

**PARACETAMOL 500MG SOLUBLE TABLETS**  
**PL 00071/0447**

**UKPAR**

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**PARACETAMOL 500MG SOLUBLE TABLETS**  
**PL 00071/0447**

**LAY SUMMARY**

The Medicines Healthcare products Regulatory Agency (MHRA) granted SmithKline Beecham (SWG) Limited a Marketing Authorisation for the medicinal product Paracetamol 500mg Soluble Tablets (PL 00071/0447) on 3<sup>rd</sup> March 2008. This general sales list (GSL) medicine is available to the general public without prescription.

Paracetamol 500mg Soluble Tablets contains the active ingredient paracetamol. It is a centrally acting analgesic (a pain killer that acts on pain centres in the brain), which is used to relieve mild to moderate pain as well as to reduce increased body temperature (anti-pyretic).

Paracetamol 500mg Soluble Tablets is indicated for headache, migraine, backache, rheumatic and muscle pain, neuralgia, toothache and period pain. They also relieve discomfort from colds, influenza, sore throats and help reduce temperature.

This application is identical to a previously granted application for Panadol Soluble Tablets (PL 00071/0072R, granted to the same Marketing Authorisation Holder on 12<sup>th</sup> January 1982) and, as such, these products can be used interchangeably.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Paracetamol 500mg Soluble Tablets outweigh the risks; hence a Marketing Authorisation has been granted.

**PARACETAMOL 500MG SOLUBLE TABLETS**  
**PL 00071/0447**

**SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

The MHRA granted a marketing authorisation for the medicinal product Paracetamol 500mg Soluble Tablets (PL 00071/0447) to SmithKline Beecham (SWG) Limited on 3<sup>rd</sup> March 2008. The product is a general sale list medicine.

The application was submitted as a simple abridged application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Panadol Soluble Tablets granted to the same Marketing Authorisation Holder, PL 00071/0072R, approved on 12<sup>th</sup> January 1982.

No new data were submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) has been generated for it.

The product contains the active ingredient paracetamol which is a centrally acting analgesic used in the management (treatment and prevention) of mild pain within the body.

# **PHARMACEUTICAL ASSESSMENT**

**LICENCE NO:** PL 00071/0447

**PROPRIETARY NAME:** Paracetamol 500mg Soluble Tablets

**ACTIVE(S):** Paracetamol

**COMPANY NAME:** SmithKline Beecham (SWG) Limited

**E.C. ARTICLE:** Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC

**LEGAL STATUS:** GSL

## **1. INTRODUCTION**

This is a simple, informed consent application for Paracetamol 500mg Soluble Tablets submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is SmithKline Beecham (SWG) Limited, 980 Great West Road, Brentford, Middlesex, TW8 9GS, UK.

The application cross-refers to the applicant's own Marketing Authorisation for Panadol Soluble Tablets, approved on 12<sup>th</sup> January 1982. The current application is considered valid.

## **2. MARKETING AUTHORISATION APPLICATION FORM**

### **2.1 Name(s)**

The proposed name of the product is Paracetamol 500mg Soluble Tablets. The product has been named in line with current requirements.

### **2.2 Strength, pharmaceutical form, route of administration, container and pack sizes**

The product contains paracetamol, equivalent to 500mg. The product is stored in blisters composed of paper-Polyethylene-Foil-Polyethylene (PPFP) laminate strips and further packed into cardboard cartons containing 4, 6, 12, 18, 24 or 30 tablets. Not all pack sizes may be marketed. The proposed shelf-life (48 months) with no specific storage conditions this is consistent with the details registered for the cross-reference product.

### **2.3 Legal status**

On approval, the product will be available as a general sale list (GSL) medicine which will be available to the general public without a prescription.

### **2.4 Marketing authorisation holder/Contact Persons/Company**

SmithKline Beecham (SWG) Limited, 980 Great West Road, Brentford, Middlesex, TW8 9GS, UK.

The QP responsible for pharmacovigilance is stated and his CV is included.

### **2.5 Manufacturers**

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

### **2.6 Qualitative and quantitative composition**

The proposed composition is consistent with the details registered for the cross-reference product.

## **2.7 Manufacturing process**

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

## **2.8 Finished product/shelf-life specification**

The proposed finished product specification is in line with the details registered for the cross-reference product.

