Diater Laboratorio de Diagnóstico
y Aplicaciones Terapéuticas, S.A

Summary of product characteristics

DAP Amoxicillin
Solution for injection

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DAP Amoxicillin, powder and solvent for skin test solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One millilitre of solution for injection contains 20 mg of amoxicillin (as sodium amoxicillin).

Excipient with known effect
One vial of reconstituted sodium amoxicillin contains 0.2364 mmol (5.43 mg) of sodium.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

White or off-white lyophilised powder.

The solvent (physiological saline solution) is a transparent and odourless liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

DAP Amoxicillin is used for the diagnostic assessment of allergy, sensitisation or type I hypersensitivity, in those cases where an allergy to aminopenicillins is suspected, through skin testing (skin prick tests or intradermal skin tests).

4.2 Posology and method of administration

Posology

For the prick test, one drop of the undiluted solution is used.

To avoid risks, it is recommended that the intradermal tests be started with a first dilution (1:10) before the intradermal tests are performed with sodium amoxicillin.

In patients whose symptoms suggest a severe reaction or high risk, the intradermal skin tests should start at a dilution of 1:1000.

Dilutions must be made under aseptic conditions and using the proper solvents.

0.02 - 0.05 ml of the respective solutions is administered intradermally.

The reconstituted solution is transparent, colourless and odourless.

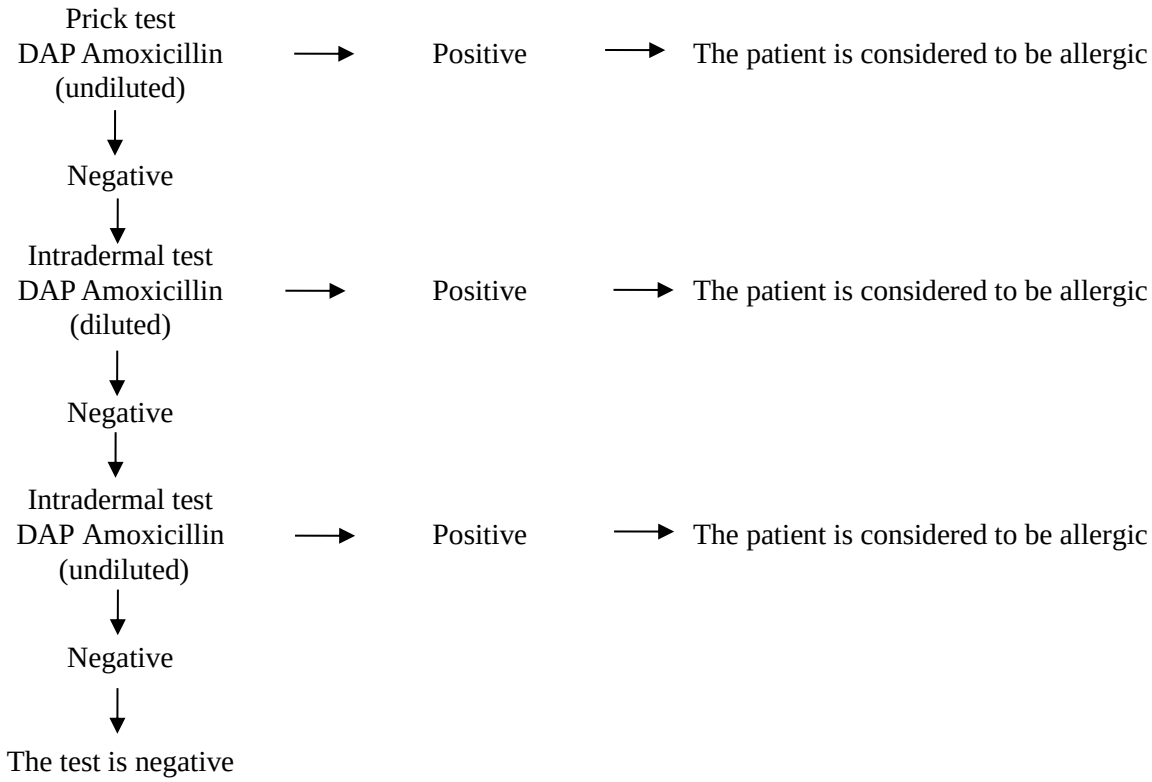
Method of administration

The skin test is performed on the inner side of the forearm.

The product must be reconstituted prior to use. For notes on reconstitution and dilution of the medicinal product prior to use, see section 6.6. Before performing the skin tests, the reconstituted vial is allowed to stand for at least 10 minutes at room temperature.

Skin tests with DAP Amoxicillin are commenced by examining skin reactivity using the prick technique. Intradermal tests should be performed only when skin prick tests have proven negative. It is recommended that the algorithm for evaluating sensitivity to amoxicillin by skin tests should be followed:

Algorithm for performing skin tests with DAP Amoxicillin



Prick test:

The skin surface is prepared and a small drop of sodium amoxicillin and positive and negative controls, with a sterile 28-32G cannula at a distance of at least 2 cm. The surface layer of the skin is punctured through the drop with a lancet. Very little pressure is required to break the continuity of the epidermis. Check the puncture site after 15-20 minutes.

