PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS

PL 00071/0448
PL 00071/0450

UKPAR

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PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS

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LAY SUMMARY

The Medicines Healthcare products Regulatory Agency (MHRA) granted SmithKline Beecham (SWG) Limited Marketing Authorisations for the medicinal product Paracetamol and Caffeine 500mg/65mg Soluble Tablets (PL 00071/0448 and PL 00071/0450) on 3rd March 2008. This general sales list (GSL) medicine is available to the general public without prescription.

Paracetamol and Caffeine 500mg/65mg Soluble Tablets are used to relieve pain (analgesic) and to reduce an increased body temperature (anti-pyretic). This formulation contains two active ingredients which as a combination are indicated for relief from headache, migraine, backache, rheumatic and muscle pain, neuralgia, toothache, period pain and also to relieve discomfort from colds, influenza, sore throats and fever.

This application is identical to a previously granted application for Panadol Soluble Tablets (PL 00071/0379, granted to the same Marketing Authorisation Holder on 23rd August 1991 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 and Caffeine 500mg/65mg Soluble Tablets outweigh the risks; hence Marketing Authorisations have been granted.

PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Marketing Authorisations for the medicinal product Paracetamol and Caffeine 500mg/65mg Soluble Tablets (PL 00071/0448 and PL 00071/0450) to SmithKline Beecham (SWG) Limited on 3rd March 2008. The product is a general sale list medicine.

The applications were submitted as simple abridged applications 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 00071/0379, approved on 23rd August 1991.

The product contains the active ingredients; paracetamol and caffeine. The active ingredients exert their effect by unrelated pharmacological mechanisms. Paracetamol 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 in the body and also acts as an antipyretic to help reduce body temperature; caffeine is a mild stimulant.

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.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 00071/0448 & PL 00071/0450
PROPRIETARY NAME: Paracetamol and Caffeine 500mg/65mg Soluble Tablets
ACTIVE(S): Paracetamol and Caffeine
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 and Caffeine 500mg/65mg Soluble Tablets 500mg/65mg 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.

This application, and its duplicate (PL 00071/0450) cross-refers to the applicant's own Marketing Authorisation for Panadol Extra Soluble Tablets, approved on 23rd August 1991. The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed name of the product is Paracetamol and Caffeine 500mg/65mg 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 and caffeine equivalent to 65mg. The product is stored in sachets composed of paper-Polyethylene-Foil-Polyethylene (PPFP) laminate 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) and storage conditions ("Do not store below 30°C) 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. Marketing Authorisations should be granted.

PRECLINICAL ASSESSMENT

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

CLINICAL ASSESSMENT

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

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for these applications are 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 applications of this type.

EFFICACY

Paracetamol is a well known drug and has been used as an analgesic for many years and caffeine is a well known stimulant. These applications are identical to the previously granted application for Panadol Extra Soluble Tablets (PL00071/0072R). No new or unexpected safety concerns arise from these applications.

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. Extensive clinical experience with paracetamol and caffeine is considered to have demonstrated the therapeutic value of the compounds. The risk benefit is therefore considered to be positive.

PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 15th October 2003.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 18th November 2003.
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 9th March 2004.
4	The applicant responded to the MHRA's requests, providing further information on 11th May 2006.
5	The application was determined on 3rd March 2008.

PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS

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STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS

PL 00071/0448
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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 arrythmias 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-methylxanine.

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
PL 00071/0450

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/03/2008

10 DATE OF REVISION OF THE TEXT

03/03/2008

PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS
PL 00071/0448
PL 00071/0450

PATIENT INFORMATION LEAFLET

DUMMY

Paracetamol and Caffeine 500mg/65mg

Soluble Tablets

Please read this leaflet carefully before you start to take **Paracetamol and Caffeine 500mg/65mg 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 and Caffeine 500mg/65mg Soluble Tablet contains the active ingredients Paracetamol Ph Eur 500mg and Caffeine Ph Eur 65mg 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 and Caffeine 500mg/65mg Soluble Tablets come in a carton containing 4, 6, 12, 18, 24 or 30 effervescent tablets.
*Not all pack sizes may be marketed.

Who makes Paracetamol and Caffeine 500mg/65mg 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 and Caffeine 500mg/65mg 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) and caffeine which acts to further help the effectiveness of paracetamol.

What are Paracetamol and Caffeine 500mg/65mg Soluble Tablets used for?

The tablets are suitable for 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.**
- **Avoid drinking too much coffee or tea when taking these tablets.**
- **Each tablet contains 427mg of sodium. This may be harmful if you are on a low sodium diet.**

Paracetamol and Caffeine 500mg/65mg Soluble Tablets should not be taken:

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

Please see your doctor before you take Paracetamol and Caffeine 500mg/65mg 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.
- 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 and Caffeine 500mg/65mg 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 and Caffeine 500mg/65mg Soluble Tablets** if you are pregnant. You can take this medicine whilst breast feeding.