## **2.9 Drug substance specification**

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

## **2.10 TSE Compliance**

A declaration is given that no materials of animal and/or human origin are contained or used in the manufacturing process for the medicinal product. This is consistent with the approved cross-reference product.

## **3. EXPERT REPORTS**

The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

## **4. PRODUCT NAME & APPEARANCE**

See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

## **5. SUMMARY OF PRODUCT CHARACTERISTICS**

The proposed summary is consistent with the details registered for the cross-reference product.

## **6. PATIENT INFORMATION LEAFLET/CARTON**

### **PIL**

The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

The marketing authorisation holder has provided a commitment to update the marketing authorisation with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 1st July 2008.

### **Carton and blister**

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

## **7. CONCLUSIONS**

The data submitted with the application are acceptable. A Marketing Authorisation should be granted.

## **PRECLINICAL ASSESSMENT**

No new preclinical data have been supplied with this application and none are required for an application of this type.



## **CLINICAL ASSESSMENT**

No new clinical data have been supplied with this application and none are required for an application of this type.

## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

The data for this application is consistent with that previously assessed for the cross-reference product and as such has been judged to be satisfactory.

### **PRECLINICAL**

No new preclinical data were submitted and none are required for an application of this type.

### **EFFICACY**

Paracetamol is a well known drug and has been used as an analgesic for many years. This application is identical to previously granted application for Panadol Soluble Tablets (PL00071/0072R). No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product which, in turn, has been shown to be interchangeable with the innovator product. Extensive clinical experience with paracetamol is considered to have demonstrated the therapeutic value of the compound. The risk benefit is therefore considered to be positive.

**PARACETAMOL 500MG SOLUBLE TABLETS  
PL 00071/0447**

**STEPS TAKEN FOR ASSESMENT**

1	The MHRA received the marketing authorisation application on 9 <sup>th</sup> October 2003.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 11 <sup>th</sup> October 2005.
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 1 <sup>st</sup> June 2006.
4	The applicant responded to the MHRA's requests, providing further information on 5 <sup>th</sup> June 2006.
5	The application was determined on 3 <sup>rd</sup> March 2008.

**PARACETAMOL 500MG SOLUBLE TABLETS  
PL 00071/0447**

**STEPS TAKEN AFTER ASSESSMENT**

<b>Date submitted</b>	<b>Application type</b>	<b>Scope</b>	<b>Outcome</b>

# PARACETAMOL 500MG SOLUBLE TABLETS

## PL 00071/0447

### SUMMARY OF PRODUCT CHARACTERISTICS

- 1 NAME OF THE MEDICINAL PRODUCT**  
Paracetamol and Caffeine 500 mg/65 mg Soluble Tablets
- 2 QUALITATIVE AND QUANTITATIVE COMPOSITION**  
Each tablet contains paracetamol 500 mg and caffeine 65 mg
- 3 PHARMACEUTICAL FORM**  
White bevel-edged scored tablets one inch in diameter  
  
Effervescent tablet.
- 4 CLINICAL PARTICULARS**
  - 4.1 Therapeutic indications**  
Paracetamol and Caffeine 500 mg/65 mg Soluble Tablets are a mild analgesic and antipyretic formulated to give extra pain relief. The soluble tablets are recommended for the treatment of most painful and febrile conditions, for example, headache including migraine, backache, toothache, neuralgia, colds and influenza, sore throat, rheumatic pain and dysmenorrhoea.
  - 4.2 Posology and method of administration**  
Paracetamol and Caffeine 500 mg/65 mg Soluble Tablets should be dissolved in at least half a tumbler of water.  
*Adults:*  
Two tablets up to 4 times daily as required.  
Do not exceed 8 tablets in 24 hours.  
  
*Elderly:*  
As for adults.  
  
*Children:*  
Not recommended for children under 12 years.  
  
*Method of administration*  
Paracetamol and caffeine 500 mg/65 mg Soluble Tablets are for oral administration only.
  - 4.3 Contraindications**  
Hypersensitivity to paracetamol, caffeine or any of the other constituents.  
  
Patients with rare hereditary problems of fructose intolerance should not take this medicine.
  - 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.  
  
Excessive intake of tea or coffee should be avoided while taking this product.  
  
Do not exceed the stated dose.  
  