The result is considered to be “positive” when the diameter of the wheal is more than 3 mm, or if it has an irregular, finger-like shape (pseudopod formation).

Largest wheal diameter	**Skin test result**
Less than or equal to 3 mm	Negative
Larger than 3 mm	Positive

If the prick test is negative, an intradermal test can be performed.

Intradermal test:

The skin area is prepared. A short 28-32G cannula and a 1 ml syringe are used. 0.02-0.05 ml of sodium amoxicillin are injected intradermally at the selected dilution.

Measure of the resulting wheal:

The puncture site is checked again after 15-20 minutes:

- The test is considered to be “positive” if the difference between the original wheal diameter and the resulting wheal is more than 3 mm.

- The test is considered to be “negative” if no increase in the size of the original wheal is observed.

- A skin test may produce a reaction even later than after 20 min. Please make sure the patient contacts the physician if the skin test produces a reaction within 48 hours.

Paediatric population

There is no relevant use of DAP Amoxicillin in the paediatric population.

4.3 Contraindications

DAP Amoxicillin must not be used:

- In case of hypersensitivity to any of the excipients listed in section 6.1.
- In the presence of a pathological condition affecting the surface of skin to be used for the skin tests, any other pathological conditions significantly affecting the patient’s general well-being.
- If the patient is suffering an acute allergic reaction caused by any allergen.
- if the patient is taking antihistamines, corticosteroids, chromones or other medicinal products that have an anti-allergic effect, it is necessary to discontinue its use 1 week before skin testing (see section 4.5).
- if, for therapeutic reasons, beta-blockers or ACE inhibitors are being taken, these must be discontinued 48 hours before skin testing, always under the approval of the physician and with control of the blood pressure (see section 4.5).
- During pregnancy and lactation.
- In patients with uncontrolled or only partly controlled bronchial asthma.

4.4 Special warnings and precautions for use

Skin tests during pregnancy and breastfeeding are not recommended due to the additional risk of a possible anaphylactic reaction, but the decision in each case is at the discretion of the physician responsible for performing the test, who must decide when best to perform the diagnostic skin tests after appraisal of the individual benefit-risk ratio (see section 4.6).

There are insufficient data on the use of this diagnostic medicinal product in children and adolescents.

After the test, the patient must remain under medical observation for at least 30 minutes.

In the hours before and after the tests, the patient is required to abstain from alcohol consumption, intense physical activity and hot baths/showers.

Sodium:
After reconstitution, this medicinal product contains less than 1 mmol (23 mg) sodium per millilitre, i.e. essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Antihistamines, corticosteroids, chromones and other medicinal products with antiallergic activity may interfere with the skin test results. These medicines must be discontinued at least one week before performing the skin tests.

Oral use of beta-blockers or ACE inhibitors must be discontinued 48 hours before the skin tests, always in consultation with the treating physician and with due monitoring of the patient's blood pressure.

If the patient is receiving allergen immunotherapy, the skin tests should be performed at least one week after administration of the last dose of immunotherapy. Similarly, the period between the skin tests and administration of an immunotherapy dose should be 2-3 days.

4.6 Fertility, pregnancy and lactation

Pregnancy and breastfeeding

Skin tests during pregnancy and breastfeeding are not recommended due to the additional risk of a possible anaphylactic reaction, but the decision in each case is at the discretion of the physician responsible for performing the test, who must decide when best to perform the diagnostic skin tests after appraisal of the individual benefit-risk ratio.

Fertility

No reproductive or developmental toxicity studies have been performed.

4.7 Effects on ability to drive and use machines

DAP Amoxicillin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions may occur immediately or hours after administration. Usually, a skin prick test causes no problems; however, due to its mechanism of action, it can cause the following IgE-mediated adverse reactions:

Local reactions
Erythema, oedema or inflammation, with or without pruritus at the puncture site. These usually manifest after 10 to 60 minutes and may persist for several hours.

Moderate systemic reactions
Large pustules, erythema and pruritus, which may progress to generalised urticaria or an exanthematous condition, with ocular or nasal symptoms and angioedema. Onset of these symptoms is usually within a few minutes to 4-6 hours after the test.

Severe systemic reactions: anaphylaxis
Anaphylaxis may develop immediately or a few minutes after performing the skin tests. It usually manifests with typical symptoms, including the onset of pruritus of the hands and feet, as well as lingual and sublingual pruritus affecting the throat. Anaphylaxis leads to severe, rapid collapse affecting multiple organs and systems: circulatory collapse with marked hypotension, nasal congestion, laryngeal oedema and bronchospasm, generalised pruritus, urticaria and angioedema, abdominal pain, nausea, vomiting and diarrhoea, intermenstrual bleeding, tinnitus, dizziness, impaired sphincter function, seizures and loss of consciousness.

