

## **Public Assessment Report**

### **Scientific discussion**

# **Paracetamol Accord 1000 mg effervescent tablets (paracetamol)**

**NL/H/4780/001/DC**

**Date: 2 March 2023**

This module reflects the scientific discussion for the approval of Paracetamol Accord 1000 mg effervescent tablets. The procedure was finalised in the United Kingdom (UK/H/1747/001/DC). After a transfer in 2019, the current RMS is the Netherlands. The report presented below reflects the original procedure at the time of finalisation in the UK and has not been changed or updated since.



# **Public Assessment Report**

## **Decentralised Procedure**

**PARACETAMOL 1000 MG EFFERVESCENT TABLETS**

**UK/H/1747/001/DC**  
**UK Licence No: PL 20075/0122**

**ACCORD HEALTHCARE LIMITED**

## LAY SUMMARY

On 6<sup>th</sup> April 2011, the UK granted Accord Healthcare Limited a Marketing Authorisation (licence) for Paracetamol 1000 mg Effervescent Tablets.

Paracetamol Effervescent Tablets contain paracetamol, which relieves pain (analgesic) and reduces the body temperature in fever (antipyretic).

Paracetamol Effervescent Tablets are recommended for use in treatment of mild to moderate pain and/or fever.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Paracetamol 1000 mg Effervescent Tablets outweigh the risks; hence a Marketing Authorisation has been granted.

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## Module 1

<b>Product Name</b>	Paracetamol 1000 mg Effervescent Tablets
<b>Type of Application</b>	Generic hybrid, Article 10.3
<b>Active Substance</b>	Paracetamol
<b>Form</b>	Effervescent Tablets
<b>Strength</b>	1000 mg
<b>MA Holder</b>	Accord Healthcare Limited, Sage House, 319 Pinner Road, North Harrow, HA1 4 HF, Middlesex, United Kingdom
<b>Reference Member State (RMS)</b>	UK
<b>CMS</b>	The Czech Republic (CZ), Germany (DE), Denmark (DK), Spain (ES), Finland (FI), France (FR), Hungary (HU), Ireland (IE), Italy (IT), the Netherlands (NL), Poland (PL), Portugal (PT), Romania (RO), Sweden (SE)
<b>Procedure Number</b>	UK/H/1747/001/DC
<b>End of Procedure</b>	Day 210 – 15 <sup>th</sup> September 2010

## Module 2

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 1000 mg Effervescent Tablets

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 1000mg of Paracetamol.

Excipients: Sodium content approximately 657 mg/tablet

Sorbitol (E420) 45 mg/tablet.

For a full list of excipient see section 6.1

#### 3 PHARMACEUTICAL FORM

Effervescent Tablet

White to off white, round, flat faced, bevelled edged tablets plain on both sides.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic indications

For adults and adolescents only:

Treatment of mild to moderate pain and/or fever.

##### 4.2 Posology and method of administration

This presentation is reserved for use in adults and in adolescents over 50kg of body weight aged 16 years and above.

Doses depend on body weight and age; a single dose ranges from 10 to 15 mg/kg body weight (= b.w.) to a maximum of 60 mg/kg b.w. for total daily dose.

Adults and adolescents > 50 kg of body weight

Take one tablet (1000 mg) every four to six hours, upto a maximum of 3 tablets (3000 mg) in 24 hours.

##### Maximum daily dose:

- The maximum daily dose of Paracetamol must not exceed 3000 mg.
- Maximum single dose is 1000 mg (1 effervescent tablet).

Paracetamol 1000 mg Effervescent Tablets are for oral administration. The tablets should be placed in a full tumbler of water immediately before use and allowed to dissolve completely before swallowing.

##### Frequency of administration:

Doses of Paracetamol 1000 mg Effervescent Tablets should not be given more frequently than every 6 hours, and not more than 3 doses should be given in any 24 hour period.

##### Renal insufficiency:

In case of renal insufficiency the dose should be reduced:

Glomerular filtration rate	Dose
10 – 50 ml/min	500 mg every 6 hours
< 10 ml/min	500 mg every 8 hours

Paracetamol 1000 mg Tablets are not suitable for patients with renal and hepatic insufficiency when reduced dose is required. More appropriate pharmaceutical forms are available in the market for use.

##### Hepatic insufficiency:

In patients with impaired hepatic or Gilbert's syndrome, the dose must be reduced or the dosing interval prolonged.

The daily effective dose should not exceed 60 mg/kg/day (upto maximum 2000 mg /day) in the following situations:

- Adults weighing less than 50 kg
- Mild to moderate hepatic insufficiency, Gilbert's syndrome (familial non-haemolytic jaundice)

- Dehydration
- Chronic malnutrition
- Chronic alcoholism

Intake of paracetamol with food and drink does not affect the efficacy of the medicinal product.

#### 4.3 Contraindications

- Hypersensitivity to Paracetamol, or any of the excipients.

#### 4.4 Special warnings and precautions for use

Prolonged or frequent use is discouraged. Patients should be advised not to take other Paracetamol containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such case unconsciousness does not occur. However, medical assistance should be sought immediately. Prolonged use except under medical supervision may be harmful. In children treated with 60mg/kg daily of Paracetamol, the combination with another antipyretic is not justified except in the case of ineffectiveness.

Caution is advised in the administration of Paracetamol to patients with moderate and severe renal insufficiency, mild to moderate hepatocellular insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (*Child-Pugh >9*), acute hepatitis, concomitant treatment with medicinal products affecting hepatic functions, glucose-6-phosphatedehydrogenase deficiency, haemolytic anaemia, dehydration, alcohol abuse and chronic malnutrition (see section 4.2).

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2000 mg in such case. Alcohol should not be used during the treatment with Paracetamol.

