SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Magnapen® 250mg/250mg Powder for Solution for Injection or Infusion
or
Co-fluampicil 250mg/250mg Powder for Solution for Injection or Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Co-fluampilcil 500mg Vials contain 250mg ampicillin as ampicillin sodium with 250mg flucloxacillin as flucloxacillin sodium (co-fluampicil 250/250).

3 PHARMACEUTICAL FORM

Powder for Solution for Injection or Infusion (injection)

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Co-fluampicil is indicated for the treatment of severe infections where the causative organism is unknown, and for mixed infections involving β-lactamase-producing staphylococci. Typical indications include:

In general practice. Chest infections, ENT infections, skin and soft tissue infections, and infections in patients whose underlying pathology places them at special risk.

In hospital (prior to laboratory results being available): severe respiratory tract infections, post-operative chest and wound infections, septic abortion, puerperal fever; septicaemia, prophylaxis in major surgery, infections in patients receiving immuno-suppressive therapy.

The spectrum of activity of co-fluampicil also makes it suitable for the treatment of many mixed infections, particularly those where β -lactamase-producing staphylococci are suspected or confirmed.

Parenteral usage is indicated where oral dosage is inappropriate.

4.2 Posology and method of administration

Usual adult dosage (including elderly patients and children over ten years):

Intramuscular/Intravenous: 500mg four times a day.

Usual children's dosage:

Intramuscular/intravenous: Under 2 years: quarter adult dose, four times a day.
2-10 years: half adult dose, four times a day.

The above dosages for adults and children may be doubled where necessary.
Therapy may be continued for as long as it is indicated by the nature of infection.

Administration:

Intramuscular: Add 1.5m1 Water for Injections BP to vial contents.
Intravenous: Dissolve 500mg in l0ml Water for Injections BP.
Administer by slow intravenous injection.
Co-fluampicil Injection may be added to infusion fluids or injected, suitably diluted into the drip tube over a period of 3 - 4 minutes.

4.3 Contraindications

Co-fluampicil contains ainpicillin and flucloxacillin which are penicillins, and should not be given to patients with a history of hypersensitivity to β-lactam antibiotics (e.g. penicillins, cephalosporins).

Co-fluampicil is contraindicated in patients with a history of flucloxacillin-associated
jaundice/hepatic dysfunction.

Ocular administration.

4.4 Special warnings and precautions for use

Before initiating therapy with co-fluampicil careful enquiries should be made concerning previous hypersensitivity reactions to -lactam antibiotics.

Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving -lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral therapy. These reactions are more likely to occur in individuals with hypersensitivity to -lactam antibiotics.

Co-fluampicil contains ampicillin and should be avoided if infectious mononucleosis and/or acute or chronic leukaemia of lymphoid origin are suspected. The occurrence of a skin rash has been associated with these conditions following the administration of ampicillin.

In case of severe and persistent diarrhoea, the possibility of pseudomembranous colitis should be considered; flucloxacillin therapy should be discontinued.

Care is required when treating some patients with spirochaete infections such as syphilis or leptospirosis because the Jarisch-Herxheimer reaction may occur shortly after treatment with a penicillin is started.

Co-fluampicil should be used with caution in patients with evidence of hepatic dysfunction (see Section 4.8).

Caution is advised when flucloxacillin is administered concomitantly with paracetamol due to the increased risk of high anion gap metabolic acidosis (HAGMA). Patients at high risk for HAGMA are in particular those with severe renal impairment, sepsis or malnutrition especially if the maximum daily doses of paracetamol are used.

After co-administration of flucloxacillin and paracetamol, a close monitoring is recommended in order to detect the appearance of acid–base disorders, namely HAGMA, including the search of urinary 5- oxoproline.

If flucloxacillin is continued after cessation of paracetamol, it is advisable to ensure that there are no signals of HAGMA, as there is a possibility of flucloxacillin maintaining the clinical picture of HAGMA (see section 4.5)

Special caution is essential in the newborn because of the risk of hyperbilirubinemia. Studies have shown that, at high dose following parenteral administration, flucloxacillin can displace bilirubin from plasma protein binding sites, and may therefore predispose to kernicterus in a jaundiced baby. In addition, special caution is essential in the newborn

because of the potential for high serum levels of flucloxacillin due to a reduced rate of renal excretion.

