IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA1077/033/008
Case No: 2073852

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

GlaxoSmithKline (Ireland) Limited

Stonemasons Way, **Rathfarnham**, **Dublin 16**, **Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Amoxil Forte Syrup 250 mg/5ml

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **24/11/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Amoxil Forte Syrup 250 mg/5ml.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 250 mg amoxicillin (as trihydrate).

Excipients: also contains sorbitol (E420), sulphur dioxide (E220) and ethanol.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral suspension.
An off-white free flowing powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of infections due to organisms sensitive to amoxicillin.
`Amoxil`is a broad spectrum antibiotic, indicated for the treatment of commonly occurring bacterial infections such as:

Upper respiratory tract infections
Otitis media
Acute and chronic bronchitis
Lobar and bronchopneumonia
Cystitis, urethritis, pylelonephritis
Bacteriuria in pregnancy
Gynaecological infections including puerperal sepsis and septic abortion
Acute uncomplicated Gonorrhoea
Peritonitis
Intra-abdominal sepsis
Septicaemia
Bacterial endocarditis
Typhoid and paratyphoid fever
Skin and soft tissue infections
Dental abscess (as adjunct to surgical management)

In children with urinary tract infection, the need for investigation should be considered.

Parenteral therapy is indicated if the oral route is considered impracticable or unsuitable and particularly for the urgent treatment of severe episodes of the above conditions.

Prophylaxis of endocarditis
`Amoxil` may be used for the prevention of bacteraemia, associated with the procedures such as dental extraction, in patients at risk of developing bacterial endocarditis.

4.2 Posology and method of administration

Route of administration: oral
The absorption of 'Amoxil' is virtually unimpaired by the presence of food.

Standard adult dosage:
The usual daily dosage is 750mg in divided doses (i.e. 250mg three times daily by the oral route).
In cases of severe infection the dosage may be doubled, or `Amoxil` given by injection.

High dosage therapy: (maximum recommended oral dosage 6g daily in divided doses): A dosage of 3g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Short course therapy: *Simple acute urinary tract infection*: two 3g doses with 10-12 hours between the doses.
Gonorrhoea: 3g as a single dose.
Dental Abscess**:** two 3g doses with 8 hours between the doses.

Children up to ten years of age:
The usual total daily dosage is 375mg in divided doses (i.e. 125mg three times daily by the oral route).
Dosage may be increased in cases of severe infection.
In severe or recurrent acute otitis media, especially where compliance may be a problem, 750mg twice a day for two days may be used as an alternative course of treatment in children aged three to ten years

Prophylaxis of endocarditis:
For dental procedures where an oral dose is appropriate.
Adults: - 3g `Amoxil` orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.

Children: Aged 5-10: half the adult dose (i.e. 1.5g given as a single 60ml dose of 'Amoxil' syrup (125mg/5ml).
Under 5: quarter the adult dose.

Renal impairment: In renal impairment the excretion of the antibiotic will be delayed and depending on the degree of impairment, it may be necessary to reduce the total daily dosage.

Glomerular filtration rate	
Adults	**Oral treatment**
> 30 ml/min	No adjustment necessary
10-30 ml/min	Amox. Max 500 mg b.d.
< 10 ml/min	Amox. Max 500 mg/day
Children under 40kg	**Oral treatment**
> 30ml/min	No adjustment necessary
10-30 ml/min	15 mg/kg given b.i.d. (maximum 500mg/twice daily)
< 10ml/min	15 mg/kg given as a single day dose (maximum 500mg)

Amoxicillin Paediatric Suspension is recommended for children under 6 months of age.

Amoxicillin may be removed from the circulation by haemodialysis.

4.3 Contraindications

Use in patients with a history of hypersensitivity to beta-lactam antibiotics including penicillins or cephalosporins.

4.4 Special warnings and precautions for use

Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.

Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving beta-lactam antibiotics. If an allergic reaction occurs, amoxicillin should be discontinued and appropriate alternative therapy instituted.

Amoxicillin should be avoided if infections mononucleosis (glandular fever) is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Prolonged use of an anti-infective may occasionally result in overgrowth of non-susceptible organisms.

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

Dosage should be adjusted in patients with renal impairment (see Section 4.2).

In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crytalluria.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid decreases the renal tubular excretion of amoxicillin. Concurrent use with amoxicillin may result in increased and prolonged blood levels of amoxicillin.