“Caution is advised in asthmatic patients sensitive to aspirin, because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested”

Abrupt discontinuation of long-term use of high-dosed analgesics, taken not as directed, may cause headache, tiredness, muscular pain, nervousness and vegetative symptoms. The withdrawal symptoms subside within a few days. Patients should be advised to consult their doctor if headaches become persistent.

Paracetamol Effervescent Tablets should not be administered in children and adolescents below 16 years of age and under 50 kg body weight.

This medicinal product contains 657 mg of sodium per tablet. To be taken into consideration by patients on a controlled sodium diet.

This medicinal product contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Do not exceed the stated dose.

If symptoms persist consult a doctor.

Treatment with an antidote is advised if an overdose is suspected.

#### 4.5 Interaction with other medicinal products and other forms of interaction

Hepatotoxic substances may increase the possibility of Paracetamol accumulation and overdose. The metabolism of paracetamol is increased in patients taking enzyme-inducing drugs such as rifampicin and some antiepileptics (carbamazepine, phenytoin, phenobarbital, primidone). Isolated reports describe unexpected hepatotoxicity in patients taking enzyme-inducing drugs and alcohol.

- Probenecid causes an almost 2-fold reduction in clearance of Paracetamol by inhibiting its conjugation with glucuronid acid. A reduction of the Paracetamol dose should be considered for concomitant treatment with probenecid.
- Salicylamide may prolong the elimination t<sub>1/2</sub> of Paracetamol.
- Metoclopramide and domperidone accelerate absorption of Paracetamol.
- Cholestyramine reduces absorption of Paracetamol and therefore should not be administered within

- an hour following Paracetamol administration.
- Concomitant use of Paracetamol (4000 mg per day for at least 4 days) with oral anticoagulants may lead to slight variations of INR values. In this case, increased monitoring of INR values should be done during the duration of the combination and after its discontinuation.
- Isoniazid : Reduction of paracetamol clearance, with possible potentiation of its action and/ or toxicity, by inhibiting its metabolism in the liver.
- Lamotrigine: decrease in the bioavailability of lamotrigine, with possible reduction of its effect, due to possible induction of liver metabolism.

Interference with laboratory tests:

Paracetamol may affect uric acid tests by wolframato phosphoric acid, and blood sugar tests by glucose-oxidase-peroxidase.

#### 4.6 Pregnancy and lactation

Epidemiological data on the oral administration of therapeutic doses of Paracetamol indicate no adverse reactions on pregnancy or on the health of the fetus/newborn child. Prospective data on overdose during pregnancy showed no increased risk of malformations. Reproduction studies investigating oral administration did not indicate any signs of malformation or fetotoxicity (see section 5.3).

Paracetamol is considered to be safe in normal therapeutic doses for short-term use as a minor analgesic/antipyretic, but patients should seek the advice of their doctor regarding its use.

#### Lactation:

Following oral administration, Paracetamol is excreted into breast milk in small quantities. To date, no adverse reactions or undesirable effects are known in association with lactation. Therapeutic doses of Paracetamol can be administered during breast-feeding

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

Paracetamol has no influence on the ability to drive and use machines.

#### 4.8 Undesirable effects

The frequency using the following convention should be: very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequency	System	Symptoms
Rare >1/10000 - < 1/1000	Blood and lymphatic system disorders	Platelet disorders, stem cell disorders, agranulocytosis, leucopenia, thrombocytopenia, haemolytic anaemia, pancytopenia
	Immune system disorders	Allergies (excluding angioedema).
	Psychiatric disorders	Depression NOS, confusion, hallucinations.
	Nervous system disorders	Tremor NOS, headache NOS.
	Eye disorders	Abnormal vision.
	Cardiac disorders	Oedema.
	Gastrointestinal disorders	Haemorrhage NOS, abdominal pain NOS, diarrhoea NOS, nausea, vomiting.
	Hepato-biliary disorders	Abnormal Hepatic function, hepatic failure, hepatic necrosis, jaundice.
	Skin and subcutaneous tissue disorders	Pruritus, rash, sweating, purpura, angioedema, urticaria
	General disorders and administration site conditions	Dizziness (excluding vertigo), malaise, pyrexia, sedation, drug interaction NOS.
	Injury, poisoning and procedural	Overdose and poisoning

	complications	
Very Rare (< 10,000)	Respiratory, thoracic and mediastinal disorders	Bronchospasm
	Hepato-biliary disorders	hepatotoxicity
	General disorders and administration site conditions	hypersensitivity reaction (requiring discontinuation of treatment)
	Metabolism and nutrition disorders	Hypoglycemia
	Renal and urinary disorders	Sterile pyuria (cloudy urine) and renal side effects

Interstitial nephritis has been reported incidentally after prolonged use of high doses. Some cases of epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme, edema of the larynx, anaphylactic shock, anemia, liver alteration and hepatitis, renal alteration (severe renal impairment, haematuria, anuresis), gastro intestinal effects and vertigo have been reported.

#### 4.9 Overdose

There is a risk of poisoning, particularly in elderly subjects, in young children, in patients with liver disease, in cases of chronic alcoholism and in patients with chronic malnutrition. Overdose of Paracetamol is potentially fatal in all populations.

Symptoms generally appear within the first 24 hours and comprise: nausea, vomiting, anorexia, pallor, and abdominal pain. Immediate emergency measures are necessary in case of paracetamol overdose, even when no symptoms are present.

- Overdose, 10g or more of Paracetamol in adults or 150 mg/kg of body weight, causes liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

#### Emergency Procedure:

- Immediate transfer to hospital.
- Blood sampling to determine initial paracetamol plasma concentration.
- IV (or oral if possible) administration of the antidote N-acetylcysteine as soon as possible or within 8 hours of the overdose.
- Activated charcoal may be used if the dose of Paracetamol ingested exceeds 12g or 150 mg/kg and should be undertaken if within 1 hour of the overdose.
- Oral methionine is also effective provided that it is given within 10 to 12 hours of the overdose.
- Symptomatic treatment should be implemented.
- Haemodialysis or haemoperfusion is possible in cases of severe poisoning.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: *other analgesics and antipyretics; anilides*  
ATC code: N02BE01

### 5.2 Pharmacokinetic properties

#### Absorption

The absorption of paracetamol by the oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes following ingestion.

