An estimated 30 million US patients report as penicillin allergic, 27 million are not.[1]

How Many Are In Your Hospital?

Nearly **10 percent** of the US population reports as penicillin allergic. When tested, **9 out of 10** who have reported the allergy **ARE NOT TRULY ALLERGIC.** This can result in the over prescribing of broad-spectrum alternative antibiotics which leads to the growing problem of drug resistance.[1]

What Is That Costing Your Hospital?

Antibiotic resistant infections cost the US healthcare system more than **$20 billion annually.**[2]

Contact ALK for assistance implementing penicillin allergy skin testing. Make it an important component of antibiotic stewardship.

ALK | PRE-PEN®
(benzylpenicilloyl polylysine injection USP)
Penicillin Skin Test Antigen

[1] Salkind, JAMA, May 16, 2001 – Vol. 285, No. 19
[2] Hospital and Societal Costs of Antimicrobial Resistance, Reported by the APUA

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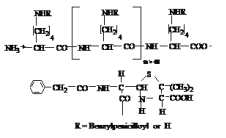
Published 10.12 S599v2

PRE-PEN® (benzylpenicilloyl polylysine injection USP) Skin Test Antigen

DESCRIPTION:

PRE-PEN® (benzylpenicilloyl polylysine injection USP) is a sterile solution of benzylpenicilloyl polylysine in a concentration of 6.0 X 10-5 M (benzylpenicil¬loyl) in 0.01 M phosphate buffer and 0.15 M sodium chloride. The benzylpeni¬cilloyl polylysine in PRE-PEN is a derivative of poly-l-lysine, where the epsilon amino groups are substituted with benzylpenicilloyl groups (50-70%) forming benzylpenicilloyl alpha amide. Each single dose ampule contains 0.25 mL of PRE-PEN.

PRE-PEN is a skin test antigen used in assessing a patient's allergic status to penicillin. The structural formula of PRE-PEN is:



CLINICAL PHARMACOLOGY:

PRE-PEN reacts specifically with benzylpenicilloyl IgE antibodies to initiate release of chemical mediators which produce an immediate wheal and flare reaction at a skin test site. All individuals exhibiting a positive skin test to PRE-PEN possess IgE against the benzylpenicilloyl group which is a hapten. A hapten is a low molecular weight chemical which, when conjugated to a carrier, e.g., poly-l-lysine, has the properties under appropriate conditions of an antigen with the hapten's specificity. The benzylpenicilloyl hapten is the major antigenic determinant in penicillin-allergic individuals.

It is to be noted that individuals who have previously received therapeutic penicillin may have positive skin test reactions to PRE-PEN as well as to a number of other non-benzylpenicilloyl haptens. The latter are designated as minor determinants, in that they less frequently engender an immune response in penicillin treated individuals than does the major determinant, benzylpenicilloyl. The minor determinants may nevertheless be associated with significant clinical hypersensitivity.

Virtually everyone who receives penicillin develops specific antibodies to the drug as measured by hemagglutination studies, but (a) immediate skin tests to various penicillin and penicillin-derived reagents become positive in fewer than 10% of patients who have tolerated penicillin in the past; and (b) acute allergic responses to penicillin treatment are infrequent (less than 1%).

Many individuals reacting positively to PRE-PEN will not develop a systemic allergic reaction on subsequent exposure to therapeutic penicillin, especially among those who have not reacted to penicillins in the past. Thus, the PRE-PEN skin test determines the presence of penicilloyl IgE antibodies which are necessary but not sufficient for acute allergic reactions due to the major penicilloyl determinant.

INDICATIONS AND USAGE:

PRE-PEN is useful as an adjunct in assessing the risk of administering peni¬cillin (benzylpenicillin or penicillin G) when it is the preferred drug of choice in adult patients who have previously received penicillin and have a history of clinical penicillin hypersensitivity. In this situation, a negative skin test to PRE-¬PEN is associated with an incidence of immediate allergic reactions of less than 5% after the administration of therapeutic penicillin, whereas the incidence may be more than 50% in a history-positive patient with a positive skin test to PRE-PEN.

These allergic reactions are predominantly dermatologic. Because of the extremely low incidence of anaphylactic reactions, there are insufficient data at present to document that a decreased incidence of anaphylactic reactions following the administration of penicillin will occur in patients with a negative skin test to PRE-PEN. Similarly, when deciding the risk of proposed penicillin treatment, there are not enough data at present to permit relative weighing in individual cases of a history of clinical penicillin hypersensitivity as compared to positive skin tests to PRE-PEN and/or minor penicillin determinants.

It should be borne in mind that no reagent, test, or combination of tests will completely assure that a reaction to penicillin therapy will not occur.

CONTRAINDICATIONS:

PRE-PEN is contraindicated in those patients who have exhibited either a sys¬temic or marked local reaction to its previous administration. Patients known to be extremely hypersensitive to penicillin should not be skin tested.

WARNINGS:

There are insufficient data to assess the potential danger of sensitization to repeated skin testing with PRE-PEN.

Rarely, a systemic allergic reaction (see below) may follow a skin test with PRE-PEN. This can be avoided by making the first application by a puncture test and very carefully following the instructions below in administering the intra¬dermal test, using the intradermal route only if the puncture test is entire¬ly negative.

PRECAUTIONS:

General:

There are insufficient data derived from well-controlled studies to determine the value of the PRE-PEN skin test alone as a means of assessing the risk of admin¬istering therapeutic penicillin (when penicillin is the preferred drug of choice) in the following situations:

(1)Adult patients who give no history of clinical penicillin hypersensitivity; and

(2)Pediatric patients.

