IRISH MEDICINES BOARD ACTS 1995 AND 2006

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

(S.I. No.540 of 2007)

PA0678/104/001
Case No: 2054166

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

GlaxoSmithKline Consumer Healthcare (Ireland) Limited

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

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

Beechams Max strength Cold and Flu 1000 mg Powder for oral solution.

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 **11/09/2008** until **01/06/2011**.

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

Beechams Max strength Cold and Flu 1000mg Powder for oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 1000mg of Paracetamol.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for Oral Solution
Pale yellow soluble powder with an odour and taste of lemon.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Short term symptomatic relief of influenza, feverishness, chills and colds including headache, sore throat pain, sinusitis, aches and pains.

4.2 Posology and method of administration

For oral administration, dissolved in hot water, as a hot lemon drink.

Adults (including the elderly) and children aged 12 years and over:
One sachet, dissolved in a cup or mug of hot water, to be taken every four to six hours as necessary up to a maximum of four sachets in any 24 hours.

Do not exceed the stated dose.

The product should not be used continuously for more than seven days without seeking medical advice.

Children under 12 years of age.
Not to be given to children under 12 years of age, except on medical advice.

4.3 Contraindications

Known hypersensitivity to paracetamol or any of the excipients.
Use in children under 12 years of age.

4.4 Special warnings and precautions for use

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Concomitant use of other ‘flu or cold medicines, or other paracetamol-containing medicines should be avoided.
If symptoms persist consult your doctor. Prolonged use except under medical supervision may be harmful.

Do not exceed the stated dose.

This product should only be used when clearly necessary.

Keep out of reach of children.

Pack Label Warnings:
Immediate medical advice should be sought in the event of an overdose, even if you feel well.
Do not take with other 'flu' or cold products.
Do not take with any other paracetamol-containing products.

Patient Information Leaflet Warnings:
Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

4.5 Interaction with other medicinal products and other forms of interaction

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding. Occasional doses have no significant effect.

4.6 Pregnancy and lactation

Pregnancy

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

Lactation

Paracetamol is excreted in breast milk but not in a clinically significant amount.

4.7 Effects on ability to drive and use machines

Normal use of the product is not known to have any affects on ability to drive or use machines.

The drug substance is not known to cause sedation.

4.8 Undesirable effects

Adverse effects of paracetamol are rare.

Skin rashes and other allergies can occasionally occur.

There have been rare reports of blood dyscrasias including thrombocytopenia and agranulocytosis but these were not necessarily causally related to paracetamol.

The frequency of adverse events associated with paracetamol is tabulated below.

Frequency table:

Frequency	**System**	**Symptoms**
Common (>1/100 - < 1/10)		
Uncommon (>1/1,000 - < 1/100)		
Rare (>1/10,000 - < 1/1,000)	Cardiovascular disorders	Oedema.
	Disorders of the eye	Abnormal vision.
	Disorders of the immune system	Allergies (excluding angioedema).
	Gastrointestinal disorders	Haemorrhage NOS, abdominal pain NOS, diarrhoea NOS, nausea, vomiting.
	General disorders	Dizziness (excluding vertigo), malaise, pyrexia, sedation, drug interaction NOS.
	Haemopoietic	Platelet disorders, stem cell disorders.
	Hepato-biliary disorders	Hepatic function abnormal, hepatic failure, hepatic necrosis, jaundice.
	Injury and poisoning	Overdose and poisoning
	Neurological disorders	Tremor NOS, headache NOS.
	Psychiatric disorders	Depression NOS, confusion, hallucinations.
	Dermatological	Pruritus, rash, sweating, purpura, angioedema, urticaria
Very Rare (< 100,000)		

4.9 Overdose

Acute systemic toxicity
Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrythmias and pancreatitis have been reported.
Liver damage is possible in adults who have taken 10 g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue.

Immediate treatment is essential in the management of paracetamol overdose.

Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention and any patient who has ingested around 7.5 g or more of paracetamol in the preceding 4 hours should undergo gastric lavage. Gastric lavage or the administration of activated charcoal may be beneficial when performed within one hour of the overdose but can be considered for up to four hours after the overdose.

Antidotes such as intravenous N-acetylcysteine (NAC) or oral methionine protect the liver if administered within 12 hours of overdose. NAC is effective up to and possibly beyond 24 hours. General supportive measures must be available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics.
ATC Code: N02B E01.

Paracetamol is an analgesic, antipyretic drug substance.

The antipyretic activity of paracetamol is thought to be mediated by its ability to selectively inhibit prostaglandin synthesis in the central nervous system.

The precise mechanism for the analgesic properties of paracetamol remains to be established. Data suggest that central prostaglandin synthetase inhibition is likely to be of primary importance. Paracetamol is a weak inhibitor of COX-1 and COX-2 leading to the suggestion that there may be another form of COX, which is more sensitive to inhibition by paracetamol.

Paracetamol does not appear to inhibit the peripheral generation of prostaglandins, e.g., it does not alter the gastric mucosal generation of prostaglandins and serious gastro-intestinal adverse events associated with paracetamol are rare. Paracetamol is, therefore, particularly suitable for patients with a history of disease or on concomitant medication where peripheral prostaglandin inhibition would be undesirable, e.g., with gastro-intestinal bleeding, cardiovascular disease or in the elderly.

5.2 Pharmacokinetic properties

Absorption and Distribution
Oral paracetamol is readily absorbed from the upper small intestine to give peak plasma concentrations of 15-20 mcg/ml in 30 to 120 minutes after oral administration of a 1000 mg dose in adults. The speed of gastric emptying modifies the rate of absorption. Plasma protein binding is minimal and there is distribution to all tissues.

Metabolism and Excretion
There is limited first-pass metabolism of paracetamol after oral administration and about 80% of a 1000 mg dose is bioavailable. Paracetamol is metabolised primarily in the liver.

After a 1000 mg oral dose in adults, 50-60% is recovered in the urine as the glucuronide conjugate, 25-35% as the sulphate conjugate, up to 5% as unchanged paracetamol and 2-5% as the cysteine or mercapturate metabolites. The latter are formed from the combination of glutathione with the oxidation metabolite of paracetamol, N-acetyl-p-benzoquinoneimine (NAPQI). Excretion via the urine is rapid and the plasma half-life after oral administration is 1-4 hours.

5.3 Preclinical safety data

The toxicity of paracetamol is well documented.

Effects of chronic toxicity in rats and mice include gastrointestinal lesions, blood count changes, degeneration and necrotic changes in testicular and lymphoid tissue in addition to hepatic and renal necrosis.

Long-term studies in rats and mice give no conclusive evidence of carcinogenic effects. There is no evidence of embryo- or foeto-toxicity from paracetamol in animal studies.

Paracetamol hepatotoxicity is directly dependent on the plasma concentration in relation to time. In man, plasma concentrations above 1.2 mmol/l at 4 hours, 0.6 mmol/l at 8 hours, and 0.3 mmol/l at 12 hours are criteria for immediate antidose treatment to prevent irreversible damage.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

List of excipients
Sucrose
Citric Acid, Anhydrous
Sodium Citrate
Maize Starch (dried)
Lemon Flavour
Sodium Cyclamate
Saccharain Sodium
Ascorbic Acid
Colour – Curcumin (E100)
Silica, Colloidal Anhydrous

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Three years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

The product is packed in laminate sachets and each pack contains 5 sachets.

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

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
Stonemasons Way
Rathfarnham
Dublin 16
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 678/104/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 02 June 2006

10 DATE OF REVISION OF THE TEXT