#### Distribution

Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood, saliva and plasma. Protein binding is low.

### Metabolism

Paracetamol is metabolized mainly in the liver following two major metabolic pathways: glucuronic acid and sulfuric acid conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dose. A minor route, catalyzed by the cytochrome P450, results in the formation of an intermediate reagent (N-acetyl-p-benzoquinoneimine) which under normal conditions of use is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cysteine and mercaptopyric acid. Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

### Elimination

Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60 to 80%) and sulphate conjugates (20 to 30%). Less than 5% is eliminated in unchanged form.

Elimination half life is about 2 hours.

### Special patient groups

Renal Insufficiency: In cases of severe renal insufficiency (creatinine clearance lower than 10 ml/min) the elimination of paracetamol and its metabolites is delayed.

Elderly Subjects. The capacity for conjugation is not modified.

## **5.3 Preclinical safety data**

In animal studies investigating the acute, subchronic and chronic toxicity of paracetamol in the rat and mouse, gastrointestinal lesions, blood count changes, degeneration of the hepatic and renal parenchyma and necrosis were observed. These changes are, on the one hand, attributed to the mechanism of action and, on the other, to the metabolism of paracetamol. The metabolites that is probably responsible for the toxic effects and the corresponding organic changes have also been found in humans. Moreover, during long term use (i.e. 1 year) very rare cases of reversible chronic aggressive hepatitis have been described in the range of maximum therapeutic doses. At subtoxic doses, symptoms of intoxication can occur following a 3-week intake period. Paracetamol should therefore not be administered over a long period of time or at high doses.

Extensive investigations showed no evidence of any relevant genotoxic risk of paracetamol in the therapeutic, i.e. non-toxic, dose range.

Long-term studies in rats and mice yielded no evidence on relevant carcinogenic effects at non-hepatotoxic dosages of paracetamol.

Paracetamol crosses the placental barrier. Animal studies and clinical experience to date have not indicated any teratogenic potential.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Anhydrous Citric acid

Sorbitol E420

Sodium Carbonate, Anhydrous

Sodium Bicarbonate

Povidone K 25 (E1201)

Simeticone emulsion (30%)

Docusate sodium

Saccharin Sodium

Macrogol 6000

Monosodium Glycine carbonate

Sodium Benzoate

### Qualitative composition of Simeticone emulsion (30%):

Water

Polydimethylsiloxane

Polyethylene glycol stearate

Polyethylene glycol

Glycerides, C14-18, mono- and di

Polyethylene glycol distearate

Polyethylene glycol palmitate

Octamethylcyclotetrasiloxane

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

24 months

**For Polypropylene tube:**

Do not use the product after 1 month from the date of first opening.

**6.4 Special precautions for storage****For Polypropylene Tube:**

Store below 25°C. Keep the polypropylene tube tightly closed. Store in the original container to protect from moisture and light.

**For Alu-Alu Strip Pack:**

Store below 25°C. Store in the original package in order to protect from moisture and light.

**6.5 Nature and contents of container**

Paracetamol 1000 mg Effervescent Tablets are packed in Alu-Alu Strip packs and Polypropylene tubes.

**Alu-Alu Strip pack:**

Strip packs are made of two plain aluminium strip foils laminated with LDPE film. Each strip has 4 or 10 tablets. The strips are packed in a carton having 4 tablets (4x1), 8 tablets (4x2), 20 tablets (4x5), 40 tablets (4x10), or 10 tablets (1 x 10) and packed with a patient information leaflet.

**Polypropylene Tubes:**

White opaque plain polypropylene tube and white opaque tamper evident polyethylene caps with inbuilt desiccant. Each tube contains 10 or 12 tablets.

Pack size: 36 (3 x 12) tablets per carton, 10 (1 x 10) tablets per carton and 20 (2 x 10) tablets per carton. Each carton has a patient leaflet for each polypropylene tube.

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal**

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

**7 MARKETING AUTHORISATION HOLDER**

Accord Healthcare Limited,  
Sage House, 319 Pinner Road,  
North Harrow, HA1 4 HF,  
Middlesex,  
United Kingdom

**8 MARKETING AUTHORISATION NUMBER(S)**

PL 20075/0122

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

06/04/2011

**10 DATE OF REVISION OF THE TEXT**

06/04/2011

## Paracetamol 1000 mg Effervescent Tablets

### Paracetamol

Read all of this leaflet carefully because it contains important information for you

This medicine is available without prescription. However, you still need to take Paracetamol Effervescent Tablets carefully to get the best results from them.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 3 days.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

The name of your medicine is "Paracetamol 1000mg Effervescent Tablets", but will be referred to as "Paracetamol Effervescent Tablets" throughout the rest of this leaflet

#### In this leaflet:

1. What Paracetamol Effervescent Tablets are and what they are used for
2. Before you take Paracetamol Effervescent Tablets
3. How to take Paracetamol Effervescent Tablets
4. Possible side effects
5. How to store Paracetamol Effervescent Tablets
6. Further information

### 1. What Paracetamol Effervescent Tablets are and what they are used for

Paracetamol Effervescent Tablets contain Paracetamol, which relieves pain (analgesic) and reduces the body temperature in fever (antipyretic).

The tablets are recommended for use in treatment of mild to moderate pain and/or fever.

### 2. Before you take Paracetamol Effervescent Tablets

#### Do not take Paracetamol Effervescent Tablets

- If you are allergic (hypersensitive) to Paracetamol or any of the ingredients of Paracetamol Effervescent Tablets.

