1.3.1 Summary of product characteristics

1. Name of the medicinal product

BRUSTAN EXTRA (Paracetamol 325 mg, Caffeine 30 mg and Ibuprofen 200 mg Capsules)

2. Qualitative and quantitative composition

Each Soft gelatin capsule contains:

Paracetamol BP 325mg

Ibuprofen BP 200mg

Caffeine BP 30mg

Qualitative

S.No	Ingredients	Specification	Functions
1.	Paracetamol	BP	Analgesic
2.	Ibuprofen	BP	NSAIDs
3.	Caffeine	BP	CNS stimulant
4.	Polyethylene glycol 400	BP	Plasticizer
5.	Propylene glycol	BP	Pharmaceutical aid.
6.	Gelatin	BP	Gelling agent
7.	Glycerol	BP	Plasticizer
8.	Liquid Sorbitol (Non Crystallizing)	BP	Plasticizer
9.	Methyl Hydroxybenzoate	BP	Antimicrobial preservative
10.	Propyl Hydroxybenzoate	BP	Antimicrobial preservative
11.	Titanium dioxide	BP	Opacifier
12.	Allura red AC	IHS	Colouring agent
13.	Purified water	BP	Vehicle

Quantitative Composition

S.No	Ingredients	Specifi-cation[1]	Over -ages %	Qty per capsule (mg)	Qty per batch (kg)*	Function
Fill Materials						
1	Paracetamol	BP	--	325.000	81.250	Analgesic
2	Ibuprofen	BP	--	200.000	50.000	NSAIDs
3	Caffeine	BP	--	30.000	7.500	CNS stimulant
4	Polyethylene glycol 400	BP	--	335.000	83.750	Plasticizer
5	Propylene glycol	BP	--	10.000	2.500	Pharmaceutical aid.
Shell materials[2]						
6	Gelatin	BP	--	190.364	47.591	Gelling agent
7	Glycerol	BP	--	50.734	12.684	Plasticizer
8.	Liquid Sorbitol (Non Crystallizing)	BP	--	25.411	6.353	Plasticizer
9.	Methyl Hydroxybenzoate	BP	--	1.142	0.286	Antimicrobial preservative
10.	Propyl Hydroxybenzoate	BP	--	0.115	0.0288	Antimicrobial preservative
11.	Titanium dioxide	BP	--	2.019	0.505	Opacifier
12.	Allura red AC	IHS	--	0.214	0.0535	Colouring agent
13.	Purified water	BP	--	q.s	q.s	Vehicle

[1] Current Pharmacopoeial Monographs are implied

[2] In the batch formula excess material is added to compensate process loss. Process loss is due to cooking tank wastages, placebo wastages, service tank/spreader box retention, net wastage and Miscellaneous.

Abbreviation:

BP : British Pharmacopoeia

IHS : In-House Specification

3. Pharmaceutical Form

Pink colour oval shaped opaque soft gelatin capsules containing white colour oily mass.

4 Clinical particulars

4.1 Therapeutic indications

Paracetamol, Ibuprofen, Caffeine Capsules are a non-steroidal anti-inflammatory drug (NSAID). It is used for relief of symptoms of arthritis, primary dysmenorrhea, fever, and as an analgesic, especially where there is an inflammatory component. Ibuprofen is known to have an antiplatelet effect, though it is relatively mild and short-lived when compared with that of aspirin or other better-known antiplatelet drugs.

Paracetamol, or acetaminophen, is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer). It is used to treat many conditions such as headaches, migraine, muscle aches, arthritis, backache, toothaches, colds, and fevers.

Caffeine, the world's most common stimulant, is used in this drug combination to speed up the action of the drug.

4.2 Posology and method of administration

Oral Route. Taken with water.

4.3 Contraindications

Hypersensitivity to paracetamol, caffeine, ibuprofen and other constituents.

- This medicine should not be used by people who have been diagnosed with hypertension or who are receiving antihypertensive medication, or who have a history of cardiac arrhythmia
- This medicine should not be used by patients recovering from chronic alcoholism who are taking disulfiram.
- This medicine should not be used if antidepressants (including lithium carbonate), anxiolytics (including clozapine) and sedatives are being used, or by persons with anxiety disorders.
- This medicine should not be used by any persons who are also taking ephedrine.
- Caffeine shares the same metabolic pathway as theophylline and therefore this medicine should be used concurrently with theophylline.
- Ibuprofen is contra-indicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.
- Active or previous peptic ulcer (two or more episodes of proven ulceration or bleeding).

