Patient with reported penicillin▪ allergy referred to outpatient clinic

▪ penicillin unspecified, penicillin VK/G, amoxicillin, amoxicillin/clavulanate, ampicillin, dicloxacillin, flucloxacillin

Assessment for Eligibility

**Inclusion Criteria**

1. Adult patients (≥ 18 years) referred to the outpatient allergy clinic for a penicillin allergy history;
2. Willing and able to give consent

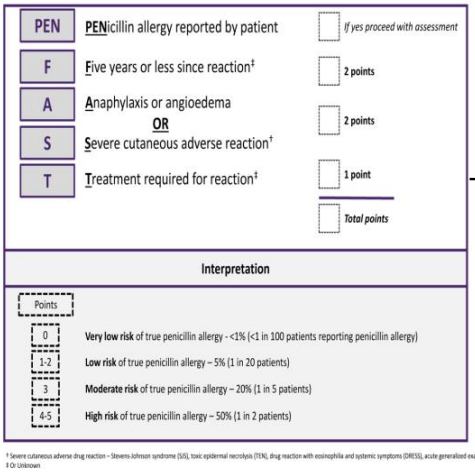
**Exclusion Criteria**

1. Pregnancy;
2. Any illness that, in the investigator's judgement, will substantially increase the risk associated with subject's participation in this study (**including a non-English speaking patient if an interpreter is not available**);
3. Patients with history of type A adverse drug reaction, drug-associated anaphylaxis, idiopathic urticaria/anaphylaxis, mastocytosis, serum sickness, blistering skin eruption or acute interstitial nephritis;
4. Patients with a concurrent history of immune-mediated cephalosporin allergy;
5. Patients where the allergy history was not able to be confirmed with patient;
6. Patients on concurrent antihistamine therapy;
7. Patients receiving more than stress dose steroids (i.e. > 50mg QID hydrocortisone [or steroid equivalent♦]).

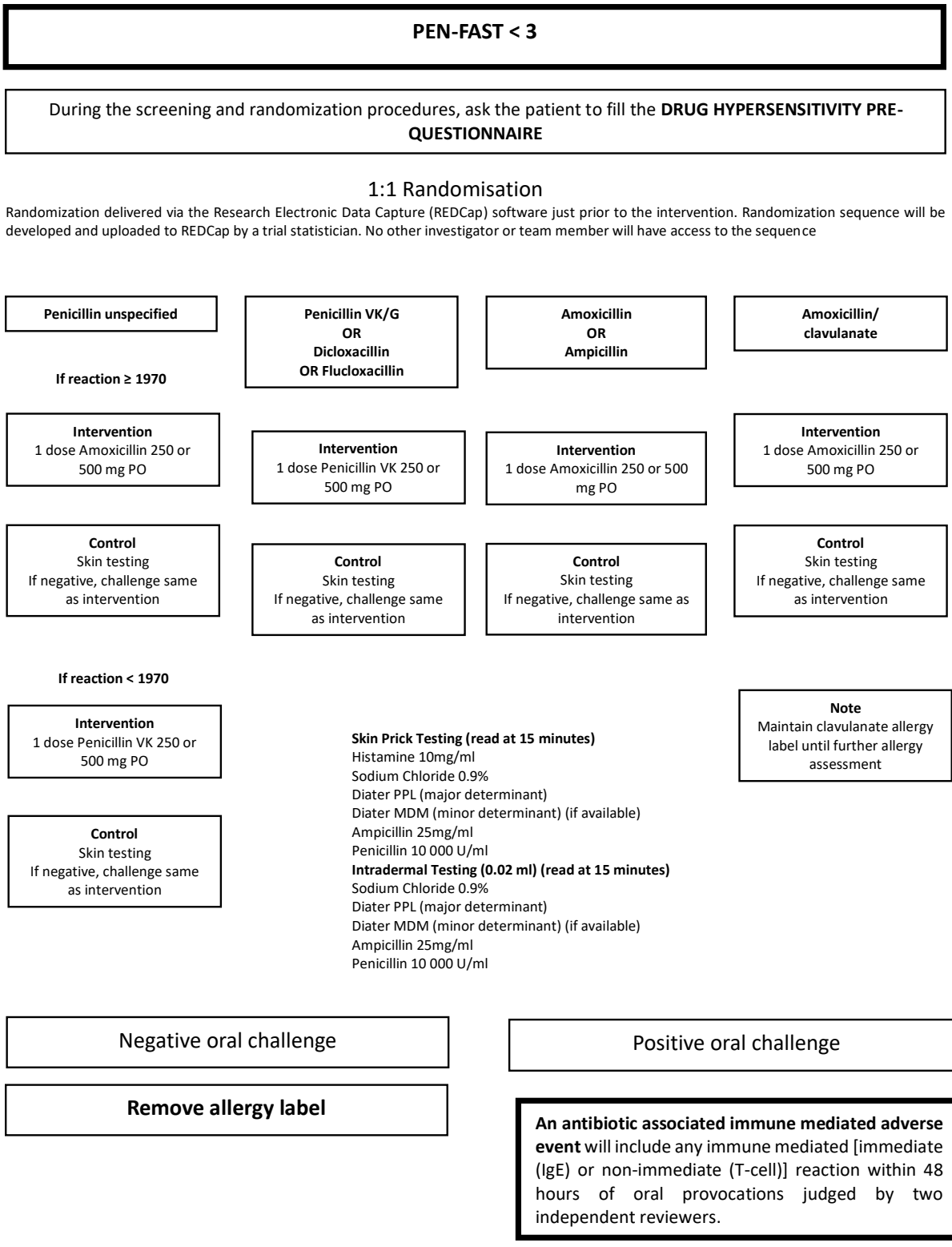
♦ **Approximate steroid equivalent**: Hydrocortisone 50 mg = Betamethasone 1.8 mg = Cortisone 62.5 mg = Dexamethasone 1.9 mg = Methylprednisolone 10 mg = Prednisone/Prednisolone 12.5 mg = Triamcinolone 10 mg

