# Antibiotic Guidelines for Management of Penicillin Allergy

## Guideline Details

- **Title**: Penicillin Allergy Management Guideline
- **Author**: Consultant Microbiologist
- **Author’s job title**: Consultant Microbiologist
- **Directorate**: Diagnostics
- **Department**: Microbiology
- **Version**: 1.2
- **Date Issued**: Dec 2018
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- **Comment / Changes / Approval**: References reviewed, guideline inserted into new Trust template, updated information on types of immune reaction included, new assessment sheet and updated poster for wards based on new rates of cross-reactivity (see references)

## Main Contact

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## Lead Director

- **Director of Medicine**

## Superseded Documents

- Guidelines for management of penicillin allergy v1.1 19Jun12

## Issue Date

- **Jan 2019**

## Review Date

- **Jan 2022**

## Review Cycle

- Three years

## Consulted with the following stakeholders:

- Clinical Audit lead?
- Antibiotic Working Group
- Drug & Therapeutics Committee
- Prescribing Interface Group
- Consultant Immunologists
- Consultant Dermatologist

## Approval and Review Process

- Antibiotic Working Group
- Drug & Therapeutics Group
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1. **Purpose**

1.1. This document sets out Northern Devon Healthcare NHS Trust’s best practice guidelines for appropriate management of patients with suspected penicillin allergy or penicillin sensitivity.

1.2. This guideline applies to all patients and must be adhered to. Special considerations exist for pregnant and breastfeeding patients; liaise with specialist clinicians as appropriate in these cases.

1.3. Non-compliance with this guideline may be for valid clinical reasons only. The reason(s) for non-compliance must be documented clearly in the patient’s notes.

1.4. This guideline is primarily aimed at all prescribing teams but other staff (e.g. nursing staff, pharmacists) may need to familiarise themselves with some aspects of the guideline.

1.5. Implementation of this guideline will ensure that:

- Penicillin allergy is managed according to current evidence and standards of practice in the wider healthcare community.
- A standard of care is specified to facilitate a consistent approach between clinical areas, microbiology and pharmacy in terms of patient management, specimen processing and drug availability.

2. **Responsibilities**

2.1. Responsibility for education and training lies with the Lead Consultant Microbiologist for Antibiotic Stewardship. It will be provided through formal study days and informal training on the ward.

2.2. The author will be responsible for ensuring the guidelines are reviewed and revisions approved by the Drug and Therapeutics Group in accordance with the Document Control Report.

2.3. All versions of these guidelines will be archived in electronic format by the author within the Antibiotic Stewardship policy archive.

2.4. Any revisions to the final document will be recorded on the Document Control Report.

2.5. To obtain a copy of the archived guidelines, contact should be made with the author.

2.6. Monitoring of implementation, effectiveness and compliance with these guidelines will be the responsibility of the Lead Clinician for Antibiotic Stewardship. Where non-compliance is found, the reasons for this must have been documented in the patient’s medical notes.

**Role of Antibiotic Working Group (AWG)**

2.7. The AWG is responsible for:
3. Contacts

3.1. Contact numbers:

- Microbiologist: Bleep 193. Via switchboard out of hours.
- Antibiotic Pharmacist: Bleep 029 (Mon-Fri only)

4. Management of Penicillin Allergy

4.1. See appendix 1

5. Monitoring Compliance with and the Effectiveness of the Guideline

Suggested audit criteria

5.1. The following could be used:

- Number of patients prescribed a beta-lactam antibiotic with a history of penicillin allergy

Process for Implementation and Monitoring Compliance and Effectiveness

5.2. Incidents involving penicillin allergy should be reported according to the Trust’s Incident Reporting Policy. Critical incident reports relating to penicillin allergy will be collated by the Antibiotic Pharmacist. Results will be reported on an annual basis to the Drug and Therapeutics Group.

