Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Phizamol 500 mg effervescent tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 500 mg of Paracetamol.

Excipients with known effect:
Sodium content approximately 418.5 mg/tablet. Also contains sorbitol (E420) 100 mg /tablet.

For the full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Effervescent Tablet

White to off white round, flat, beveled edged plain on both side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of mild to moderate pain and/or fever.

4.2 Posology and method of administration

Posology

This presentation is reserved for use only in adults and in adolescents aged 12 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.

Pediatric Patients:

- Children below 12 years of age: Phizamol effervescent Tablet is not recommended in children aged less than 12 years.
- Adolescents of 12 to 15 years and weighing 41 to 50 kg the posology is one tablet per dose, repeated if necessary 4-6 hours later, without exceeding 4 tablets daily.

- Adolescents of 16 to 18 years and weighing more than 50 kg: as adults.

Adults:

The usual adults dose is one to two tablets of 500mg, repeated if necessary 4 hours later, without exceeding 3g of Paracetamol a day (i.e. 6 tablets).

Maximum daily dose:

- The maximum daily dose of Paracetamol must not exceed 3g.

- Maximum single dose is 1g (2 effervescent tablets)

Frequency of administration:

The specific dose interval depends on the symptoms and the maximum daily dose. Systematic administration enables to avoid pain or fever oscillation. Depending on the reoccurrence of symptoms (fever and/or pain), repeated administration is allowed. It should, however, preferably never fall below 6 hours and in no case fall below 4 hours. In adolescents administration should be regularly spaced, including nighttime, preferably at 6 hour intervals, otherwise at intervals of a minimum of 4 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.

Renal Insufficiency:

In case of renal insufficiency the dose should be reduced:

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

Impaired liver function:
In patients with impaired hepatic function 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 2g/day) in the following situations :

- adults weighing less than 50 kg
- mild to moderate hepatic insufficiency, Gilberts'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.

Method of administration

Phizamol 500 mg Effervescent Tablets are for oral administration. The tablets should be placed in a full tumbler of water and allowed to dissolve completely before swallowing.

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 adolescents 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 hepatic 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, hemolytic anemia, alcohol abuse dehydration 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 2 grams 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.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin, If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

This medicine contains 100 mg sorbitol in each tablet. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product

This medicinal product contains 418.5 mg sodium per dose, equivalent to 20.92% of the WHO recommended maximum daily intake for sodium.

The maximum daily dose of this product is equivalent to 125.55 % of the WHO recommended maximum daily intake for sodium.

Phizamol 500 mg Effervescent Tablet is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

In the case of high fever, or signs of secondary infection or persistence of symptoms a doctor should be consulted.

Immediate medical advice should be sought in the event of overdosage even if the patient feels well because of the risk of irreversible liver damage (see section 4.9).

4.5 Interaction with other medicinal products and other forms of interaction

Hepatotoxic substances may increase the possibility of Paracetamol accumulation and overdose. The risk of hepatotoxicity of paracetamol may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants, 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 t1/2 of Paracetamol
- Metoclopramide and Domperidone: accelerate absorption of Paracetamol
- Cholestyramine: reduces absorption of Paracetamol
- Concomitant use of Paracetamol (4 g 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. 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.
- 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 its metabolism in the liver.

Interference with laboratory tests: Paracetamol may affect uric acid tests by wolframatop phosphoric acid, and blood sugar tests by glucose-oxydase-peroxydase.
Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4)

4.6 Fertility, pregnancy and lactation

A large amount of data on pregnant women indicate neither malformative, norfeto/neonatal toxicity. Epidemiological studies on neurodevelopment inchildren exposed to paracetamol in utero show inconclusive results. Ifclinically needed, paracetamol canbe usedduring pregnancy however it should beused at the lowest effective dose for theshortest possible time and at the lowest possible frequency.

Breast-feeding:
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

Adverse events of paracetamol from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class and frequency.

