includes:

- the generic and proprietary name of the drug or drugs suspected to have caused the reaction, including the strength and formulation

- a description of the reaction (see recommendation 1.1.1)
- the indication for the drug being taken (if there is no clinical diagnosis, describe the illness)
- the date and time of the reaction
- the number of doses taken or number of days on the drug before onset of the reaction
- the route of administration
- which drugs or drug classes to avoid in future.

Maintaining and sharing drug allergy information

- 1.2.4 Prescriptions (paper or electronic) issued in any healthcare setting should be standardised and redesigned to record information on which drugs or drug classes to avoid to reduce the risk of drug allergy.
- 1.2.5 Ensure that drug allergy status is documented separately from adverse drug reactions and that it is clearly visible to all healthcare professionals who are prescribing drugs.
- 1.2.6 Check a person's drug allergy status and confirm it with them (or their family members or carers as appropriate) before prescribing, dispensing or administering any drug (see also recommendation 1.3.4). Update the person's medical records or inform their GP if there is a change in drug allergy status.
- 1.2.7 Ensure that information about drug allergy status is updated and included in all:
- GP referral letters
 - hospital discharge letters.
- 1.2.8 Carry out medicines reconciliation for people admitted to hospital in line with recommendations in the NICE guideline on [medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes](#).

Documenting information after specialist drug allergy investigations

For recommendations on referral to specialist services see section 1.4.

1.2.9 After specialist drug allergy investigations, allergy specialists should document:

- the diagnosis, drug name and whether the person had an allergic or non-allergic reaction
- the investigations used to confirm or exclude the diagnosis
- drugs or drug classes to avoid in future.

1.3 Providing information and support to patients

1.3.1 Discuss the person's suspected drug allergy with them (and their family members or carers as appropriate) and provide structured written information (see recommendation 1.2.3). Record who provided the information and when.

1.3.2 Provide information in line with the recommendations in the NICE guideline on [patient experience in adult NHS services](#).

1.3.3 Ensure that the person (and their family members or carers as appropriate) is aware of the drugs or drug classes that they need to avoid, and advise them to check with a pharmacist before taking any over-the-counter preparations.

1.3.4 Advise people (and their family members or carers as appropriate) to carry information they are given about their drug allergy at all times and to share this whenever they visit a healthcare professional or are prescribed, dispensed or are about to be administered a drug.

Providing information and support to people who have had specialist drug allergy investigations

For recommendations on referral to specialist services see section 1.4.

1.3.5 Allergy specialists should give the following written information to people who have undergone specialist drug allergy investigation:

- the diagnosis – whether they had an allergic or non-allergic reaction
- the drug name and a description of their reaction (see recommendation 1.1.1)
- the investigations used to confirm or exclude the diagnosis
- drugs or drug classes to avoid in future
- any safe alternative drugs that may be used.

1.3.6 Explain to people in whom allergy to a drug or drug class has been excluded by specialist investigation that they can now take this drug or drug class safely and ensure that their medical records are updated.

1.4 Non-specialist management and referral to specialist services

General

1.4.1 If drug allergy is suspected:

- consider stopping the drug suspected to have caused the allergic reaction and advising the person to avoid that drug in future
- treat the symptoms of the acute reaction if needed; send people with severe reactions to hospital
- document details of the suspected drug allergy in the person's medical records (see recommendations 1.2.3 and 1.2.6)
- provide the person with information (see section 1.3).

1.4.2 Refer people to a specialist drug allergy service if they have had:

- a suspected anaphylactic reaction (also see the NICE guideline on [anaphylaxis](#)) or
- a severe non-immediate cutaneous reaction (for example, drug reaction with eosinophilia and systemic symptoms [DRESS], Stevens–Johnson Syndrome, toxic epidermal necrolysis).

Non-steroidal anti-inflammatory drugs (including selective

cyclooxygenase 2 inhibitors)

- 1.4.3 Explain to people with a suspected allergy to a non-selective non-steroidal anti-inflammatory drug (NSAID) (and their family members or carers as appropriate) that in future they need to avoid all non-selective NSAIDs, including over-the-counter preparations.
- 1.4.4 For people who have had a mild allergic reaction to a non-selective NSAID but need an anti-inflammatory:
- discuss the benefits and risks of selective cyclooxygenase 2 (COX-2) inhibitors (including the low risk of drug allergy)
 - consider introducing a selective COX-2 inhibitor at the lowest starting dose with only a single dose on the first day.
- 1.4.5 Do not offer a selective COX-2 inhibitor to people in a non-specialist setting if they have had a severe reaction, such as anaphylaxis, severe angioedema or an asthmatic reaction, to a non-selective NSAID.
- 1.4.6 Refer people who need treatment with an NSAID to a specialist drug allergy service if they have had a suspected allergic reaction to an NSAID with symptoms such as anaphylaxis, severe angioedema or an asthmatic reaction.
- 1.4.7 Be aware that people with asthma who also have nasal polyps are likely to have NSAID-sensitive asthma unless they are known to have tolerated NSAIDs in the last 12 months.