Paediatric population

There is no relevant data in the paediatric population.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose

DAP Amoxicillin is administered for skin tests only.

In case of accidental overdose or incorrect skin test technique, adverse reactions may occur with varying degrees of severity, including anaphylaxis, usually as a result of injury to a blood vessel and subsequent endovenous administration. The adverse reactions can be treated as follows:

Treatment of local reactions

The skin test should be interpreted after 15-20 minutes (IgE-mediated reaction) and the person tested should be kept under medical surveillance for at least 30 minutes. The wheal should have receded within 1-6 hours after the test.

Usually, they do not require medical treatment, although the use of oral antihistamines and/or corticosteroid-based topical creams may be appropriate if the wheal fails to recede and has a diameter of more than 5 cm. Only in the event of severe local reactions is it advisable to apply a tourniquet above the area where the skin test was performed and to infiltrate subcutaneously the adjacent areas with adrenaline.

Treatment of moderate systemic reactions

A tourniquet must be applied above the area where the skin test was performed and pharmacological treatment must be initiated immediately. In those cases where urticaria and angioedema occurs, intravenous antihistamines and adjuvant intravenous corticosteroids (i.e. prednisolone) are to be administered. If required, the test area can be subcutaneously infiltrated with adrenaline, which can be repeated every 15 minutes; the use of bronchodilator aerosols and a slow intravenous theophylline injection may also be considered.

The patient’s blood pressure and pulse must be constantly monitored.

Treatment of severe systemic reactions: anaphylaxis

Instructions for treating anaphylaxis must comply with the current guidelines for management of anaphylaxis and must be regularly adapted to the latest state of knowledge.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Group V (Various), ATC code: V04CL10. Tests for allergic diseases.

Mechanism of action

The most common hypersensitivity reactions to betalactam antibiotics are IgE-mediated (type I). In these, proteins present in plasma bind with penicillin to form haptens, which are recognized by IgE-antibodies in the surface of basophils/mast cells, inducing a fast release of histamine and other inflammatory mediators responsible for the allergic response (Antúnez et al. 2006).

These newly formed determinants can, *in situ*, induce a type I immediate reaction (IgE-mediated). In the case of amoxicillin, the side chain has been proven a relevant part of the allergenic determinant (Torres et al. 2010).

Clinical efficacy and safety

A multicentre study was carried out to demonstrate the equivalence between DAP Amoxicillin and injectable amoxicillin. The study included 68 healthy volunteers and 55 patients with positive prick tests with injectable amoxicillin, who were re-evaluated within six months through skin testing, basophil activation test (BAT), Radioallergosorbent test (RAST) using both reagents. It was observed no significant differences in skin tests with DAP Amoxicillin (25 positives with prick test and 28 with intradermal test) and with injectable amoxicillin (24 positive with prick test and 29 with intradermal test), basophil activation test or the radioallergosorbent test. Only one patient showed mild systemic symptoms with both compounds with intradermal test (Torres et al. 2011).

Paediatric population

There is no relevant data in the paediatric population.

Literature References

- Antúnez C. et al. (2006). Immediate hypersensitivity to penicillins and other betalactams. *Curr Pharm Des*, 12(26):3327-33.
- Torres M.J. et al. (2010). Role of minor determinants of amoxicillin in the diagnosis of immediate allergic reactions to amoxicillin. *Allergy*, 65: 590–596
- Torres M.J. et al. (2011). Immunoglobulin E mediated hypersensitivity to amoxicillin: *in vivo* and *in vitro* comparative studies between an injectable therapeutic compound and a new commercial compound. *Clinical & Experimental Allergy*, 41: 1595–1601

5.2 Pharmacokinetic properties

There is no data on pharmacokinetic and metabolism.

5.3 Preclinical safety data

There is no preclinical safety data on DAP Amoxicillin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months.

6.4 Special precautions for storage

Non-reconstituted vials (lyophilised powder): store in refrigerator (2ºC-8ºC).

After reconstitution, store in refrigerator (2ºC-8ºC) with a shelf life of 24 hours.

6.5 Nature and contents of container

DAP Amoxicillin is presented in Type I transparent glass vials, with rubber stoppers and aluminum flip-off capsule.

Each pack contains:
- 6 vials of sodium amoxicillin 20 mg
- 12 vials of solvent (physiological saline solution) for reconstitution 1.2 ml.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

This medicinal product must be reconstituted prior to use. Under sterile conditions and using a sterile syringe and cannula, 1 ml diluent is added to the vial of lyophilised powder.

The reconstituted solution is transparent, colourless and odourless.

For intradermal use, dilutions must be made. Dilutions should be prepared under the appropriate, required aseptic conditions with diluents which can also be ordered separately.

To use DAP Amoxicillin, 1 ml diluent is added to the vial containing sodium amoxicillin. In the package there are additional vials of solvent provided. For information on dilution series, see section 4.2.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

March 2022.