NEW ZEALAND DATA SHEET

1. PHENOXYMETHYLPENICILLIN–AFT

Phenoxymethylpenicillin-AFT (granules for oral solution, 125 mg/5 mL and 250 mg/ 5 mL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Phenoxymethylpenicillin-AFT 125 mg/5 mL:
Following reconstitution, each 5 mL of solution contains 125 mg phenoxymethylpenicillin (as potassium salt).

Phenoxymethylpenicillin-AFT 250 mg/5 mL:
Following reconstitution, each 5 mL of solution contains 250 mg phenoxymethylpenicillin (as potassium salt).

Excipient(s) with known effect:
This product also contains sugar: approximately 2.8 g per 5 mL in the 125 mg/5 mL strength, and 2.9 g per 5 mL in the 250 mg/5 mL strength.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Granules for oral solution.

Pale orange granular powder with an orange odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of mild to moderately severe infections caused by penicillin-sensitive organisms. The following infections will usually respond to an adequate dosage of Penicillin.

Streptococcal infections
Mild to moderate infections of the upper respiratory tract, scarlet fever and erysipelas.
Note: Streptococci in groups A C G H L and M are very sensitive to penicillin.

Pneumococcal infections
Mild to moderately severe infections of the respiratory tract.
Prevention of bacterial endocarditis in patients with congenital and/or rheumatic heart lesions who are

about to undergo dental procedures or minor upper respiratory tract surgery or instrumentation.

Oral penicillin should not be used as adjunctive prophylaxis for genitourinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy or complications of childbirth.

4.2 Dose and method of administration

Dose

The usual dosage is 250 mg every four to six hours for adults and children. For younger children the dosage is 125 mg every four hours. Higher doses may be used in more severe infections. To ensure maximum absorption each dose should be taken one hour before meals. 250 mg two or three times daily may be used in the prophylaxis of recurrent streptococcal infections.

Method of administration

Oral

For instructions on reconstitution of the medicine before administration, see section 6.6.

4.3 Contraindications

Phenoxymethylpenicillin-AFT is contraindicated in patients who have had previous experience of a major allergy or anaphylaxis to a cephalosporin or penicillin.

Hypersensitivity to any of the excipients (see section 6.1).

4.4 Special warnings and precautions for use

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, the medicine should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including phenoxymethylpenicillin. A toxin produced with *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea of colitis in association with antibiotic

use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to medicine discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered.

Massive doses of penicillin can cause hypokalaemia and sometimes hypernatraemia. Use of a potassium-sparing diuretic may be helpful. In patients undergoing high-dose treatment for more than 5 days, electrolyte balance, blood counts and renal functions should be monitored.

Prolonged use of penicillin may occasionally result in an overgrowth of non-susceptible organisms or yeast and patients should be observed carefully for superinfections.

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving penicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Fluids, electrolytes and protein replacement should be provided when indicated. Agents which delay peristalsis, e.g. opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the condition and should not be used. Phenoxymethylpenicillin is not recommended for chronic, severe or deep seated infections as therapeutic concentrations may not be achieved in the relevant tissues. Oral administration should not be relied upon to achieve therapeutic levels in some patients with severe illness or with nausea, vomiting, gastric dilation, cardio-spasm or intestinal hypermotility. Occasionally patients will not absorb therapeutic amounts of oral penicillin. Parenteral administration of suitable antibiotics is recommended in these patients.

In a streptococcal infection, therapy should continue for a minimum of ten days. Cultures should be taken following completion of treatment to determine whether Streptococci have been eradicated.

Use of an alternative or additional method of contraception is strongly recommended if an oestrogen-containing contraceptive is taken concurrently (see section 4.5).

4.5 Interaction with other medicines and other forms of interaction

Bacteriostatic agents may antagonise the effect of penicillin.

Probenecid reduces the tubular excretion of penicillin, thereby increasing concentrations in the blood stream of concomitantly administered penicillin.

Food has a variable effect, generally delaying absorption.

Antacids may reduce absorption of the medicine.