Beta-lactam antibiotics

- 1.4.8 Refer people with a suspected allergy to beta-lactam antibiotics to a specialist drug allergy service if they:
- need treatment for a disease or condition that can only be treated by a beta-lactam antibiotic or
 - are likely to need beta-lactam antibiotics frequently in the future (for example, people with recurrent bacterial infections or immune deficiency).
- 1.4.9 Consider referring people to a specialist drug allergy service if they are not able

to take beta-lactam antibiotics and at least 1 other class of antibiotic because of suspected allergy to these antibiotics.

Local anaesthetics

- 1.4.10 Refer people to a specialist drug allergy service if they need a procedure involving a local anaesthetic that they are unable to have because of suspected allergy to local anaesthetics.

General anaesthesia

- 1.4.11 Refer people to a specialist drug allergy service if they have had anaphylaxis or another suspected allergic reaction during or immediately after general anaesthesia.

^[2] Note that these boxes describe common and important presenting features of drug allergy but other presentations are also recognised

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline.

2.1 Designing systems for documenting drug allergy

Which documentation strategies would be most clinically and cost effective to minimise the number of people who are re-exposed to drugs to which they have a suspected or confirmed allergy, looking in particular at:

- electronic health records that include features specifically designed to record and alert clinicians to drug allergy information, compared with systems without such features and
- different formats for patient-held, structured drug allergy documentation?

Why this is important

Evidence from patient safety incident reports to the National Reporting and Learning System and from published research shows that a large number of NHS patients with known drug allergies are being re-exposed to these drugs in error each year. Over the past few decades, many people have been inaccurately diagnosed and recorded as either having or not having a drug allergy. While re-exposure to a drug has not caused harm in the majority of people, a minority of these incidents have caused harm or death.

The systematic review undertaken for this guideline identified a wide range of documentation strategies, including patient-held records; information worn by patients; hospital-based notices worn by patients (such as coloured arm bands); automated messages (for example, screensavers); mandatory reporting of drug allergy status in paper or electronic medication records; mandatory documentation of details related to adverse drug reactions; design of drug charts; use of Summary Care Records; and computerised physician or prescriber order entry (CPOE) systems.

Most of the studies included in the systematic review were from the USA and their focus was largely on adverse drug events or medication prescribing errors, and not specifically on drug allergy. In addition, few studies assessed the effectiveness of patient-held documentation strategies. The quality of the evidence from studies was generally very low. Research is therefore

needed to determine which strategy or combination of strategies is most effective in reducing harm by minimising accidental re-exposure to a known drug allergen.

2.2 Communicating information about drug allergy

In people with suspected or confirmed drug allergies, are patient-focused information strategies more effective than standard NHS practice in increasing people's likelihood of disclosing their drug allergy (or their suspected drug allergy) and therefore reducing the risk of being re-exposed to the affected drug?

Why this is important

Administering drugs to which patients have a reported allergy can be fatal, but inadvertent prescription or administration of such drugs is common. Data from the UK General Practice Research Database indicate that the incidence of contraindicated antibiotics being re-prescribed to patients with suspected penicillin allergy is as high as 48.5%, suggesting that even electronic systems with reminders do not eliminate the risk of inappropriate prescribing. Also, few allergy documentation systems communicate across healthcare organisations, so this information may be lost when patients move to new areas.

Patients and their families and carers have been identified as a resource to prevent inappropriate prescribing. This is in line with the concept of 'patient responsibility' described in the NHS Constitution (2010). Patients and their families and carers are encouraged to be involved in decisions about their care and this includes decisions about drug choice. However, in current practice information is usually not provided unless drug allergy is confirmed by specialists. Suitable information provision is important to encourage people to volunteer their allergy status (be it suspected or confirmed) and make sure that this is appropriately documented by healthcare professionals.

The British Society for Allergy and Clinical Immunology (BSACI) recommends giving patients written details about their allergy, including information on drugs they should avoid. However, it is unclear what factors influence patients to disclose their allergy status to healthcare professionals and what would empower them to do so, to improve safety.

Research is therefore needed to determine which information strategy would be most effective (and preferred by patients) to:

- increase patients' knowledge about their allergy and ability to remember this information

- increase patient empowerment and confidence to discuss their drug allergy with healthcare professionals
- minimise harm from inadvertent re-exposure to a suspected drug allergen.