Patients should be advised not to take other paracetamol-containing products concurrently.  
  
If symptoms persist, consult your doctor.  
  
Keep out of the reach and sight of children.  
  
Pack Label:  
  
Immediate medical advice should be sought in the event of an overdose, even if you feel well.  
  
Do not take with other paracetamol-containing products.

#### Patient Information Leaflet:

Immediate medical advice should be sought in the event of 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 metaclopramide or domperidone and absorption reduced by colestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

#### **4.6 Pregnancy and lactation**

Epidemiological studies in human pregnancy have shown no ill effect due to paracetamol and caffeine used at the recommended dosage, but patients should follow the advice of their doctor regarding its use. Paracetamol and caffeine are excreted in breast milk but not in a clinically significant amount.

Available published data do not contraindicate breast feeding.

#### **4.7 Effects on ability to drive and use machines**

None.

#### **4.8 Undesirable effects**

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been very rare reports of blood dyscrasias including thrombocytopenia and agranulocytosis but these were not necessarily causally related to paracetamol.

#### **4.9 Overdose**

##### Paracetamol

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

##### *Risk factors*

If the patient

a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

or

b) Regularly consumes ethanol in excess of recommended amounts.

or

c) Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

##### *Symptoms*

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, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

##### *Management*

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. Symptoms may be limited to nausea or vomiting and may not reflect the severity of the

overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24 h from ingestion should be discussed with the NPIS or a liver unit.

## Caffeine

### *Symptoms*

Overdose of caffeine may produce nervousness, restlessness, insomnia, excitement, diuresis, facial flushing, muscle twitching, GI disturbance, tachycardia or cardiac arrhythmia, “rambling” flow of thought and speech, psychomotor agitation, or periods of inexhaustibility.

### *Management*

Patients should receive general supportive care (e.g. hydration and maintenance of vital signs). 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. The CNS effects of overdose may be treated with intravenous sedatives.

## **5 PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

The combination of paracetamol and caffeine is a well established analgesic combination.

### **5.2 Pharmacokinetic properties**

Paracetamol is rapidly and almost completely absorbed from the gastro-intestinal tract. It is relatively uniformly distributed throughout most body fluids and exhibits variable protein binding. Excretion is almost exclusively renal in the form of conjugated metabolites.

Caffeine is absorbed readily after oral administration, maximal plasma concentrations are achieved within one hour and the plasma half-life is about 3.5 hours. 65 --80% of administered caffeine is excreted in the urine as 1-methyluric acid and 1-methylxanthine.

### **5.3 Preclinical safety data**

There are no preclinical 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**

Sodium bicarbonate  
Sorbitol powder  
Saccharin sodium  
Sodium lauryl sulphate  
Citric acid (anhydrous)  
Sodium carbonate (anhydrous)  
Polyvidone  
Dimethicone (Silicone fluid 200/350)

### **6.2 Incompatibilities**

None known

- 6.3 Shelf life**  
48 months
- 6.4 Special precautions for storage**  
The product should be stored below 30°C
- 6.5 Nature and contents of container**  
PPFP laminate sachets in cardboard cartons containing 4, 6, 12, 18, 24 or 30 tablets.  
\*Not all pack sizes may be marketed.
- 6.6 Special precautions for disposal**  
None
- 7 MARKETING AUTHORISATION HOLDER**  
SmithKline Beecham (SWG) Limited  
980 Great West Road  
Brentford  
Middlesex  
TW8 9GS  
United Kingdom
- Trading as GlaxoSmithKline Consumer Healthcare, Brentford TW8 9GS, UK
- 8 MARKETING AUTHORISATION NUMBER(S)**  
PL 00071/0448
- 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**  
03/03/2008
- 10 DATE OF REVISION OF THE TEXT**  
03/03/2008



**PARACETAMOL 500MG SOLUBLE TABLETS**  
**PL 00071/0447**

**PATIENT INFORMATION LEAFLET**

**SUMMARY**

## Paracetamol 500mg Soluble Tablets

Please read this leaflet carefully before you start to take **Paracetamol 500mg Soluble Tablets**.  
If you have any questions, or if you do not understand anything, ask your doctor or pharmacist. Keep this leaflet, you may want to read it again.