#### Take special care with Paracetamol Effervescent Tablets

##### Tell your doctor:

- If you are suffering from kidney problems
- If you are suffering from liver problems including liver problems due to excessive alcohol consumption.
- If you have Gilbert's syndrome (mild jaundice)
- If you have hemolytic anemia (abnormal breakdown of red blood cells)
- If you are an asthmatic and sensitive to aspirin.
- If you are suffering from dehydration or chronic malnutrition.
- If you are on paracetamol containing drugs
- If you have fever after paracetamol therapy
- If you suffer from glucose-6-phosphate dehydrogenase deficiency (enzyme deficiency)

Do not use paracetamol unless prescribed by your doctor if you have an addiction to alcohol or liver damage. If this concerns you do not use with alcohol. If you are already taking other pain medication containing paracetamol do not use Paracetamol Effervescent Tablets without first speaking to your doctor or a pharmacist.

Never take more Paracetamol Effervescent Tablets than recommended. A higher dose does not increase pain relief; instead it can cause severe liver damage. The symptoms of liver damage occur first after a few days. It is important therefore that you contact your doctor as soon as possible if you have taken more Paracetamol Effervescent Tablets than recommended in this leaflet.

Do not use Paracetamol 1000 mg Effervescent Tablets in children and adolescents below 10 years of age and under 50 kg body weight.

#### Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Tell your doctor before you take Paracetamol Effervescent Tablets if you are taking:

- Drugs to thin the blood (anti-coagulant drugs e.g. warfarin)
- Medicines used to relieve sickness (e.g. metoclopramide, domperidone)
- Medicines used to treat high cholesterol (cholestyramine)
- Probenecid (Medicine used to treat high levels of uric acid in the blood stream i.e gout)
- Medicine to treat fever or mild pain (Aspirin, salicylamide)
- Drugs such as rifampicin (drug that helps to fight infection) and some antiepileptics such as carbamazepine, phenytoin, phenobarbital, primidone (drugs used to treat or cure convulsions).
- Medicines used to treat epilepsy (lamotrigine)
- Medicines to treat tuberculosis (isoniazid)

Effects of Paracetamol Effervescent Tablets on laboratory tests

Uric acid and blood sugar tests may be affected.

#### Taking Paracetamol Effervescent Tablets with food and drink

Meals will not affect how much Paracetamol gets into the body.

#### Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

If you are pregnant see your doctor before you take Paracetamol Effervescent Tablets. The dose of Paracetamol recommended for this product is acceptable if you are breast-feeding.

#### Driving and using machines

Paracetamol Effervescent Tablets have no influence on the ability to drive and use machines.

#### Important information about some of the ingredients of Paracetamol Effervescent Tablets

This medicinal product contains 657mg of sodium. This should be taken into consideration by patients on a controlled sodium (salt) diet.

This medicinal product also contains sorbitol. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicinal product.

### 3. How to take Paracetamol Effervescent Tablets

You should take Paracetamol Effervescent Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Paracetamol Effervescent Tablets are for oral administration. Place the tablet in a full glass of water. Allow it to completely dissolve. Then drink the solution straight away.

If you have doubts on the correct dose of Paracetamol Effervescent Tablets to use please consult your doctor.

This medicinal product is for use, only in adults and adolescents aged 16 years and above.

#### Adults and adolescents > 50 kg of body weight

Take one tablet (1000 mg) every four to six hours, upto a maximum of 3 tablets (3000 mg) in 24 hours.

#### Maximum daily dose:

- The maximum daily dose of Paracetamol must not exceed 3 tablets (3000 mg).
- Maximum single dose is 1000 mg (1 effervescent tablet)

The minimum time interval between two doses should be 4 to 6 hours.

If the pain persists for more than 5 days or the fever lasts for more than 3 days, or gets worse or other symptoms appear, you should stop the treatment and consult a doctor.

#### Kidney problems:

In moderate kidney problems: The usual dose is 500 mg repeated every 6 hours.

In severe kidney problems: The usual dose is 500 mg repeated every 8 hours

#### Liver problems:

In case of problems with your liver please consult your doctor. Your doctor may decide to reduce the dose.

In chronic alcoholics, a dose of 2000 mg per day should not be exceeded

Do not divide the 1000 mg tablet into two equal halves for the lower doses. Paracetamol tablets of lower strengths are available in the market.

Do not exceed the stated dose. Do not give to adolescents of 16 years of age and younger. Cap contains desiccant. Do not eat.

#### If you take more Paracetamol Effervescent Tablets than you should:

Symptoms of paracetamol overdose in the first 24 hours may include paleness, nausea (feeling sick), vomiting, lack of desire to eat and stomach pain. If you or someone you know accidentally takes more than the stated dose (overdose) you should contact a doctor immediately even if you feel well, because there is risk of serious, delayed liver damage.

#### If you forget to take Paracetamol Effervescent Tablets:

If you forget to take a dose, take it as soon as you remember, unless it is almost time for your next dose. The minimum time interval between two doses should be 4 to 6 hours. Never take a double dose to make up for the one you have missed.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

### 4. Possible side effects

Like all medicines Paracetamol Effervescent Tablets can cause side effects, although not everybody gets them.

You should stop taking Paracetamol Effervescent Tablets and see your doctor immediately if you experience symptoms like swelling in the face, tongue or throat, difficulty swallowing, red and itchy swellings on the skin and difficulty in breathing.