The following convention has been utilised for the classification of the undesirable effects: very common (≥1/10); common (≥1/100 to < 1/10); uncommon (≥1/1000 to < 1/100); rare (≥1/10000 to < 1/1000); very rare (< 1/10000), including isolated reports; not known: frequency cannot be estimated from the available data. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Body System	Undesirable effect	Frequency
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis Leukopenia Hemolytic anemia	Very rare
Immune system disorders	Allergies (excluding angioedema)	Rare
	Anaphylactic shock Cutaneous hypersensitivity reactions including, among others, skin rashes and angiodema Hypersensitivity reaction (requiring discontinuation of treatment)	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm*	Very rare
	edema of the larynx	Unknown
Hepatobiliary disorders	Hepatic failure hepatic necrosis jaundice	Rare
	Hepatic dysfunction Hepatotoxicity	Very rare
Skin and subcutaneous tissue disorders	Pruritus rash sweating purpura urticaria	rare
	Toxic epidermal necrolysis Stevens Johnson syndrome Erythema multiforme	Unknown
Psychiatric disorders	Depression NOS confusion hallucinations	Rare

Nervous system disorders	Tremor NOS headache NOS	Rare
Eye disorders	Abnormal vision	Rare
Cardiac disorders	Oedema	Rare
Gastrointestinal disorders	Haemorrhage NOS abdominal pain NOS diarrhoea NOS nausea vomiting	Rare
General disorders and administration site conditions	Dizziness (excluding vertigo) malaise pyrexia sedation drug interaction NOS	Rare
Injury, poisoning and procedural complications	Overdose and poisoning	Rare
Metabolism and nutrition disorders	Hypoglycaemia	Very rare
	High anion gap metabolic acidosis	Not known
Renal and urinary disorders	Sterile pyuria (cloudy urine) and renal side effects (Severe renal impairment, Tubulointerstitial nephritis, Haematuria, Enuresis)	Very rare

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Description of selected adverse reactions
High anion gap metabolic acidosis
Cases of high anion gap metabolic due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

There is a risk of poisoning, particularly in elderly subjects, in young adolescents, in patients with liver disease, in cases of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal.

Liver damage is possible in adults who have taken 10g 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 overdosage 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. 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.

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

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.

High doses of sodium bicarbonate may be expected to induce gastrointestinal symptoms including belching and nausea. In addition, high doses of sodium bicarbonate may cause hypernatraemia; electrolytes should be monitored and patients managed accordingly.

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.

Biotransformation
Paracetamol is metabolized mainly in the liver following two major metabolic pathways: glucuronic acid and sulphuric 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 cystein and mercaptopuric 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.

Physiopathological Variations
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, sub chronic 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 sub toxic 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.

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous citric acid
Sodium hydrogen carbonate
Sorbitol E420
Sodium carbonate anydrous
Povidone K 25 (E1201)
Simeticone
Saccharin sodium
Lemon flavour (containing maize maltodextrin, acacia gum (E414) and alpha-tocopherol (E307))
Macrogol 6000

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 30°C. Keep the polypropylene tube tightly closed. Store in the original container to protect from the moisture and light.

6.5 Nature and contents of container

White opaque plain polypropylene tube and white opaque tamper evident polyethylene cap with inbuilt desiccant. Contains 24 tablets, 20 tablets, 8 tablets or 10 tablets in a tube.
Pack size: 60 (3 x 20) tablets per carton.
20 (1 x 20) tablets per carton
10 (1 x 10) tablets per carton
16 (2 x 8) tablets per carton
30 (3 x 10) tablets per carton
24 (3 x 8) tablets per carton.
24 (1 x 24) tablets per carton

100 (5 x 20) tablets per carton

Pack size: 20 tablets in a tube per carton.
10 tablets in a tube per carton.
8 tablets in a tube per carton.
24 tablets in a tube per carton.

Strip packs:

Pack size(s) for Alu-Alu strip pack:
4's tablets per carton
8's tablets per carton
10's tablets per carton
16 tablets per carton
20 tablets per carton
24 tablets per carton
30 tablets per carton
32 tablets per carton
60 tablets per carton
100 tablets per carton

Pack size(s) for Paper/PE/Aluminium/Surlyn strip pack:
8's tablets per carton
10's tablets per carton
16 tablets per carton
20 tablets per carton
24 tablets per carton
30 tablets per carton
32 tablets per carton
60 tablets per carton
100 tablets per carton

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Ireland Ltd.
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Euro Business Park
Little Island
Cork T45 K857
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2315/065/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 30th May 2012

10 DATE OF REVISION OF THE TEXT

March 2025