Care is necessary if very high doses of flucloxacillin are given, especially if renal function is poor, because of the risk of nephrotoxicity and/or neurotoxicity. The intrathecal route should be avoided. Care is also necessary if large doses of sodium (salts) are given to patients with impaired renal function or heart failure. Flucloxacillin should be used with caution in patients with evidence of hepatic dysfunction (see section 4.8). Renal, hepatic and haematological status should be monitored during prolonged and high-dose therapy (e.g. osteomyelitis, endocarditis). Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Sodium content: Co-fluampicil 500mg vials contains 29.9mg (1.3 mmol) sodium per vial. This should be included in the daily allowance of patients on sodium restricted diets.

4.5 Interaction with other medicinal products and other forms of interaction

Other antibacterials: There may be antagonism between penicillins, including ampicillin and bacteriostatic agents such as chloramphenicol, erythromycins or tetracyclines. This may reduce the effectiveness of penicillins particularly in the treatment of infections such as pneumococcal meningitis and scarlet fever.

Cytotoxics: Penicillins reduce the excretion of methotrexate (increased risk of toxicity).

In common with other oral broad-spectrum antibiotics, co-fluampicil may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

Probenecid decreases the renal tubular secretion of co-fluampicil. Concurrent use with co-fluampicil may result in increased and prolonged blood levels of both ampicillin and flucloxacillin.

Concurrent administration of allopurinol during treatment with ampicillin can increase the likelihood of allergic skin reactions.

Caution should be taken when flucloxacillin is used concomitantly with paracetamol as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risk factors. (see section 4.4.)

Interference with diagnostic tests: Penicillins may produce false-positive results with the direct antiglobulin (Coombs') test, falsely high urinary glucose results with the copper sulphate test and falsely high urinary protein results, but glucose enzymatic tests (e.g. Clinistix) and bromophenol blue tests (e.g. Multistix or Albustix) are not affected

4.6 Fertility, pregnancy and lactation

Pregnancy: Animal studies with co-fluampicil have shown no teratogenic effects. The product has been in clinical use since 1971 and the limited number of reported cases of use in human pregnancy have shown no evidence of untoward effects. The decision to administer any drug during pregnancy should be taken with the utmost care. Therefore co-fluampicil should only be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Lactation: Trace quantities of ampicillin and flucloxacillin can be detected in breast milk. The possibility of hypersensitivity reactions must be considered in breast-fed infants. Therefore co-fluampicil should only be administered to a breast-feeding mother when the potential benefit outweigh the potential risks associated with treatment.

4.7 Effects on ability to drive and use machines

Adverse effects on the ability to drive or operate machinery have not been observed.

4.8 Undesirable effects

Blood and lymphatic system disorders:
As with other b-lactam antibiotics haematological effects including reversible leucopenia, reversible thrombocytopenia and haemolytic anaemia have been reported rarely.

Immune System Disorders:
Anaphylaxis (see Item 4.4-warnings) has been reported rarely.
If any hypersensitivity reaction occurs, the treatment should be discontinued. Late sensitivity reactions may include serum sickness-like reactions (featuring symptoms such as arthralgia, rash, urticaria, fever, angioedema, lymphadenopathy), haemolytic anaemia and acute interstitial nephritis.

Metabolism and nutrition disorders:
Electrolyte disturbances, such as hypokalaemia, due to administration of large amounts of sodium

Post marketing experience: very rare cases of high anion gap metabolic acidosis, when flucloxacillin is used concomitantly with paracetamol, generaly in the presence of risk factors (see section 4.4.)

Psychiatric disorders:
There is a potential for hallucinations to occur rarely with flucloxacillin.

Nervous System Disorders
Convulsions may be associated with IV administration of high doses to patients with underlying renal failure.
Coma may develop with high doses of Flucloxacillin.

Respiratory, thoracic and mediastinal disorders:
Bronchospasm may occur as a result of penicillin allergy.
There is a potential for acute, severe dyspnoea to occur with flucloxacillin.

Gastrointestinal disorders:
Minor gastrointestinal disturbances, including occasionally nausea, vomiting and diarrhoea may occur during treatment. Pseudomembranous colitis has been reported rarely.

Hepatobiliary disorders:
Hepatitis and cholestatic jaundice have been reported rarely. These may be delayed for up to two months after withdrawal of treatment. In some cases the course of these conditions has been protracted and lasted for several months. Very rarely deaths have been reported from hepatic effects but are mostly limited to patients with serious underlying disease.