- History of upper gastrointestinal bleeding or perforation, related to pervious NSAID therapy.
- Should not be given to patients who are pregnant or breastfeeding.
- Patients with severe hepatic failure, renal failure or severe heart failure

4.4 Special warnings and precautions for use

- Kidney problems can sometimes occur with the use of NSAID medications, including Ibuprofen. Problems are more likely to occur if you are dehydrated, have heart failure or kidney disease, are an older adult, or if you take certain medications.
- This drug may make you dizzy or drowsy. Do not drive, use machinery, or do any activity that requires alertness until you are sure you can perform such activities safely. Limit alcoholic beverages.
- This medicine may cause stomach bleeding. Daily use of alcohol and tobacco, especially when combined with this medicine, may increase your risk for stomach bleeding. Daily use of alcohol and tobacco, especially when combined with this medicine, any increase your risk for stomach bleeding. Limit alcohol and stop smocking.
- Older adults may be more sensitive to the effects of this drug, especially stomach/intestinal bleeding and kidney problems.
- Patients should be advised to consult their doctor if their headache becomes persistent.
- Do not exceed the stated dose
- Do not take with any other paracetamol ibuprofen and caffeine containing products.
- Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non cirrhotic alcoholic liver disease.
- Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.
- Caution should be taken when ibuprofen is given to patients with SLE and autoimmune diseases

4.5 Interaction with other medicinal products and other forms of interaction

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

Ibuprofen should be avoided in combination with aspirin. Ibuprofen should be used with caution in combination with Anticoagulants, Antihypertensives and diuretics, corticosteroids, Anti-platelet agents and selective serotonin reuptake inhibitors (SSRI's), Cardiac glycosides, Lithium, Methotrexate, Cyclosporin, Mifepristone, Tacrolimus, Zidovudine and Quinolone antibiotics.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no experience of use of this product in humans during pregnancy. Congenital abnormalities have been reported in association with NSAID administration in man; however these are low in frequency and do not appear to follow any discernible pattern. In view of the known affects of NSAIDs on the foetal cardiovascular system (risk of closure of ductus arteriosus), use in the last trimester is contraindicated. The onset of labour may be delayed and duration increased with an increased bleeding tendency in both mother and child (see Section 4.3). NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus. Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol use at the recommended dosage. Therefore if possible, the use of this product should be avoided in the first six months of pregnancy and contraindicated in the last three months of pregnancy (see Section 4.3).

Lactation

Ibuprofen and its metabolites can pass in very small amounts (0.0008% of the maternal dose) into the breast milk. No harmful effects to infants are known. Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breastfeeding. Therefore it is not necessary to interrupt breastfeeding for short-term treatment with the recommended dose of this product.

4.7 Effects on ability to drive and use machines

Some undesirable effects (e.g. dizziness/vertigo, drowsiness, visual disturbances) may impair the patient's ability to concentrate and react, and therefore may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

4.8 Undesirable effects

Central Nervous System: headache, shaky feeling, tingling, agitation, fainting, fatigue, heavy eyelids, high energy, hot spells, numbness, sluggishness, seizure. Mental confusion, excitement, or depression can also occur due to intolerance, particularly in elderly or debilitated patients

Autonomic Nervous System : Dry mouth, hyperhidrosis.

Gastrointestinal : Difficulty swallowing, heartburn, flatulence, constipation.

Cardiovascular : Tachycardia.

Musculoskeletal : Leg pain, muscle fatigue.

Genitourinary : Diuresis.

Miscellaneous : Pruritus, fever, earache, nasal congestion, tinnitus, euphoria, allergic reactions.

4.9 Overdose

Paracetamol:

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

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.

Caffeine:

Overdose of caffeine may result in epigastric pain, vomiting, diuresis, tachycardia or cardiac arrhythmia, CNS stimulation. 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 administration.