Patient recruitment
Consent form discussed and signed

Penicillin allergy assessment with **PEN-FAST** tool
All penicillin allergy assessment should take place during the **same medical appointment**




PEN-FAST ≥ 3
Excluded


PEN-FAST < 3
During the screening and randomization procedures, ask the patient to fill the DRUG HYPERSENSITIVITY PRE-QUESTIONNAIRE
1:1 Randomisation
Randomization delivered via the Research Electronic Data Capture (REDCap) software just prior to the intervention. Randomization sequence will be developed and uploaded to REDCap by a trial statistician. No other investigator or team member will have access to the sequence
Penicillin unspecified
Penicillin VK/G OR Dicloxacillin OR Flucloxacillin
Amoxicillin OR Ampicillin
Amoxicillin/ clavulanate
If reaction ≥ 1970
Intervention 1 dose Amoxicillin 250 or 500 mg PO
Intervention 1 dose Penicillin VK 250 or 500 mg PO
Intervention 1 dose Amoxicillin 250 or 500 mg PO
Intervention 1 dose Amoxicillin 250 or 500 mg PO
Control Skin testing If negative, challenge same as intervention
Control Skin testing If negative, challenge same as intervention
Control Skin testing If negative, challenge same as intervention
Control Skin testing If negative, challenge same as intervention
If reaction < 1970
Intervention 1 dose Penicillin VK 250 or 500 mg PO
Control Skin testing If negative, challenge same as intervention
Note Maintain clavulanate allergy label until further allergy assessment
Skin Prick Testing (read at 15 minutes)
Histamine 10mg/ml
Sodium Chloride 0.9%
Diater PPL (major determinant)
Diater MDM (minor determinant) (if available)
Ampicillin 25mg/ml
Penicillin 10 000 U/ml
Intradermal Testing (0.02 ml) (read at 15 minutes)
Sodium Chloride 0.9%
Diater PPL (major determinant)
Diater MDM (minor determinant) (if available)
Ampicillin 25mg/ml
Penicillin 10 000 U/ml
Negative oral challenge
Positive oral challenge
Remove allergy label
An antibiotic associated immune mediated adverse event will include any immune mediated [immediate (IgE) or non-immediate (T-cell)] reaction within 48 hours of oral provocations judged by two independent reviewers.

**A serious adverse event** will be defined as any adverse drug event/experience occurring at any dose that in the opinion of the investigators is causal for any of these outcomes: (1) death; (2) life threatening reaction; (3) inpatient hospitalization; (4) results in persistent or significant disability/incapacity; (5) congenital anomaly or birth defect; or (6) requires intervention to prevent permanent impairment or damage.

**An antibiotic associated adverse event** will include any non-immune mediated reaction (e.g. nausea, vomiting, diarrhea etc.) within 48 hours of oral provocations judged by two independent reviewers.

**Report to Data safety management board (DSMB)**