6. Equality Impact Assessment

6.1. The author must include the Equality Impact Assessment Table and identify whether the policy has a positive or negative impact on any of the groups listed. The Author must make comment on how the policy makes this impact.

Table 1: Equality impact Assessment

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### 7. References


#### 7.3. NICE 2014. CG 183: Drug Allergy: Diagnosis and Management. [https://www.nice.org.uk/guidance/cg183/chapter/1-Recommendations](https://www.nice.org.uk/guidance/cg183/chapter/1-Recommendations)


#### 7.5. Drug and Therapeutics Bulletin. 2017. Drugs and Therapeutics Bulletin: Penicillin allergy—getting the label right. BMJ 2017; 358:j3402 doi: [https://doi.org/10.1136/bmj.j3402](https://doi.org/10.1136/bmj.j3402) (Published 04 August 2017) [https://www.bmj.com/content/358/bmj.j3402](https://www.bmj.com/content/358/bmj.j3402)


#### 7.7. Nasser, S; Queen, J. 2015. Attaching a label of beta-lactam allergy can be costly. [online] [https://www.guidelinesinpractice.co.uk/allergy/attaching-a-label-of-beta-lactam-allergy-can-be-costly/352615.article](https://www.guidelinesinpractice.co.uk/allergy/attaching-a-label-of-beta-lactam-allergy-can-be-costly/352615.article)
7.8. Trubiano, JA; Stone, CA; Grayson, LM; Urbancic, K; Slavin, MA; Thursky, KA; Phillips, EJ. 2017. The Three C’s of Antibiotic Allergy – Classification, Cross-Reactivity and Collaboration. Journal of Allergy and Clinical Immunology Practice 5(6): 1532–1542. doi:10.1016/j.jaip.2017.06.017


7.10. Hoetzenecker, W; Nägeli, M; Mehra, ET; Jensen, AN; Saulite, I; Schmid-Grendelmeier, P; Guenova, E; Cozzio, A; French, LE. Adverse cutaneous drug eruptions: current understanding. Seminars in Immunopathology, November 2015. DOI: 10.1007/s00281-015-0540-2


8. Associated Documentation

- Incident reporting policy
- Resuscitation guidelines
- Antibiotic prescribing policy
- Antibiotic guidelines for surgical prophylaxis
9. **Appendix 1**

9.1. Name of guideline on app

Approach to Reported Penicillin Allergy

9.2. Location on app

Secondary Care
Infection

Approach to Reported Penicillin Allergy

9.3. Header

It is estimated that 90% of patients with a ‘penicillin allergy’ could safely be given a penicillin. These guidelines are an attempt at providing guidance for the management of a difficult area, and are aimed at offsetting the increased risk of drug reactions in certain patient groups against the risk of denying a group of patients safe and effective medication.

9.4. Type of Allergic Reaction [open/closed]

**SERIOUS previous reaction to penicillin [closed]**
Anaphylaxis or Stevens Johnson Syndrome

- Symptoms usually occur less than 1 hour after exposure, and include:
  - Mucous membrane erosions, blisters, Nikolsky skin
  - Confluent erythema
  - Angioedema and tongue swelling
  - Bronchospasm
  - Palpable purpura, skin necrosis
  - Hypotension

**MODERATE: development of type 1 reaction [closed]**
History, or development, of Accelerated Type 1 Reaction to Penicillins

- Symptoms include:
  - Pruritic skin eruptions or urticarial
  - May involve airways e.g. wheeze
  - Usually occurs within 4 hours of first dose
  - 15-70% chance of IgE mediated reaction

**SERIOUS: development of Haematological / Cell Dysfunction [closed]**
Type II antibody mediated reaction, most commonly affects haematological cells, precise mechanism not understood, uncommon