Ibuprofen:

In children ingestion of more than 400mg/kg may cause symptoms. In adults the dose response is less clear cut. The half-life in overdose is 1.5-3 hours. Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, Vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Paracetamol:

Paracetamol is an antipyretic analgesic. The mechanism of action is probably by the inhibition of prostaglandin synthesis. The inhibition appears, however, to be on a selective basis.

Caffeine:

Caffeine, a methylxanthine, is a phosphodiesterase inhibitor. It has an antagonistic effect at central adenosine receptors. It is a CNS and respiratory stimulant. It has bronchodilating and diuretic properties and it facilitates the performance of muscular work.

Caffeine is a central nervous system and metabolic stimulant, and is used both recreationally and medically to reduce physical fatigue and to restore alertness when drowsiness occurs. It produces increased wakefulness, faster and clearer flow of thought, increased focus, and better general body coordination. The amount of caffeine needed to produce effects varies from person to person, depending on body size and degree of tolerance. Effects begin less than an hour after consumption, and a moderate dose usually wears off in about five hours. Caffeine has a number of effects on sleep. It improves performance during sleep deprivation but may lead to subsequent insomnia.

Ibuprofen:

Ibuprofen: Ibuprofen is a nonsteroidal antiinflammatory agent (NSAID) or nonsteroidal anti-inflammatory drug (NSAID), with analgesic and antipyretic properties. Ibuprofen is a

propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis.

5.2 Pharmacokinetic properties

Paracetamol:

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. The concentration in plasma reaches a peak in 30 to 60 minutes and the half life in plasma is 1 to 4 hours after therapeutic doses. Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of the drug to plasma proteins is variable; 20 to 50% may be bound at the concentrations encountered during acute intoxication. Following therapeutic doses 90 to 100% of the drug may be recovered in the urine within the first day. However, practically no paracetamol is excreted unchanged, and the bulk is excreted after hepatic conjugation.

Caffeine:

Absorption : Readily absorbed after oral admin.

Distribution : Widely distributed throughout the body.

Metabolism : Metabolised almost completely hepatically via oxidation, demethylation and acetylation.

Excretion : Excreted in the urine as 1-methyluric acid, 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine, 5-acetylamino-6-formylamino-3-methyluracil and other metabolites with only about 1% unchanged.

Ibuprofen:

Absorption: 80% absorbed from 01 tract .Time to reach peak plasma concentration 47 minutes (suspension), 62 minutes (chewable tablets), 120 minutes (conventional tablets).

Protein binding: 90-99% to whole human plasma and Site 11 of purified albumin, binding appears to be saturable and becomes non-linear at concentrations exceeding 20 meg/mI.

Excretion: ibuprofen is rapidly metabolized and eliminated in the urine.

Half life: 2-4 hours

5.3 Preclinical safety data

The toxicological safety profile of paracetamol, caffeine & ibuprofen capsules has been established in animal experiments and in humans from extensive clinical experience. There are no new preclinical data of relevance to the prescriber which are additional to the data already presented in this Summary of Product Characteristics.

6. Pharmaceutical particulars

6.1 List of excipients

S.No	Ingredients	Specification	Reason for inclusion
1.	Polyethylene glycol 400	BP	Plasticizer
2.	Propylene glycol	BP	Pharmaceutical aid.
3.	Gelatin	BP	Gelling agent
4.	Glycerol	BP	Plasticizer
5.	Liquid Sorbitol (Non Crystallizing)	BP	Plasticizer
6.	Methyl Hydroxybenzoate	BP	Antimicrobial preservative
7.	Propyl Hydroxybenzoate	BP	Antimicrobial preservative
8.	Titanium dioxide	BP	Opacifier
9.	Allura red AC	IHS	Colouring agent
10.	Purified water	BP	Vehicle

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

Keep out of reach of children.

6.5 Nature and contents of container

BRUSTAN EXTRA (Paracetamol 325 mg, Caffeine 30 mg and Ibuprofen 200 mg Capsules) are packaged into 1 x 10's Blister Pack along with insert.

6.6 Special Precautions for Disposal and Other Handling

Not applicable.

6.7 Marketing authorization holder

6.8 Marketing authorization Number

6.9 Date of first authorization/renewal of the authorization

6.10 Date of revision of the text-Nil