**Rare (affects less than 1 in 1,000 patients):**

- Bleeding problems or clotting disorders (Platelet disorders), decreased formation of cells, severe decrease in white blood cells which may lead to severe infections (agranulocytosis), frequent infections due to poorly functioning white blood cells or decrease in white blood cells (leucopenia), reduction in blood platelets, which increases the risk of bleeding or bruising (thrombocytopenia) abnormal breakdown of red blood cells, which may cause weakness or pale skin (haemolytic anaemia), decrease in blood count (pancytopenia), reduced neutrophil count in blood (neutropenia).
- Allergies (excluding swelling on the face, mouth, hands).
- Depression, confusion, sensing unreal things
- Tremor, headache
- Abnormal vision.
- Abnormal accumulation of fluid under the skin (oedema)
- Stomach pain, diarrhoea, nausea (feeling sick), vomiting, bleeding (haemorrhage)
- Abnormal liver function, liver failure, death of liver cells (hepatic necrosis), jaundice
- Dizziness, feeling of general discomfort or uneasiness (malaise), fever, drowsiness, drug interaction.
- Overdose and poisoning.

**Very rare (affects less than 1 in 10,000 patients):**

- Damage caused to the liver (hepatotoxicity)
- Immediate severe allergic reaction (hypersensitivity reaction requiring discontinuation of treatment)
- Low levels of glucose in the blood (hypoglycaemia)
- Cloudy urine and kidney disorders.
- Life-threatening skin disease causing rash, skin peeling and sores (epidermal necrolysis)
- Allergic reaction of the skin (erythema multiforme)
- Severe life-threatening skin disease causing rash, skin peeling, sores (Stevens–Johnson syndrome)
- Accumulation of fluid in the voice box (larynx)
- Severe allergic reaction (anaphylactic shock)
- Decrease in red blood cells (anemia)
- Severe kidney impairment (renal alteration)
- Kidney disorder (nephritis interstitial)
- Blood in urine (haematuria)
- Inability to urinate (anuresis)
- Stomach ulcers and bleeding (gastrointestinal effects)
- Uneasiness.

If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

### 5. How to store Paracetamol Effervescent Tablets

- Keep out of the reach and sight of children and adolescents.
- Do not use Paracetamol Effervescent Tablets after expiry date which is stated on the label after EXP. The expiry date refers to last day of that month.
- For Polypropylene tube: Do not use the product after 1 month from the date of first opening.
- For Polypropylene Tube: Store below 25°C. Keep the polypropylene tube tightly closed. Store in the original container to protect from moisture and light.
- For Alu-Alu Strip Pack: Store below 25°C. Store in the original package in order to protect from moisture and light.
- Do not use the product if you notice visible signs of deterioration, like brown or black spots, bulging of tablets or discoloration.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

### 6. Further information

**What Paracetamol Effervescent Tablets contains:**

The active substance is Paracetamol. Each effervescent tablet contains 1000 mg of Paracetamol.

The other ingredients are:

Anhydrous Citric acid, Sorbitol E420, Sodium Carbonate Anhydrous, Sodium Hydrogen Carbonate, Povidone K 25, Simeticone emulsion (30%), Docusate sodium, Saccharin Sodium, Macrogol 6000, Monosodium glycane carbonate, Sodium Benzoate.

Simeticone emulsion 30% contains:

Water, polydimethylsiloxane, polyethylene glycol stearate, polyethylene glycol, glycerides C14-18 mono- and di Polyethylene glycol distearate, Polyethylene glycol palmitate, Octamethylcyclotetrasiloxane.

**What Paracetamol Effervescent Tablets look like and contents of the pack:**

Paracetamol 1000 mg Effervescent Tablets are white to off-white, round, flat faced and bevelled edged tablets, plain on both sides.

This medicinal product is available in two different types of packaging: Alu-Alu strip pack or polypropylene tubes.

**Alu-Alu Strip pack:**

The effervescent tablets are packed in aluminium strip foils laminated with LDPE film. Each strip has 4 tablets or 10 tablets. The strips are packed in a carton containing 4 tablets (4x1), 8 tablets (4x2), or (10 x 1) 10 tablets .

**Polypropylene Tubes:**

The effervescent tablets are packed in white polypropylene tube with tamper evident polyethylene cap containing an inbuilt desiccant. Each tube contains 10 tablets. One tube (1 x 10) is packed in a carton.

**CAUTION:**

Cap contains desiccant. Do not eat. Not all pack sizes may be marketed.

**Marketing Authorisation Holder and Manufacturer:**

Accord Healthcare Limited,  
Sage House, 319 Pinner road,  
North Harrow,  
Middlesex,  
HA1 4 HF,  
United Kingdom

The leaflet was last approved in 03/2011.



## Module 4 Labelling

**Paracetamol 1000 mg Effervescent Tablets**  
4 tablets

**1000 mg**  
PL 20075/0122

**Paracetamol 1000 mg Effervescent Tablets**

Each effervescent tablet contains 1000 mg Paracetamol.

**Maximum strength in a single tablet.  
Take only one tablet at a time.  
Do not take more than one tablet 3 times a day.**

Also contains sodium and sorbitol (E420).  
See package leaflet for further information.

For oral use.  
Read the package leaflet before use.  
Dissolve one tablet in a glass of water immediately before use.  
Allow to dissolve completely before use.

Contains Paracetamol.  
Do not take with any other Paracetamol containing products.

Immediate medical advice should be sought in the event of overdose even if you feel well.  
Please read the enclosed leaflet carefully.  
Prolonged use except on the doctor's advice may be harmful.  
This product should be used only when clearly necessary.

**1000 mg**      **accord**

PL Holder: Accord Healthcare Limited,  
Sage House, 319 Pinner Road,  
North Harrow, Middlesex, HA1 4HF,  
United Kingdom      Store below 25°C.  
Store in the original package in order to  
protect from moisture and light.

4

tablets

Varnish free area for batch coding

LOT:      EXP:

---

**Paracetamol 1000 mg Effervescent Tablets**  
4 tablets

**Paracetamol 1000 mg Effervescent Tablets**  
4 tablets

**1000 mg**      **P**

**Keep out of the reach and sight of children and adolescents.**

Warning: Taking higher doses than recommended can cause serious liver damage. Do not use Paracetamol unless prescribed by your doctor if you have an addiction to alcohol or liver damage or if you are concomitantly taking other pain medication containing paracetamol.