- Symptoms include:
  - Haemolytic anaemia – dyspnoea, fatigue, pallor, jaundice, dark urine, splenomegaly, bounding pulses, “roaring in the ears”
  - Thrombocytopenia – petechial rash, splenomegaly, hepatomegaly neutropenia
  - Platelets (decrease from within normal range prior to treatment, to < 150 x10^9/L)
Neutrophils (decrease from within normal range prior to treatment, to \(< 1 \times 10^9/L\))
Haemoglobin (decrease from within normal range prior to treatment, to \(< 100 \text{ g/dL}\))
Typically develops at least 5-8 days after exposure, may begin after much longer periods of treatment. Symptoms can occur within hours if the causative drug is stopped, then restarted

**SERIOUS: development of Vasculitis ± End-organ impairment [closed]**
Type III antigen-antibody mediated reaction, may include serum sickness, Arthus reaction or vasculitis. Uncommon. Usually seen in the context of high-dose prolonged drug administration. Vasculitis reactions are most strongly associated with exposure to penicillins.

- Symptoms include:
  - Palpable purpura and/or petechiae (usually lesions affect lower extremities)
  - Arthralgias
  - ± Acute glomerulonephritis.
  - Renal injury / AKI (uncommon). Classed as significant if: >50% reduction in eGFR from baseline; OR absolute serum creatinine increase >26.5µmol/L; OR transplantation / dialysis following injury
  - Liver dysfunction (Liver enzymes ≥ 5 x upper limit of normal (ULN) ALT alone; OR ≥ 3 x ULN ALT with ≥ 2 x ULN of either bilirubin/ALP; OR requires transplant following injury
  - GI tract may be involved (uncommon)
  - Complement levels are low (not usually measured unless requested by Immunology service)
  - Typically develops after at least 1-2 weeks of continuous exposure, since significant quantities of antibody are needed to generate symptoms.

**Development of Rash with Systemic Symptoms on Treatment [closed]**

Occurs after weeks of uncomplicated treatment, whereupon the patient suddenly develops signs and symptoms of a fulminant immune reaction (T-cell mediated, type IV), which may include end-organ impairment. Various sub-types differing in severity, ranging from Stevens-Johnson to AGEP.

Not including accelerated type 1 reaction

**SERIOUS: Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN).**

- Symptoms include:
  - A prodrome of acute-onset febrile illness and malaise.
  - A painful rash that progresses rapidly.
  - Erythematous macules, targetoid lesions, or diffuse erythema progressing to vesicles and bullae
  - Positive Nikolsky sign and/or "bullae spread sign."
  - Oral, ocular, and/or genital mucositis with painful mucosal erosions
  - Necrosis and sloughing of the epidermis of varying degree
Typical onset is 1-4 weeks after initial drug exposure, re-exposure after a break may result in onset of symptoms in as little as 48 hours.

SERIOUS: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), or Drug Hypersensitivity Syndrome (DHS).

- Symptoms include:
  - Widespread red macules, papules or erythroderma
  - Fever
  - Lymphadenopathy
  - Eosinophilia (increase from within normal range to > 0.7 x 10^9/L)
  - Usually occurs 2-6 weeks after first drug exposure, or within 3 days of second exposure

SERIOUS: Acute generalised exanthematous pustulosis (AGEP)

- Symptoms include:
  - Widespread pustules
  - Fever
  - Neutrophilia
  - Usually occurs 3-5 days after first drug exposure

MODERATE: Symmetrical drug-related intertriginous and flexural exanthem (SDRIFE) [formerly called Baboon syndrome]

- Symptoms include:
  - More common in men
  - Demarcated, V-shaped erythema in gluteal/perianal or inguinal/perigenital areas
  - Often involves at least one other flexural area – axillae, elbows or knees
  - Typically develops from 6 hours to 10 days after drug exposure
  - No mucosal involvement
  - Rarely: high fever, malaise, visceral organ involvement (if present, then falls into “SERIOUS” category for management)
  - If symptoms develop within 6 hours following initial dose, then falls into “SERIOUS” category for management

Other types of reaction [closed]