When used concurrently with an oestrogen-containing oral contraceptive, the effectiveness of the oral contraceptive may be decreased because of stimulation of oestrogen metabolism or reduction of enterohepatic circulation of oestrogens, resulting in menstrual irregularities, intermenstrual bleeding and unplanned pregnancies. Patients should be advised to use an alternative or additional method of contraception while taking this penicillin.

Penicillins reduce the excretion of methotrexate thereby increasing the risk of methotrexate toxicity.

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving penicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Penicillins may interfere with:

- Urinary glucose test
- Coomb's tests
- Tests for urinary or serum proteins
- Tests which use bacteria e.g. Guthrie test.

4.6 Fertility, pregnancy and lactation

Pregnancy

Limited or no data are available from the use of phenoxymethylpenicillin in pregnant women. As a precautionary measure, it is preferable to avoid the use of Phenoxymethylpenicillin-AFT during pregnancy, unless the benefits clearly outweigh any potential risk.

Breast-feeding

Trace quantities of penicillin can be detected in breast milk with the potential for hypersensitivity reactions (e.g. drug rashes) or gastrointestinal disorders (e.g. diarrhoea or candidosis) in the breast-fed infant. Consequently, breastfeeding might have to be discontinued.

4.7 Effects on ability to drive and use machines

During treatment with penicillin, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions) which may influence the ability to drive and use machines. Patients should be cautious when driving or operating machinery.

4.8 Undesirable effects

The most common reactions to oral penicillin are gastrointestinal effects and hypersensitivity reactions. Although hypersensitivity reactions have been reported much less frequently after oral than parenteral therapy, it should be remembered that all forms of hypersensitivity, including fatal

anaphylaxis have been observed with oral penicillin.

Blood and lymphatic disorders
There have been very rare reports of changes in blood counts, including, thrombocytopenia, neutropenia, leucopenia, eosinophilia and haemolytic anaemia. Coagulation disorders (including prolongation of bleeding time and defective platelet function) have also been reported.

Gastrointestinal disorders
Nausea, vomiting, abdominal pain, diarrhoea are common. Sore mouth and black hairy tongue (discolouration of tongue) have been reported occasionally.

Rare: Superficial discolouration of the teeth (especially with the suspension). Usually the discoloration can be removed by teeth brushing.

Hepatobiliary disorders
Hepatitis and cholestatic jaundice have been reported very rarely.

Immune disorders
Allergic reactions may commonly occur and typically manifest as skin reactions (See Skin and subcutaneous disorders). Severe allergic reactions causing angioedema, laryngeal oedema and anaphylaxis have been reported rarely. Serum sickness-like reactions characterized by fever, chills, arthralgia and oedema have also been reported.

Infections and infestations
Pseudomembranous colitis has occasionally been reported.

Nervous system disorders
Central nervous system toxicity including convulsions has been reported (especially with high doses or in severe renal impairment); paraesthesia may occur with prolonged use.

Neuropathy is an infrequent reaction and is usually associated with high doses of parenteral penicillin.

Renal and urinary disorders
Interstitial nephritis has occurred in very rare cases.

Nephropathy is an infrequent reaction and is usually associated with high doses of parenteral penicillin.

Skin and subcutaneous disorders
Urticarial, erythematous or mobilliform rash and pruritus occur most frequently, while exfoliative dermatitis occurs rarely. Cutaneous vasculitis has also been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows

continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Phenoxymethylpenicillin has low toxicity. However, if there is gross renal impairment, the medicine may accumulate in the blood, and the dose should be reduced accordingly. Large quantities of parenterally administered penicillin (greater than 20 million units per day) have been associated with CNS effects e.g. lethargy, confusion, epileptiform seizures.

Treatment
Management of overdose should include monitoring of electrolyte balance, cardiovascular status and renal function.

Penicillin may be removed by haemodialysis.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta-lactamase sensitive penicillins; ATC code: J01CE02.