Recommended for:  
Treatment of mild to moderate pain and/or fever.  
See package leaflet for further information.

This medicinal product is for use only in adults and in adolescents aged 16 years and above and over 50 kg of body weight.


Adults and adolescents over 50 kg of body weight  
Take one tablet (1000 mg) every four to six hours, up to a maximum of 3 tablets (3000 mg) in 24 hours.

Maximum daily dose:  
• The maximum daily dose of Paracetamol must not exceed 3000 mg.

• Maximum single dose is 1000 mg (1 effervescent tablet)  
If the pain persists for more than 5 days or the fever lasts for more than 3 days, or gets worse or other symptoms appear, you should stop the treatment and consult a doctor.

Do not exceed the stated dose.  
If symptoms persist consult your doctor.

Do not give to children below 16 years of age and under 50 kg body weight.



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Code: GJ/Drugs/133

**1000 mg**

**Paracetamol 1000 mg Effervescent Tablets**  
8 tablets

**1000 mg**

PL 20075/0122

**Paracetamol 1000 mg Effervescent Tablets**

Each effervescent tablet contains 1000 mg Paracetamol

**Maximum strength in a single tablet.  
Take only one tablet at a time.  
Do not take more than one tablet 3 times a day.**

Also contains sodium and sorbitol (E420).  
See package leaflet for further information.

For oral use.  
Read the package leaflet before use.  
Dissolve one tablet in a glass of water immediately before use.  
Allow to dissolve completely before use.

**Contains Paracetamol.  
Do not take with any other Paracetamol containing products.**

**Immediate medical advice should be sought in the event of  
overdosage even if you feel well.  
Please read the enclosed leaflet carefully.  
Prolonged use except on the doctor's advice may be harmful.  
This product should be used only when clearly necessary.**

**1000 mg**

**accord**

PL Holder:  
Accord Healthcare Limited,  
Sage House, 319 Pinner Road,  
North Harrow, Middlesex, HA1 4HF,  
United Kingdom

Store below 25°C.  
Store in the original package in order  
to protect from moisture and light.

**8**  
tablets

Varnish free area for batch coding

LOT:  
EXP:

**Paracetamol 1000 mg Effervescent Tablets**  
8 tablets

**Paracetamol 1000 mg Effervescent Tablets**  
8 tablets

**1000 mg**

**P**

**Keep out of the reach and sight of children and adolescents.**

Warning: Taking higher doses than recommended can cause serious liver damage. Do not use Paracetamol unless prescribed by your doctor if you have an addiction to alcohol or liver damage or if you are concomitantly taking other pain medication containing paracetamol.

Recommended for:  
Treatment of mild to moderate pain and/or fever.  
See package leaflet for further information.

This medicinal product is for use only in adults and in adolescents aged 16 years and above and over 50 kg of body weight.

Adults and adolescents over 50 kg of body weight  
Take one tablet (1000 mg) every four to six hours, up to a maximum of 3 tablets (3000 mg) in 24 hours.

Maximum daily dose:  
• The maximum daily dose of Paracetamol must not exceed 3000 mg.

• Maximum single dose is 1000 mg (1 effervescent tablet)  
If the pain persists for more than 5 days or the fever lasts for more than 3 days, or gets worse or other symptoms appear, you should stop the treatment and consult a doctor.

**Do not exceed the stated dose.  
If symptoms persist consult your doctor.**

Do not give to children below 16 years of age and under 50 kg body weight.



Code: Gyl/Drugs/1339

**1000 mg**

Varnish free area for batch coding

LOT:  
EXP:

**accord**

**1000 mg**

**Paracetamol 1000 mg Effervescent Tablets**

**Paracetamol 1000 mg Effervescent Tablets**

10 (1 x 10) tablets

Keep out of the reach and sight of children and adolescents.  
Warning: Taking higher doses than recommended can cause serious liver damage.  
Do not use Paracetamol unless prescribed by your doctor if you have an addiction to alcohol or liver damage or if you are concomitantly taking other pain medication containing paracetamol.

Recommended for:  
Treatment of mild to moderate pain and/or fever.  
See package leaflet for further information.

This medicinal product is for use only in adults and in adolescents aged 16 years and above and over 50 kg of body weight.

**Adults and adolescents over 50 kg of body weight**  
Take one tablet (1000 mg) every four to six hours, up to a maximum of 3 tablets (3000 mg) in 24 hours.

Maximum daily dose:

- The maximum daily dose of Paracetamol must not exceed 3000 mg.
- Maximum single dose is 1000 mg (1 effervescent tablet)

If the pain persists for more than 5 days or the fever lasts for more than 3 days, or gets worse or other symptoms appear, you should stop the treatment and consult a doctor.

Do not exceed the stated dose.  
If symptoms persist consult your doctor.

Do not give to children below 16 years of age and under 50 kg body weight.  
CAUTION: Cap contains desiccant.  
Do not eat.



Code GupDrugs1339

**Paracetamol 1000 mg Effervescent Tablets**

10 (1 x 10) tablets

PL Holder:  
Accord Healthcare Limited,  
Sage House,  
319 Pinner Road,  
North Harrow,  
Middlesex,  
HA1 4HF,  
United Kingdom

**Paracetamol 1000 mg Effervescent Tablets**

Each effervescent tablet contains 1000 mg Paracetamol.

Maximum strength in a single tablet.

Take only one tablet at a time.

Do not take more than one tablet 3 times a day.

Also contains sodium and sorbitol (E420).  
See package leaflet for further information.

For oral use.

Read the package leaflet before use.

Dissolve one tablet in a glass of water immediately before use.

Allow to dissolve completely before use.

Contains Paracetamol.

Do not take with any other Paracetamol containing products.

Immediate medical advice should be sought in the event of overdose  
Even if you feel well. Please read the enclosed leaflet carefully.  
Prolonged use except on the doctor's advice may be harmful.  
This product should be used only when clearly necessary.