MODERATE: Severe neurological or CNS manifestation

- Symptoms include:
  - Seizures
  - Psychosis

9.5. Management

- SERIOUS REACTIONS [closed]
STEVENS JOHNSON SYNDROME, TEN, ANAHPYLAXIS, VASCULITIS, AGE, DRESS/DHS, HAEMATOLOGICAL ABNORMALITIES, RENAL INJURY, LIVER INJURY, BLOOD DYSCRASIAS, VASCULITIS, END-ORGAN DYSFUNCTION MEETING CRITERIA

- Stop all beta-lactam antibiotics – penicillins, cephalosporins and carbapenems.
- Monobactams e.g. aztreonam are regarded as having no cross-reactivity, contact microbiology to discuss use.
- Do not rechallenge with any beta-lactam antibiotics unless life-threatening illness (as defined in appropriate infection management guideline).
- Check for recent history of penicillin administration without complication.
- Discuss further management with Consultant Immunologist at Derriford or RD&E (RD&E only for children) if beta-lactams likely to be indicated in future, for outpatient antibiotic allergy assessment ± testing.

**MODERATE REACTIONS [closed]**

ACCELERATED TYPE 1 REACTION, SDRIFE, SEVERE NEUROLOGICAL REACTION

- Stop implicated antibiotics.
- Avoid the implicated class of antibiotic and use other beta lactams with caution (theoretical cross-reactivity between penicillins, cephalosporins and carbapenems). See appendix in BOB document policy for cross-reactivity diagram to aid choosing suitable alternative agents.
- History should be checked for evidence of any inadvertent administration of a beta-lactam since the allergy label.
- If penicillin is frequently indicated for recurrent infection in the patient, check specific IgE to penicillins (Penicillin V, G and Amoxicillin). If negative, consider referral to immunology service in Derriford or RD&E (children should only be referred to RD&E) for skin testing followed by provocation test.

**Development of Other Rash on Treatment [closed]**

Non-urticarial rash with no blistering, mucous membrane involvement; or pruritic rash without eruptions.

Not including accelerated type 1 reaction

- **Symptoms include:**
  - Exanthem/exanthema typically symmetrical
  - Often confluent erythematous macules and papules sparing the palms and soles
  - Typically develops within 2 weeks after the onset of therapy

- **Management**
  - Continue to treat, and consider use of anti-histamine or steroid
  - Watch for blistering / mucous membrane involvement / skin sloughing
- Do not label as allergic to penicillins if symptoms do not progress on treatment

**Vague History of Allergy / Rash [closed]**
History of non-urticarial rash with no blistering or mucous membrane involvement, vague history, or unsubstantiated history of allergy from family.

Low risk of penicillin allergy

- **Management**
  - Check the history for evidence of inadvertent administration of a penicillin
  - In hospital, it is reasonable to give a provocation test to adult patients (children require referral to RD&E allergy clinic), and if this is tolerated, remove the allergy label. Ensure adequate communication to other healthcare providers and the patient regarding the removal of the allergy label to avoid confusion in the future
  - In the community, treat as for accelerated type 1 reaction

**Non-allergic Reactions to Penicillin [closed]**
History of diarrhoea / vomiting / minor CNS / joint symptoms / MILD raised LFTs (not meeting threshold for immune mediated reaction) / MILD raised creatinine (not meeting threshold for immune mediated reaction) after penicillin:

Risk of adverse reaction to penicillins will be approximately the same as the general population.