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

In common with other antibiotics, amoxicillin may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

In the literature there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin.

4.6 Pregnancy and lactation

Use in pregnancy:
Animal studies with `Amoxil` have shown no teratogenic effects. The product has been in extensive clinical use since1972 and its suitability in human pregnancy has been well documented in clinical studies. Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Use in lactation:
Amoxicillin may be administered during the period of lactation. With the exception of the risk of sensitisation associated with the excretion of trace quantities of amoxicillin in breast milk, there are no know detrimental effects for the infant.

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

The following convention has been utilised for the classification of undesirable effects: Very common (more than 1/10), common (more than 1/100, less than 1/10), uncommon (more than 1/1000, less than 1/100), rare (more than 1/10,000, less than 1/1000), very rare (less than 1/10,000).
The majority of the side-effects listed below are not unique to amoxicillin and may occur when using other penicillins. Unless otherwise stated, the frequency of adverse events (AEs) has been derived from more than 30 years of post-marketing reports.

Blood and lymphatic system disorders	
Very rare:	Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.
	Prolongation of bleeding time and prothrombin time.
Immune system disorders	
Very rare:	As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis *(see Warnings and Precautions)*, serum sickness and hypersensitivity vasculitis.
If a hypersensitivity reaction is reported, the treatment must be discontinued. (*See also Skin and subcutaneous tissue disorders*).	
Nervous system disorders	
Very rare:	Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.
Infections and Infestations	
Very rare:	Mucocutaneous candidiasis
Gastrointestinal disorders	
#Common:	Diarrhoea and nausea.
#Uncommon:	Vomiting.
Very rare:	Antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis). Black hairy tongue
	Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing ***(for suspension and chewable tablet formulations only)***
Hepato-biliary disorders	
Very rare:	Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT.
The significance of a rise in AST and/or ALT is unclear.	
Skin and subcutaneous tissue disorders	
#Common:	Skin rash.
#Uncommon:	Urticaria and pruritus.
Very rare:	Skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP).
	(*See also Immune system disorders*).
Renal and Urinary tract disorders	
Very rare:	Interstitial nephritis, crystalluria (*see Overdosage*)

#The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

4.9 Overdose

Gross overdosage will produce very high urinary concentrations, more so after parenteral administration. Symptoms of water/electrolyte imbalance should be treated symptomatically. Problems are unlikely to occur if adequate fluid intake and urinary output are maintained; however, amoxicillin crystalluria in some cases leading to renal failure, has been observed *(see Section 4.4, Special Warnings and Special Precautions for Use)*. More specific measures may be necessary in patients with impaired renal function: the antibiotic is removed by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

`Amoxil` is a broad-spectrum antibiotic which possesses the safety profile of the penicillins and is rapidly bactericidal against a wide range of Gram-negative and Gram-positive organisms.

5.2 Pharmacokinetic properties

`Amoxil` is well absorbed by the oral and parenteral routes, peak blood levels are achieved one to two hours after administration. Oral administration produces high serum levels independent of the time at which the food is taken. `Amoxil` gives good penetration into the bronchial secretions and the high urinary concentrations of unchanged antibiotic. The average serum half life is 60 minutes. Elimination is mainly via the urine.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E420)
Disodium edetate
Sodium benzoate (E211)
Sodium saccharin
Anhydrous silicon dioxide
Colloidal anhydrous silica
Xanthan gum (E415)
Peach, strawberry and lemon dry flavours
(containing sulphur dioxide (E220) and ethanol).

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Unopened: 5 years.
Reconstituted: 14 days.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the container tightly closed.

6.5 Nature and contents of container

Clear glass bottles (Ph.Eur. Type III) (150 ml volume) with either a metal cap with flowed-in sealing compound, a polypropylene wadless cap or a ROPP, internally lacquered closure containing a flowed-in PVC liner.
Contains 100 ml.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

At time of dispensing, the dry powder should be reconstituted to form a white to off white oral suspension, as detailed below:

Volume of water to be added to reconstitute	Nominal bottle size	Final volume of reconstituted oral suspension.
85 ml	150 ml	100 ml

When necessary dilute to half-strength using water.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
Stonemasons Way
Rathfarnham
Dublin 16

8 MARKETING AUTHORISATION NUMBER

PA 1077/33/8

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1977

Date of last renewal: 01 April 2007

10 DATE OF REVISION OF THE TEXT

November 2009