**What is in the pack?**

Each **Paracetamol 500mg Soluble Tablet** contains the active ingredient **Paracetamol Ph Eur 500 mg** in a fizzy base designed to dissolve the tablet.

The tablets also contain: sodium bicarbonate, sorbitol powder (E 420), saccharin sodium, sodium lauryl sulphate, citric acid, sodium carbonate, polyvidone and dimeticone.

**Paracetamol 500mg Soluble Tablets** come in a carton containing 4, 12 or 24 effervescent tablets.  
\* Not all pack sizes may be marketed.

**Who makes Paracetamol 500mg Soluble Tablets?**

The product licence holder is **GlaxoSmithKline Consumer Healthcare**, Brentford, TW8 9GS, U.K. and all enquiries should be sent to this address.

The manufacturer is **GlaxoSmithKline Dungarvan Ltd.**, Co. Waterford, Ireland or **Famar SA**, Anthousa Av., 153 44 Pallini, Attikis, Greece.

**What do Paracetamol 500mg Soluble Tablets do?**

The tablets contain paracetamol which

is an analgesic (pain killer) and antipyretic (helps to reduce body temperature when you have a fever).

**What are Paracetamol 500mg Soluble Tablets used for?**

The tablets are suitable for headache, tension headache, migraine, backache, rheumatic and muscle pain, neuralgia, toothache and period pain. They also relieve discomfort in colds, influenza, sore throats and help reduce temperature.

**Check before you take these tablets**

**IMPORTANT:**

- Do not take with any other paracetamol-containing products.
- Each tablet contains 427 mg of sodium. This may be harmful if you are on a low sodium diet.

**Paracetamol 500mg Soluble Tablets should not be taken:**

- if you are sensitive to paracetamol or to any of the other ingredients listed above.

**Please see your doctor before you take Paracetamol 500mg Soluble Tablets:**

- if you are taking metoclopramide or domperidone - used to treat nausea and vomiting.
- if you are taking colestyramine - used to treat high cholesterol.
- if you have severe liver or kidney disease, including alcoholic liver disease.

*continued*

- if you are taking anti-coagulants (drugs to thin the blood e.g. warfarin) and you need to take a painkiller *on a daily basis over a long period*. However, you can take *occasional* doses of **Paracetamol 500mg Soluble Tablets**.
- If your headaches become persistent, see your doctor.
- If you have been told by your doctor that you have an intolerance to some sugars.

**If you are pregnant or breast feeding:**

Please see your doctor before you take **Paracetamol 500mg Soluble Tablets** if you are pregnant. You can take this medicine whilst breast feeding.

**How to take Paracetamol 500mg Soluble Tablets:**

The tablets must be dissolved in water before taking.

For oral use:

*Adults, including the elderly:*

Take 1-2 tablets dissolved in at least half a tumbler of water up to 4 times daily as required. Do not take more frequently than every 4 hours. Do not take more than 8 tablets in 24 hours.

*Children (6-12 years):*

Give 1/2 to 1 tablet dissolved in water up to 4 times daily as required. Do not give more frequently than every 4 hours. Not more than 4 tablets should be given in 24 hours.

Do not give to children for more than 3 days without consulting a doctor.

Do not give to children under 6 years of age.

Do not exceed the stated dose.

**If symptoms persist consult your doctor.**

**What should you do if you take too many Paracetamol 500mg Soluble Tablets?**

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.

**Will Paracetamol 500mg Soluble Tablets suit you ?**

Most people taking these tablets find they cause them no problems. However, occasionally some people may get allergic reactions, such as skin rash. In all the years paracetamol has been used there have been very rare reports of blood disorders, but these were not necessarily caused by paracetamol. These effects should go away once you stop taking the medicine.

If you are concerned about these effects, or if these tablets affect you in any other way, stop taking them and talk to your doctor or pharmacist.

**Storage Instructions**

Store below 25°C.

Do not use this medicine after the "Use by end of" date shown on the pack.

**Remember: Keep all medicines out of reach and sight of children.**

Leaflet prepared: July 2004



GlaxoSmithKline Consumer Healthcare, Brentford, TW8 9GS, U.K.



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PARACETAMOL 500MG SOLUBLE TABLETS  
PL 00071/0447

LABELLING

CARTON  
PACK SIZE-24



**CONTAINER  
BLISTER FOIL**