- **Management**
  - Give beta-lactams in all settings
  - Remove label of allergy without provocation testing
  - Ensure adequate communication to other healthcare providers and the patient regarding the removal of the allergy label to avoid confusion in the future

**9.6. If Inadvertent Administration… [closed]**

Management of a patient where there is a history of inadvertent administration of a penicillin since the application of the allergy label

History of reaction after administration of a specific beta-lactam antibiotic, with subsequent well-tolerated administration of the same antibiotic:

- The label of penicillin allergy should be removed
- Ensure adequate communication to other healthcare providers and the patient regarding the removal of the allergy label to avoid confusion in the future

History of reaction after administration of a specific beta-lactam antibiotic, with subsequent administration of a different beta-lactam antibiotic, or unable to remember/identify beta-lactam antibiotic implicated in original reaction. (Possible reaction to moiety other than beta-lactam ring):

- If there is a history of serious or life-threatening reaction:
Avoid all beta lactams and discuss further management with Consultant Immunologist or Microbiologist

- If there is a history of accelerated type 1 reaction with the initial antibiotic, and no reaction to the subsequent antibiotic:
  - It is safe to use the subsequent antibiotic that was inadvertently administered in all settings.
  - If other penicillins are intended:
    - In the community, avoid all other penicillins and caution with cephalosporins and carbapenems
    - In hospital, use the provocation test for adult patients (children require referral to RD&E allergy clinic), and if tolerated, remove penicillin allergy label. Ensure adequate communication to other healthcare providers and the patient regarding the removal of the allergy label to avoid confusion in the future. See appendix in BOB document policy for cross-reactivity diagram to aid choice of alternative agents.

- If vague history of non-urticarial rash with no blistering or mucous membrane involvement, or vague history, or unsubstantiated history of allergy from family:
  - Remove label of penicillin allergy. Ensure adequate communication to other healthcare providers and the patient regarding the removal of the allergy label to avoid confusion in the future.

9.7. Ward Provocation Test – ADULTS ONLY [closed]

- Ensure provocation test is carried out in an area with resuscitation facilities and trained staff
- The patient, or their carers / representatives should be appropriately consented and the risks and benefits of the procedure explained before the test.
- Ensure patient is cannulated before the test, and observed closely throughout
- Give the lowest available oral dose of the intended beta-lactam antibiotic (consider use of paediatric suspensions) and monitor continuously for at least one hour. If piperacillin-tazobactam (Tazocin®) is indicated, use co-amoxiclav as the oral alternative
  - 125mg/5mL amoxicillin, 125+31mg/5mL co-amoxiclav, or 125mg/5mL penicillin V suspensions are usually in stock from NDDH Pharmacy
- If no reaction in the hour following initial test dose, give the oral treatment dose of the intended beta-lactam antibiotic. Monitor continuously for at least one hour.
- If no reaction in the hour following full oral dose, administer the lowest licensed intravenous dose by infusion over 60 minutes, monitoring continuously.
- If no reaction during the 60 minute low-dose infusion, administer the treatment intravenous dose by infusion over 60 minutes, monitoring continuously
• If no reaction during the 60 minute treatment-dose infusion, the patient can be treated with the intended beta-lactam antibiotics intravenously (if indicated). Ensure to take into account when the test dose was given when writing up a course subsequently in the drug chart.
• The label of penicillin allergy should be removed. A letter must be sent to other care providers regarding the outcome of the test, and subsequent removal of the penicillin allergy label to avoid confusion in the future.

9.8. Cross Reaction Between Beta Lactams [closed]

There is now thought to be much less than 10% cross-reactivity between penicillins, cephalosporins and carbapenems, depending on their chemical structure and side-rings. Monobactam cross-reactivity is not thought to be significant due to the different structure of the moiety around a single, unattached beta lactam ring.

➢ See appendix in BOB document policy for cross-reactivity diagram to aid choosing suitable alternative agents.