How to take Paracetamol and Caffeine 500mg/65mg Soluble Tablets:

The tablets must be dissolved in water before taking.

For oral use:

Adults, including the elderly:

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

Do not exceed the stated dose.

Do not give to children under 12 years of age.

If symptoms persist consult your doctor.

What should you do if you take too many Paracetamol and Caffeine 500mg/65mg 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 and Caffeine 500mg/65mg 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 30°C.
Do not use this medicine after the "Use by end of" date shown on the pack.

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

Leaflet prepared: July 2004

GlaxoSmithKline

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

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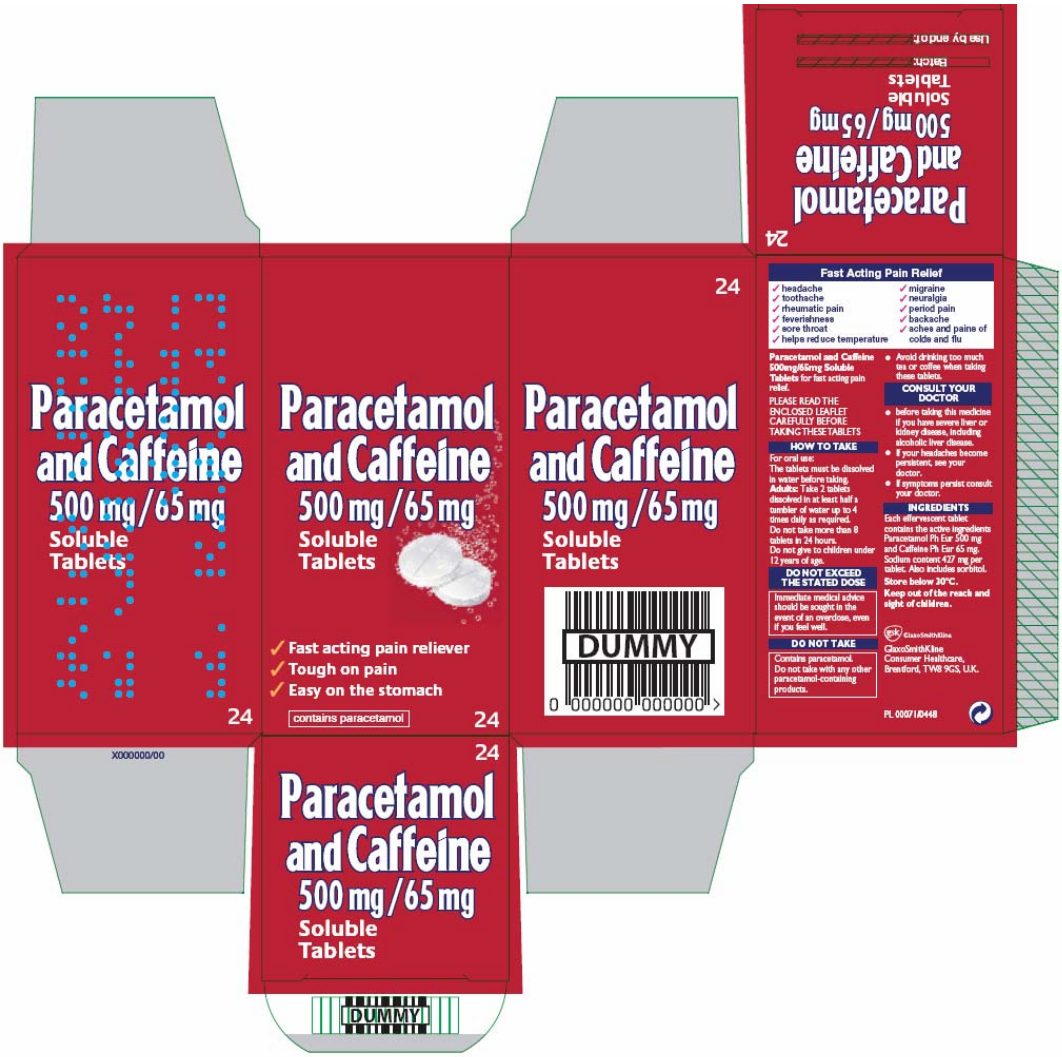
PARACETAMOL AND CAFFEINE 500MG/65MG SOLUBLE TABLETS
PL 00071/0448
PL 00071/0450

LABELLING

CARTON
PACK SIZE-24



CONTAINER
BLISTER FOIL