As with most other antibiotics, a moderate transient increase in transaminases has been reported.

Skin and subcutaneous tissue disorders:
Skin rash, puritis and urticaria have been reported. The incidence of rash is higher in patients suffering from infectious mononucleosis and acute or chronic leukaemia of lymphoid origin. Purpura, fever, eosinophilia and sometimes angioneurotic oedema have also been reported. Rarely, skin reactions such as erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. Reactions such as fever, arthralgia, and myalgia can develop more than 48 hours after the start of the treatment.

Erythema nodosum may occur rarely with flucloxacillin.
Potential for pemphigoid reactions to occur rarely with flucloxacillin.
There is potential for non-thrombocytopenic purpura to occur rarely with flucloxacillin.
Vasculitis may occur rarely with flucloxacillin.

Renal and urinary disorders
Interstitial nephritis may occur but it is reversible when treatment is

discontinued.

Congenital, familial and genetic disorders:
Potential for acute attacks of porphyria to occur with flucloxacillin.

General disorders and administration site conditions:
Some patients with spirochaete infections such as syphilis or leptospirosis may experience a Jarisch-Herxheimer reaction shortly after treatment with a penicillin is started. Symptoms include fever, chills, headache and reaction at the site of lesions. The reaction can be dangerous in cardiovascular syphilis or where there is a serious risk of increased local damage such as with optic atrophy

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 Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

4.9 Overdose

Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically.

Co-fluampicil contains flucloxacillin. Haemodialysis does not lower the serum levels of flucloxacillin.

Co-fluampicil contains ampicillin, which may be removed from the circulation by haemodialysis

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Co-fluampicil is indicated for the treatment of severe infections where the causative organism is unknown, and for mixed infections involving β-lactamase-producing staphylococci.

5.2 Pharmacokinetic properties

Co-fluampicil is excreted via the kidneys with a plasma half life of approximately one hour.

5.3 Preclinical safety data

Not relevant

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

Co-fluampicil should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates) or with intravenous lipid emulsions.

If co-fluampicil is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because of loss of activity of the aminoglycoside can occur under these conditions.

The following drugs are incompatible with Magnapen® 250mg/250mg Powder for Solution for Injection or Infusion or Co-fluampicil 250mg/250mg Powder for Solution for Injection or Infusion:

Amikacin sulphate

Amiodarone

Amphotericin B cholesteryl sulphate complex

Atropine Sulphate

Buprenorphine

Calcium gluconate

Chlorpromazine hydrochloride

Ciprofloxacin

Clarithromycin

Diazepam

Dobutamine Hydrochloride
Dopamine hydrochloride
Erythromycin lactobionate
Gentamicin sulphate
Heparin sodium
Hydralazine hydrochloride
Hydrocortisone sodium succinate
Kanamycin sulphate
Lincomycin hydrochloride
Morphine Sulphate
Metoclopramide hydrochloride
Netilmicin Sulphate
Ofloxacin
Papaveretum
Pethidine Hydrochloride
Polymyxin B sulphate
Prochlorperazine edisylate
Prochlorperazine mesylate
Promethazine Hydrochloride
Sodium bicarbonate
Tobramycin
Verapamil Hydrochloride

6.3 Shelf life

Three years.
See also Section 6.6.

6.4 Special precautions for storage

Co-fluampicil Vials for Injection should be stored in a dry place at, or below 25ºC.

6.5 Nature and contents of container

5 or 10 ml glass vials fitted with butyl rubber disc and an aluminium seal. Boxes of 10 vials with instructions for use.

6.6 Special precautions for disposal

Co-fluampicil solutions for injection should be used immediately. Co-fluampicil may be added to most intravenous fluids (e.g. Water for Injections, sodium chloride 0.9%, glucose 5%, sodium chloride 0.18% with glucose 4%). In intravenous solutions containing glucose or other carbohydrates, co-fluampicil should be infused within two hours of preparation. Intravenous solutions of co-fluampicil in Water for Injections or sodium chloride 0.9% should be infused within 24 hours of preparation. Full particulars are given in the package enclosure leaflet. Preparation of co-fluampicil infusion solutions must be carried out under appropriate aseptic conditions if these extended storage periods are required.

7 MARKETING AUTHORISATION HOLDER

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