2.3 Using selective cyclooxygenase 2 inhibitors in people with previous severe allergic reactions to non-selective non-steroidal anti-inflammatory drugs

Should all patients who have experienced a severe allergic reaction to a non-selective non-steroidal anti-inflammatory drug (NSAID) be assessed by specialist drug allergy services or should they be advised to take a selective cyclooxygenase 2 (COX 2) inhibitor without further investigations if clinically appropriate?

Why this is important

There are about 5.4 million people with asthma in the UK, 1–5% of whom are unable to take non-selective NSAIDs without developing a severe and sometimes life-threatening asthma attack. In addition, 0.1–1% of the general population report allergic reactions to NSAIDs with symptoms ranging from urticaria and angioedema to anaphylaxis. NSAIDs are extremely widely used, available over the counter and present within many compound preparations (for example, cold and flu remedies). People who are allergic to NSAIDs are therefore at risk of inadvertent exposure and this presents a significant public health issue.

Commonly encountered NSAIDs such as aspirin, ibuprofen, diclofenac and naproxen are non-selective COX-2 inhibitors that block the enzymatic effects of both cyclooxygenase 1 (COX-1) and COX-2. More recently introduced NSAIDs include a group which are selective inhibitors of the COX-2 isoform alone. Studies have shown that the allergic response to NSAIDs is mediated through inhibition of COX-1 and therefore the majority of people with a history of allergic reactions to non-selective NSAIDs are able to tolerate selective COX-2 inhibitors. However, the same studies have also reported that a small proportion of these people also react adversely to selective COX-2 inhibitors. This group has not been properly characterised and therefore it is not possible to predict who should be offered a selective COX-2 inhibitor without undertaking specialist drug allergy investigations. This clinical guideline recommends that people who have had a mild reaction to a non-selective NSAID could be offered a selective COX-2 inhibitor but that all those who have had a severe reaction, such as anaphylaxis, severe angioedema or an asthmatic reaction, should not be offered a selective COX-2 inhibitor in a non-specialist setting.

Well-designed, appropriately powered, controlled studies characterising people with a history of severe reactions to non-selective NSAIDs may enable them to have treatment with an anti-inflammatory without specialist drug allergy investigation.

2.4 Oral antibiotic challenge for diagnosing antibiotic allergy in children

In children who have a suspected allergy to an antibiotic, is it clinically and cost effective to proceed directly (without prior skin or intradermal tests) to a diagnostic oral antibiotic challenge rather than referring them to specialist drug allergy services?

Why this is important

Antibiotics are an important class of drug and one of the most common groups of drugs prescribed to children. Many childhood illnesses are associated with skin rashes, and it can be clinically difficult in the acute setting to be certain if an atypical rash is caused by the underlying illness, the antibiotic, or both. Adverse drug reactions to antibiotics are common and frequently result in a child being diagnosed with 'drug allergy', a diagnosis which generally remains for life.

Current clinical experience suggests that most patients in a community setting who are believed to be allergic to an oral antibiotic (approximately 3% for children, 10–20% for adults) will be challenge 'negative' – that is, they are able to tolerate the oral antibiotic on the day of the challenge and on subsequent days. While patients who are correctly diagnosed with an allergy are kept safe through avoidance, there are health and cost implications for patients who are incorrectly diagnosed with an antibiotic allergy.

The evidence review for this clinical guideline found no evidence to support the reliability of allergy testing (skin, intradermal or IgE determination) for the diagnosis of antibiotic allergy in children. In addition, these tests are painful and restricted to only a few specialist centres in the UK. The result is that only a small fraction of children in the UK with a diagnosis of antibiotic allergy ever undergo investigations to confirm or exclude this diagnostic 'label'. It would therefore be beneficial to prospectively investigate the use of the oral supervised challenge in a safe clinical setting without prior allergy testing. This novel diagnostic approach could be compared with an intervention of 'antibiotic avoidance'.

If the oral antibiotic challenge is found to be safe, acceptable and cost effective, it could be rolled out across all centres that offer paediatric allergy services. This would substantially reduce the number of children who receive a lifelong label of antibiotic allergy.

Finding more information and resources

You can see everything NICE says on drug allergy in our interactive flowchart on [drug allergy](#).

To find out what NICE has said on topics related to this guideline, see our web page on [allergies](#).

For full details of the evidence and the guideline committee's discussions, see the [full version](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources](#) to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see [resources to help you put guidance into practice](#).

Update information

Minor changes since publication

November 2018: After a surveillance review, a link to other NICE guidance was updated as the original guidance had been replaced.

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Accreditation