**1000 mg**

**accord**

**Paracetamol 1000 mg Effervescent Tablets**

10 (1 x 10) tablets

Store below 25°C.  
Keep the polypropylene tube tightly closed.

Store in the original container to protect from moisture and light.

Do not use the product after one month from the date of first opening.

PL 20075/0122

**P**

**1000 mg**

**accord**  
**PARACETAMOL 1000 MG**  
**EFFERVESCENT TABLETS**  
 MAXIMUM STRENGTH IN A  
 SINGLE TABLET

DO NOT EXCEED THE STATED DOSE  
 DISSOLVE ONE TABLET IN A GLASS  
 OF WATER IMMEDIATELY BEFORE USE

PL 20075/0122

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PL 20075/0122

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 SINGLE TABLET

DO NOT EXCEED THE STATED DOSE  
 DISSOLVE ONE TABLET IN A GLASS  
 OF WATER IMMEDIATELY BEFORE USE

PL 20075/0122

## Paracetamol 1000 mg Effervescent Tablets

Each effervescent tablet contains 1000 mg Paracetamol. Also contains sodium and sorbitol (E420). See package leaflet for further information. For oral use. Read the package leaflet before use. Dissolve one tablet in a glass of water immediately before use. Allow to dissolve completely before use.

**Maximum strength in a single tablet. Take only one tablet at a time. Do not take more than one tablet 3 times a day.**

**Keep out of the reach and sight of children and adolescents.**

**Contains Paracetamol. Do not take with any other Paracetamol containing products.**

**Immediate medical advice should be sought in the event of overdose even if you feel well. Please read the enclosed leaflet carefully. Prolonged use except on the doctor's advice may be harmful. This product should be used only when clearly necessary.**

**1000 mg**

PL 20075/0122

**Warning:** Taking higher doses than recommended can cause serious liver damage. Do not use Paracetamol unless prescribed by your doctor if you have an addiction to alcohol or liver damage or if you are concomitantly taking other pain medication containing paracetamol. Do not use the product after one month from the date of first opening. Store below 25°C. Keep the polypropylene tube tightly closed. Store in the original container to protect from moisture and light.

**For information on uses and doses, please refer to the outer packaging or carton.**

Do not exceed the stated dose. If symptoms persist consult your doctor.

Do not give to children below 16 years of age and under 50 kg body weight.

**CAUTION:**

Cap contains desiccant. Do not eat.

PL Holder:

Accord Healthcare Limited,  
Sage House, 319 Pinner Road,  
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HA1 4HF, United Kingdom

**P**

**accord**

Code: Guj/Drugs/1339

## **Module 5**

### **Scientific discussion during initial procedure**

#### **I INTRODUCTION**

Based on the review of the data on quality, safety and efficacy, the Czech Republic (CZ), Germany (DE), Denmark (DK), Spain (ES), Finland (FI), France (FR), Hungary (HU), Ireland (IE), Italy (IT), the Netherlands (NL), Poland (PL), Portugal (PT), Romania (RO), Sweden (SE) and the UK considered that the application for Paracetamol 1000 mg Effervescent Tablets could be approved. This product is supplied through pharmacies only (P) and is indicated for the treatment of mild to moderate pain and/or fever.

This application for Paracetamol 1000 mg Effervescent Tablets is submitted as an abridged application according to Article 10.3 of Directive 2001/83/EC, claiming to be a generic hybrid medicinal product to Panodil brus, 500 mg Brustablett, first authorised in Sweden to Glaxo Smithkline, Customer Healthcare A/S on 12th January 1982.

The UK reference product is given as Panadol Soluble 500 mg Effervescent Tablets, first authorised in the UK to Glaxo SmithKline, Consumer Healthcare in November 1997 (PL 00071/0072).

Paracetamol has both analgesic and antipyretic activity, which are mediated through inhibition of prostaglandin synthesis within the central nervous system.

No new non-clinical studies were conducted, which is acceptable given that the product contains a widely-used, well-known active substance. No clinical studies have been performed and none are required for this application as the pharmacology of paracetamol is well-established.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the community, the RMS has accepted copies of current GMP Certificates or satisfactory inspection summary reports, 'close-out letters' or 'exchange of information' issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

The RMS considers that the pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Marketing Authorisation Holder has provided adequate justification for not submitting a Risk Management Plan.

**II. ABOUT THE PRODUCT**

Name of the product in the Reference Member State	Paracetamol 1000 mg Effervescent Tablets
Name(s) of the active substance(s) (INN)	Paracetamol
Pharmacotherapeutic classification (ATC code)	Other analgesics and antipyretics; anilides (N02BE01)
Pharmaceutical form and strength(s)	1000 mg Effervescent Tablets
Reference numbers for the Decentralised Procedure	UK/H/1747/001/DC
Reference Member State	United Kingdom
Member States concerned	The Czech Republic (CZ), Germany (DE), Denmark (DK), Spain (ES), Finland (FI), France (FR), Hungary (HU), Ireland (IE), Italy (IT), the Netherlands (NL), Poland (PL), Portugal (PT), Romania (RO), Sweden (SE)
Marketing Authorisation Number(s)	PL 20075/0122
Name and address of the authorisation holder	Accord Healthcare Limited, Sage House, 319 Pinner Road, North Harrow, HA1 4 HF, Middlesex, United Kingdom

### III SCIENTIFIC OVERVIEW AND DISCUSSION

#### III.1 QUALITY ASPECTS

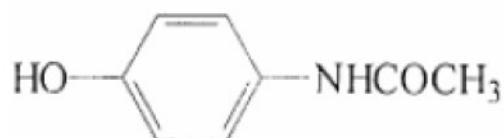
##### S. Active substance

###### Paracetamol

INN/Ph.Eur name: Paracetamol

Chemical name: *N*-(4-Hydroxyphenyl)acetamide

Structural formula:



Molecular formula: C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>

Molecular weight: 151.2

Appearance: white crystalline powder

Solubility: sparingly soluble in water, freely soluble in alcohol and very slightly soluble in ether and in methylene chloride

Paracetamol is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture of the active substance from its starting materials are controlled by a Certificate of Suitability.