• Antibiotics containing penicillin [closed]
➢ AVOID if history of penicillin allergy:
  ➢ Amoxicillin
  ➢ Ampicillin
  ➢ Co-amoxiclav (Augmentin®)
  ➢ Flucloxacillin
  ➢ Penicillin G (benzylpenicillin)
  ➢ Penicillin V (phenoxymethyl-penicillin)
  ➢ Piperacillin
  ➢ Pivmecillinam
  ➢ Tazocin® (piperacillin plus tazobactam)
  ➢ Temocillin
  ➢ Ticarcillin
  ➢ Timentin® (ticarcillin plus clavulanic acid)

• Non-Penicillin Beta-Lactam Antibiotics [closed]
➢ Use with caution in penicillin allergy, especially if history of serious reaction:
  ➢ Cefalexin
  ➢ Cefixime
  ➢ Cefotaxime
  ➢ Cefradine
  ➢ Ceftazidime
  ➢ Ceftaroline
  ➢ Ceftolazole / Tazobactam
  ➢ Ceftriaxone
  ➢ Cefuroxime
  ➢ Ertapenem
  ➢ Imipenem plus cilastin
  ➢ Meropenem

• Non Beta-Lactam Antibiotics [closed]
➢ Can be used safely in penicillin allergy
  ➢ Amikacin
Azithromycin
Aztreonam
Chloramphenicol
Ciprofloxacin
Clarithromycin
Clindamycin
Colistin
Co-trimoxazole
Daptomycin
Doxycycline
Erythromycin
Gentamicin
Levofloxacin
Linezolid
Lymecycline
Metronidazole
Minocycline
Moxifloxacin
Nitrofurantoin
Norfloxacin
Ofloxacin
Oxytetracycline
Rifampicin
Rifaximin
Sodium Fusidate
Sulfadiazine
Synercid®
Teicoplanin
Tetracycline
Tigecycline
Tinidazole
Trimethoprim
Tobramycin
Vancomycin

9.9. Other Relevant Guidelines [closed]
- Antimicrobial prescribing policy
- Medicines Policy

9.10. Version Control [closed]
- Guidelines for management of penicillin allergy v1.3 230119
## 10. Appendix 2 – Table of Cross-Sensitivities in Beta Lactam Antibiotics

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**Legend**

- *In vitro* data proposed cross-reactivity between cefotaxim and cephalothin based upon shared but not shared R1
- Exactly the same drug
- R1 – Identical R1 side chain
- R1* – Almost identical R1 side chain
- R2 – Identical R2 and non-identical R1 with some cross-reactivity
- R2* – Non-identical R1 with some clinical cross-reactivity
- Shared class specific ring but no shared side chain structure
- No shared class specific ring, only shared beta-lactam ring
- No shared cross-reactivity with beta-lactam ring

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Microbiology

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11. Appendix 3 – Penicillin Allergy Poster for Display on Wards

PENICILLIN ALLERGY – Antibiotic prescribing in a penicillin allergic patient

CONTRA-INDICATED

- Amoxicillin
- Ampicillin
- Co-amoxiclav (Augmentin®)
- Flucloxacillin
- Penicillin G (benzylpenicillin)
- Penicillin V (phenoxymethylpenicillin)
- Piperacillin
- Pivmecillinam
- Tazocin® (piperacillin plus tazobactam)
- Temocillin
- Ticarcillin
- Timentin (ticarcillin plus clavulanic acid)

CAUTION*

- Cefalexin
- Cefixime
- Cefotaxime
- Cefradine
- Ceftaroline
- Ceftazidime
- Ceftolozane/Tazobactam
- Ceftriaxone
- Cefuroxime
- Ertapenem
- Imipenem plus cilastatin
- Meropenem

CONSIDERED SAFE

- Amikacin
- Azithromycin
- Aztreonam
- Chloramphenicol
- Ciprofloxacin
- Clarithromycin
- Clindamycin
- Colistin
- Co-trimoxazole
- Daptomycin
- Doxycycline
- Erythromycin
- Gentamicin
- Levofloxacin
- Linezolid
- Lymecycline
- Metronidazole
- Minocycline