In addition, there are no data at present to assess the clinical value of PRE-¬PEN where exposure to penicillin is suspected as a cause of a current drug reaction or in patients who are undergoing routine allergy evaluation.

Furthermore, there are no reliable data relating the clinical value of PRE-PEN skin tests alone to the risk of administering semi-synthetic penicillins (phenoxymethyl penicillin, ampicillin, carbenicillin, dicloxacillin, methicillin, nafcillin, oxacillin, amoxicillin) ,cephalosporin-derived antibiotics, and penem antibiotics.

Recognition that the following clinical outcomes are possible makes it impera¬tive for the physician to weigh risk to benefit in every instance where the deci¬sion to administer or not to administer penicillin is based in part on a PRE-PEN skin test:

(1)A serious allergic reaction to therapeutic penicillin may occur in a patient with a negative skin test to PRE-PEN.

(2)It is possible for a patient to have an anaphylactic reaction to therapeu¬tic penicillin in the presence of a negative PRE-PEN skin test and a neg¬ative history of clinical penicillin hypersensitivity.

(3)If penicillin is the drug of choice for a life-threatening infection, successful desensitization with therapeutic penicillin may be possible irrespective of a positive skin test and/or a positive history of clinical penicillin hypersensitivity.

Pregnancy – Pregnancy Category C:

Animal reproduction studies have not been conducted with PRE-PEN. It is not known whether PRE-PEN can cause fetal harm when administered to a preg¬nant woman or can affect reproduction capacity. The hazards of skin testing in such patients should be weighed against the hazard of penicillin therapy with¬out skin testing.

ADVERSE REACTIONS:

Occasionally, patients may develop an intense local inflammatory response at the skin test site. Rarely patients will develop a systemic allergic reaction, manifested by generalized erythema, pruritus, angioedema, urticaria, dyspnea, and/or hypotension. The usual methods of treating a skin test anti¬gen-induced reaction — the applications of a venous occlusion tourniquet proximal to the skin test site and administration of epinephrine are recommended and will usually control the reaction. As a rule, systemic allergic reactions following skin test proce¬dures are of short duration and controllable, but the patient should be kept under observation for several hours.

DOSAGE AND ADMINISTRATION:

SKIN TESTING DOSAGE AND TECHNIQUE

Skin testing responses can be attenuated by interfering drugs (e.g. H1-antihistamines and vasopressors). Skin testing should be delayed until the effects of such drugs have dissipated, or a separate skin test with histamine can be used to evaluate persistent antihistaminic effects in vivo.

Puncture Testing:

Skin testing is usually performed on the inner volar aspect of the forearm. The skin test antigen should always be applied first by the puncture technique. After preparing the skin surface, apply a small drop of PRE-PEN solution using a sterile 22-28 gauge needle. The same needle can then be used to make a single shallow puncture of the epidermis through the drop of PRE-PEN. Very little pressure is required to break the epidermal continuity. Alternatively an allergy prick testing device (eg. duo tip or bifurcated needle) may be employed. Observe for the appearance of a wheal, erythema, and the occurrence of itching at the test site during the succeeding 15 minutes at which time the solution over the puncture site may be wiped off. A positive reaction is unmistakable and consists of the develop¬ment within 10 minutes of a pale wheal, sometimes with pseudopods, surrounding the puncture site and varying in diameter from 5 to 15 mm (or more). This wheal may be surrounded by a variable diameter of erythema, and accompanied by a variable degree of itching. The most sensitive individuals develop itching quickly, and the wheal and erythema are prompt in their appearance. As soon as a positive response as defined above is clearly evident, the solu¬tion over the scratch should be immediately wiped off. If the puncture test is either negative or equivocally positive (less that 5 mm wheal and little or no erythema, and no itching), an intradermal test may be performed.

The Intradermal Test:

Using a tuberculin syringe with a 3/8" to 5/8"long, 26 to 30 gauge, short bevel needle, withdraw the remaining contents of the ampoule. Prepare with an alcohol swab a skin test area on the upper, outer arm, sufficiently below the deltoid muscle to permit prox¬imal application of a tourniquet later, if necessary. Be sure to eject all air from the syringe through the needle, then insert the needle, bevel up immediately below the skin surface. Inject an amount of PRE-PEN sufficient to raise a small intradermal bleb of about 3 mm in diameter, in duplicate at least 2 cm apart. Using a separate syringe and needle, inject a like amount of sterile saline or allergen diluting solution as a control at least 5 cm removed from the antigen test sites. Most skin reac¬tions will develop within 5-15 minutes and response to the skin test is read at 20 min as follows:

Negative response — no increase in size of original bleb and no greater reaction than the control site.Ambiguous response — wheal only slightly larger than initial injection bleb, with or without accompanying erythematous flare and slightly larger than the control site; OR discordance between duplicates.

Positive response — itching and significant increase in size of original blebs to at least 5mm. Wheal may exceed 20 mm in diameter and exhibit pseu¬dopods.

If the control site exhibits a wheal greater than 2-3 mm, repeat the test, and if the same reaction is observed, a physician experienced with allergy skin testing should be consulted.

HOW SUPPLIED: NDC 65044-9997-5

PRE-PEN® (benzylpenicilloyl polylysine injection USP) is a clear, colorless, sterile solution supplied in ampoules containing 0.25 mL.

Box of 5 single dose ampoules. Ampoules are opened by snapping the neck of the vial using two forefingers of each hand. Visually inspect for glass chards before use. Each vial is for single patient use only—discard any unused portion.

PRE-PEN is optimally stored under refrigeration (2-8°C). It is recom¬mended that test antigenubjected to ambient temperatures for more than 24 hours be discarded. As with all parenteral drug products, PRE-PEN should be inspected visually for particulate matter and discoloration prior to administration.

Rx only

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