Appropriate proof of structure data has been supplied for the active pharmaceutical ingredient. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance, with suitable test methods and limits. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all reference standards used.

Satisfactory specifications and Certificates of Analysis have been provided for all aspects of the container-closure system. A declaration has been provided that the primary packaging complies with current regulations concerning contact with foodstuff.

Appropriate stability data have been generated showing the active substance to be a physically and chemically stable drug, and supporting an appropriate retest period.

##### P. Medicinal Product

###### Other Ingredients

Other ingredients consist of pharmaceutical excipients anhydrous citric acid, sorbitol E420, anhydrous sodium carbonate, sodium bicarbonate, povidone K 25 (E1201), simeticone emulsion (30%), docusate sodium, saccharin sodium, macrogol 6000, monosodium glycine carbonate and sodium benzoate.

The ingredients in the simeticone emulsion (30%) are water, polydimethylsiloxane, polyethylene glycol stearate, polyethylene glycol, glycerides (C14-18, mono- and di),

polyethylene glycol distearate, polyethylene glycol palmitate and octamethylcyclotetrasiloxane.

With the exception of simethicone emulsion 30% and monosodium glycine carbonate, all excipients comply with their respective European Pharmacopoeia monographs. Simethicone emulsion 30% complies with the United States Pharmacopoeia. Monosodium glycine carbonate complies with in-house specifications.

None of the excipients used contain material of animal or human origin.

No genetically modified organisms (GMO) have been used in the preparation of this product.

### **Pharmaceutical Development**

The objective of the development programme was to produce a paracetamol containing product that could be considered a generic medicinal product of Panadol Soluble 500 mg Effervescent Tablets, first authorised in the UK to Glaxo SmithKline, Consumer Healthcare in November 1997 (PL 00071/0072).

The applicant has provided a suitable product development section. Justifications for the use and amounts of each excipient have been provided and are valid.

Comparative *in vitro* dissolution profiles and impurity profiles have been provided for the finished product versus the reference product.

### **Manufacturing Process**

A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Process validation data on commercial-scale batches have been provided. The results are satisfactory.

### **Finished Product Specification**

The finished product specification proposed for the product is acceptable. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for any working standards used.

### **Container-Closure System**

This product is packaged in:

- i) White opaque plain polypropylene tube and white opaque tamper evident polyethylene caps with inbuilt desiccant. Pack sizes are 36, 10 and 20 tablets.
- ii) Strip packs made of two plain aluminium strip foils laminated with LDPE film. The strips are packed in cartons and come in pack sizes of 4, 8, 20, 40 and 10 tablets.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary product packaging complies with EU legislation regarding contact with food.

**Stability of the product**

Stability studies were performed on batches of the finished product in the packaging proposed for marketing and in accordance with current guidelines. These data support a shelf-life of 24 months. Additionally for the polypropylene tube, do not use the product after 1 month from the date of first opening.

Storage instructions are 'Store in the original package/container to protect from moisture and light' and 'Do not store above 25°C'. The polypropylene tube has the additional sentence 'Keep the polypropylene tube tightly closed'.

**Summary of Product Characteristics (SmPCs), Patient Information Leaflet (PIL), Labels**

The SmPC, PIL and labelling are pharmaceutically acceptable.

User testing results have been submitted for a typical PIL for this product. The results indicate that the PIL is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that they contain.

**MAA forms**

The MAA form is pharmaceutically satisfactory.

**Expert report**

The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

**Conclusion**

It is recommended that a Marketing Authorisation is granted for this application.

### **III.2 NON-CLINICAL ASPECTS**

The pharmacodynamics, pharmacokinetics and toxicological properties of paracetamol are well-known. As paracetamol is a widely used, well-known active substance, the applicant has not provided any additional studies and none are required.

The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environmental Risk Assessment.

### **III.3 CLINICAL ASPECTS**

#### **CLINICAL PHARMACOLOGY**

This medicinal product is an effervescent preparation; therefore the submission of a bioequivalence study is not applicable according to the “Note for guidance on the investigation of bioavailability and bioequivalence” (CPMP/EWP/QWP/1401/98), which states that if the product is an aqueous oral solution at the time of administration and contains an active substance in the same concentration as an oral solution currently approved as a medicinal product, no bioequivalence study is required, provided the excipients contained in it do not affect gastrointestinal transit, absorption or *in vivo* stability of the active substance.

#### **EFFICACY**

No new efficacy data were submitted with this application and none were required.

#### **SAFETY**

No new safety data were submitted with this application and none were required.

#### **SUMMARY OF PRODUCT CHARACTERISTICS (SmPC), PATIENT INFORMATION LEAFLET (PIL) AND LABELLING**

The SmPC, PIL and labelling are medically satisfactory and consistent with those for the reference product, where appropriate.

#### **CLINICAL EXPERT REPORT**

The clinical expert report has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

#### **MAA FORM**

The MAA Form is medically satisfactory.

#### **CONCLUSIONS**

It is recommended that a Marketing Authorisation is granted for this application.

#### **IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT QUALITY**

The important quality characteristics of Paracetamol 1000 mg Effervescent Tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

#### **NON-CLINICAL**

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

#### **EFFICACY**

The applicant's Paracetamol 1000 mg Effervescent Tablets and the reference product Panadol Soluble 500 mg Effervescent Tablets are considered to be bioequivalent.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory and consistent with that for the reference product.

#### **RISK-BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. 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.

## Module 6

### STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

Date submitted	Application type	Scope	Outcome