IRISH MEDICINES BOARD ACT 1995, as amended

Medicinal Products (Control of Placing on the Market) Regulations, 2007, as amended

PA0172/004/007
Case No: 2086521

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

Pfizer Consumer Healthcare Ltd

Ramsgate Road, **Sandwich**, **Kent**, **CT13 9NJ**, **United Kingdom**

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

Aniall 500/50 mg Tablets

the particulars of which are set out in 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 **28/07/2010** until **06/09/2012**.

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

Aniall 500 / 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Tablet contains:

Aspirin (Acetylsalicylic acid)	500 mg
Caffeine	50 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet.

White, round, biconvex tablets, with diametrically opposite notches, engraved on both sides with “AMX”.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of headaches, neuralgia, rheumatic pain, period pain, dental pain, and the symptoms of colds and flu.

4.2 Posology and method of administration

Oral.

Adults and children over 12 years:
1 tablet every three to four hours.
Do not exceed 8 tablets in 24 hours.

Elderly:
Non-steroidal anti-inflammatory drugs should be used with particular caution in elderly patients who are prone to adverse events. The lowest dose compatible with adequate safe clinical control should be employed. See also Section 4.4.

4.3 Contraindications

- Use in patients hypersensitive (e.g. bronchospasm, rhinitis, urticaria) to the active ingredients or any of the other constituents.
- Use in the presence of active peptic ulceration and those with a history of peptic ulceration.
- Use in patients with haemophilia.
- Use in children under 12 and when breastfeeding.

4.4 Special warnings and precautions for use

- Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration. Patients treated with NSAIDs longterm should undergo regular medical supervision to monitor for adverse events.
- Elderly patients are particularly susceptible to the adverse effects of NSAIDs.
- Patients with a history of, or existent, peptic ulceration or inflammatory bowel disease, coagulation disorders, or asthma should consult a doctor before using this product.
- Aspirin may induce asthmatic attacks in hypersensitive patients.
- There is a possible association between Aspirin and Reye's syndrome when given to children. Reye's syndrome is a very rare disease, which affects the brain and liver and can be fatal. For this reason, Aspirin should not be given to children and adolescents aged under 16 years unless specifically indicated.
- Caution should be exercised in patients with allergic disease or dehydration.
- In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function.
- If symptoms persist for more that 3 days, or symptoms unrelated to the original condition are experienced the patient should contact their doctor.
- If the patient is taking any other medications or are under the care of a doctor he/she should consult the doctor before using.

4.5 Interaction with other medicinal products and other forms of interaction

It is considered unsafe to take NSAID's in combination with warfarin or heparin unless under direct medical supervision.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Care should be taken in patients treated with any of the following drugs as interactions have been reported.

Anti-hypertensives:	reduced anti-hypertensive effect.
Diuretics:	reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.
Cardiac glycosides:	NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.
Methotrexate:	decreased elimination of methotrexate.
Cyclosporin:	increased risk of nephrotoxicity with NSAIDs
Other NSAID's	avoid concomitant use of two or more NSAIDs
Corticosteroids:	increased risk of gastrointestinal bleeding
Aminoglycosides:	reduction in renal function in susceptible individuals decreased elimination of aminoglycoside and increased plasma concentrations.
Probenecid:	reduction in metabolism and elimination of NSAID and metabolites.

Oral hypoglycaemic agents:	inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.
Phenytoin:	The effect of phenytoin may be enhanced by aspirin. However, no special precautions are needed.
Valproate:	The effect of valproate may be enhanced by aspirin.

4.6 Pregnancy and lactation

There is clinical and epidemiological evidence of safety of aspirin in pregnancy, but it may prolong labour and contribute to maternal and neonatal bleeding. This product should only be taken during pregnancy on the advice of a doctor and should not be used in the third trimester of pregnancy.

Aspirin appears in breast milk and regular high doses may affect neonatal clotting. Taking aspirin is not recommended while breast feeding due to possible risk of Reye's Syndrome as well as neonatal bleeding due to hypoprothrombinaemia.

Caffeine appears in breast milk. Irritability and poor sleeping pattern in the infant have been reported.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Undesirable effects are mild and infrequent, but the following have been reported:

Gastrointestinal: Gastro-intestinal irritation with slight asymptomatic blood loss. Gastrointestinal disorders have been reported for aspirin-containing products e.g. nausea, diarrhoea, vomiting and gastro-intestinal bleeding which may lead to anaemia in some cases. Gastrointestinal ulceration leading to haemorrhage and perforation may occur.
Blood: Increased bleeding time.
Hypersensitivity Reactions: Aspirin may precipitate bronchospasm and induce asthma attacks or other hypersensitivity reactions in susceptible individuals.

Other: Aspirin may precipitate gout in susceptible individuals. There is a possible risk of Reye's Syndrome in children under 12 years.

High doses of caffeine can cause tremor and palpitations.

4.9 Overdose

Severe intoxication from heavy overdose is shown by hyperventilation, fever, restlessness, ketosis, respiratory alkalosis, metabolic acidosis and convulsions.

A worthwhile recovery of salicylate can be achieved up to 24 hours after ingestion. Treatment must be in hospital where plasma salicylate pH and electrolytes can be measured. Fluid losses are replaced and forced alkaline diuresis is considered when the plasma salicylate concentration is greater than 500mg / litre in adults or 300mg/litre (2.2mmol/litre) in children.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Aspirin is a non-steroidal anti-inflammatory agent. It has analgesic antipyretic and anti-inflammatory properties.

Caffeine increases the pain relieving effect of the product.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release aspirin dosing (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

5.2 Pharmacokinetic properties

ASPIRIN

Absorption and fate

Absorption is generally rapid and complete following oral administration. It is largely hydrolysed in the gastrointestinal tract., liver and blood to salicylate which is further metabolised primarily in the liver.

CAFFEINE

Absorption and Fate

Caffeine is completely and rapidly absorbed after oral administration with peak concentrations occurring between 5 and 90 minutes after dose in fasted subjects. There is no evidence of presystemic metabolism. Elimination is almost entirely by hepatic metabolism in adults.

In adults, marked individual variability in the rate of elimination occurs. The mean plasma elimination half-life is 4.9 hours with a range of 1.9 – 12.2 hours. Caffeine distributes into all body fluids. The mean plasma protein binding of caffeine is 35%.

Caffeine is metabolised almost completely via oxidation, demethylation and acetylation and is excreted in the urine. The major metabolites are 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine). Minor metabolites include 1-methyluric acid and 5-acetylamino-6 formylamino-3-methyluracil (AMFU).

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch
Microcrystalline Cellulose

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

2 Years

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package to protect from moisture.

6.5 Nature and contents of container

Cartons containing blister strips of 12 and 16 tablets. The blister is composed of:

- Blister: White opaque uPVC, with PVdC coating, heat-sealed to the foil.
- Foil: Glassine / Aluminium foil / Heatseal lacquer.

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

No special requirements

7 MARKETING AUTHORISATION HOLDER

Pfizer Consumer Healthcare Ltd
Ramsgate Road
Sandwich
Kent
CT13 9NJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 172/4/7

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 7th September 2007

10 DATE OF REVISION OF THE TEXT

July 2010