- Moxifloxacin
- Nitrofurantoin
- Norfloxacin
- Ofloxacin
- Oxytetracycline
- Rifampicin
- Rifaximin
- Sodium Fusidate
- Sulfadiazine
- Synercid®
- Teicoplanin
- Tetracycline
- Tigecycline
- Tinidazole
- Trimethoprim
- Tobramycin
- Vancomycin
## 12. Appendix 4 – Penicillin Allergy Type Assessment and Management Planning Sheet for Individual Patients

<table>
<thead>
<tr>
<th>Dermatological</th>
<th>Respiratory or Systemic</th>
<th>Unknown Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Manifestation</strong></td>
<td><strong>Recommendation and resultant allergy type</strong></td>
<td><strong>Clinical Manifestation</strong></td>
</tr>
<tr>
<td><strong>Childhood exanthem (unspecified)</strong></td>
<td>Unlikely to be significant (non-severe)</td>
<td>Laryngeal involvement (“throat tightness” or “hoarse voice”)</td>
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<tr>
<td>Details of rash timing unknown and no severe features or hospitalisation</td>
<td></td>
<td>Unknown reaction ≤ 10 years ago</td>
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<tr>
<td><strong>Immediate diffuse rash (“itchy immediate rash”) &lt;2 hours post-antibiotic dose</strong></td>
<td>Immediate hypersensitivity (non-severe)</td>
<td>Respiratory compromise (“wheeze” or “SOB”)</td>
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<tr>
<td>Diffuse rash or localised rash with no other symptoms &gt;24 hours post starting antibiotic</td>
<td>≤10 years ago</td>
<td>Delayed hypersensitivity (non-severe)</td>
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<tr>
<td>&gt;10 years ago</td>
<td>Delayed hypersensitivity (non-severe, low-risk)</td>
<td>Fever (“high temperature”) – not explained by infection or other cause</td>
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<td><strong>Rash and mucosal ulceration (“mouth, eye or genital ulcers”). Be alert for history of SCAR</strong></td>
<td>Delayed hypersensitivity (severe)</td>
<td>Haematological</td>
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<tr>
<td><strong>Postural, blistering or desquamating (“skin shedding”) rash. Be alert for history of SCAR</strong></td>
<td>Delayed hypersensitivity (severe)</td>
<td>Platelets &lt; 150x10⁹/L or unknown</td>
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<tr>
<td><strong>Angioedema (“lip, facial or tongue swelling”)</strong></td>
<td>Immediate hypersensitivity (severe)</td>
<td>Neutrophils &lt; 1 x10⁹/L or unknown</td>
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<td><strong>Swelling (outside of angioedema)</strong></td>
<td>Immediate hypersensitivity (severe)</td>
<td>Haemoglobin &lt; 100g/L or unknown</td>
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<td><strong>Urticaria (“wheals and hives”)</strong></td>
<td>Immediate hypersensitivity (severe)</td>
<td>EOSINOPHILIA &gt; 0.7 x10⁹/L or unknown</td>
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<tr>
<td><strong>DRESS</strong></td>
<td>Immediate hypersensitivity (severe, if DRESS)</td>
<td><strong>EXAMINE HISTORY FOR DRESS</strong></td>
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### ABBREVIATIONS:

- DRESS: drug reaction with eosinophilia and systemic symptoms
- AIN: acute interstitial nephritis
- DILI: drug induced liver injury
- SCAR: severe cutaneous drug reactions
- **Gastro-intestinal symptoms** "nausea, vomiting, diarrhoea"
- Mild neurological or CNS manifestation "headache, confusion, depression, mood disorder"
- Unlikely immune mediated (non-severe, low risk)
| Refer to microbiology for consideration of skin testing / direct oral re-challenge | Severe neurological or CNS manifestation "seizures, psychosis", Other reaction, OR; Anaphylactoid / infusion reaction | Unknown or unclear mechanism – contact Microbiologist and Medicines Information (Pharmacy) for advice |
| Refer to immunology for further allergy assessment | | |

Refer to microbiology for consideration of skin testing / direct oral re-challenge
Refer to immunology for further allergy assessment