Phenoxymethylpenicillin exerts a bactericidal action against penicillin sensitive micro-organisms during the stage of active multiplication. It is not active against the penicillinase producing bacteria, which includes many strains of staphylococci. Sensitive organisms include the following:

- Gram-positive cocci, e.g. Streptococci (groups A,C,G,H,L and M), and non-penicillinase producing *Staphylococcus pyogenes*.
- Gram-positive bacilli, e.g. Clostridium tetani, Cl. Perfrigens, Corynebacterium diphtheriae and Bacillus anthracis.
- Gram-negative bacteria, both *Neisseria meningitidis* and *N. gonorrhoeae* are sensitive to a degree but *Haemophilus influenzae* is moderately resistant and other aerobic Gram-negative bacilli are highly resistant.
- *Treponema pallidum* is sensitive, but treatment of syphilis with oral penicillins is not recommended.

Phenoxymethylpenicillin produces a bacterial effect on penicillin sensitive organisms during the stage of active multiplication through inhibition of biosynthesis of cell wall mucopeptides. The antibacterial spectrum of phenoxymethylpenicillin is similar to that of benzyl penicillin, however, it has the advantage of being acid stable and hence better absorbed from the gastrointestinal tract than benzyl

penicillin.

5.2 Pharmacokinetic properties

Usually, up to 60% of phenoxymethylpenicillin potassium is absorbed into the blood stream after oral administration. Absorption is usually rapid and may produce peak serum concentrations within 30 minutes and demonstrable levels are maintained for 4 hours.

Approximately 80% of phenoxymethylpenicillin is serum protein bound. Tissue levels are highest in the kidneys with lesser amounts in the liver, skin and intestines. Small amounts are found in other body tissues and the cerebrospinal fluid. About 56% of a 500 mg oral dose of the medicine is metabolised into inactive metabolite and about 23 to 36% is excreted unchanged in the urine. Bile excretion is dependent upon renal function, being low in normal renal function and high in renal impairment. The oral plasma half-life is about 30 minutes in healthy adults and about 1 to 3 hours in neonates. The half-life is greatly extended in patients with renal or hepatic impairment.

The medicine is excreted rapidly in individuals with normal kidney function but is considerably delayed in neonates, young infants and individuals with impaired kidney function.

Tissue levels are highest in the kidneys with lesser amounts in the liver, skin and intestines. Small amounts are found in all other body tissues and the cerebrospinal fluid.

It is resistant to inactivation by gastric acid. It may be given with meals; however, blood levels are slightly higher when given on an empty stomach. Average blood levels are two to five times higher than the levels following the same dose of oral penicillin G and show much less individual variation.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Orange colour
Orange flavour
Saccharin sodium
Sodium benzoate
Sucrose

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

Powder:
Phenoxymethylpenicillin-AFT 125 mg/5mL: 18 months
Phenoxymethylpenicillin-AFT 250 mg/5mL: 24 months

Reconstituted solution: not more than 10 days in a refrigerator (2–8 °C). Protect from light.

6.4 Special precautions for storage

Powder: Store below 25°C. Protect from light.

For storage conditions after reconstitution of the medicine, see section 6.3.

6.5 Nature and contents of container

HDPE bottle containing sufficient powder that when correctly prepared, the bottle will contain 100 mL of solution. Pack sizes of 1 bottle.

6.6 Special precautions for disposal and other handling

Solution Preparation
Add 63 mL purified water to Phenoxymethylpenicillin-AFT granules for oral solution 125 mg/5 mL.

Add 60 mL purified water to Phenoxymethylpenicillin-AFT granules for oral solution 250 mg/5 mL.

When correctly prepared, each bottle will contain 100 mL of clear orange solution with an orange odour and flavour.

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

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9. DATE OF FIRST APPROVAL

14 June 2001

10. DATE OF REVISION OF THE TEXT

03 June 2022

Summary table of changes:

Section changed	**Summary of new information**
4.3	Wording of contraindications updated.
4.4	Information added on massive dose effects, prolonged use, and use with oral anticoagulants.
4.5	Interactions added – methotrexate, oral anticoagulants, and potential interference with tests.
4.6	Wording of pregnancy and breast-feeding information updated.
4.7	Wording of information regarding ability to drive updated.
4.8	Cutaneous vasculitis added.
4.9	Treatment of overdose information updated.
8	Sponsor address updated.
All	Format update.
6.3	Shelf life correction as per TPDR