SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Finished Pharmaceutical Product

1.1 Proprietary Name

GOFEN 400MG SOFT GEL CAPSULES

1.2 Strength

EACH SOFT GELATIN CAPSULE CONTAINS : IBUPROFEN EQUIVALENT TO IBUPROFEN 400MG (PRESENT AS FREE ACID AND POTASSIUM SALT)

1.3 Pharmaceutical Form

Capsules, Soft Gelatin

2. Qualitative and Quantitative Composition

2.1 Qualitative Declaration

2.2 Quantitative Declaration

Active Ingredient	Specification	Claim (mg/cap)	Content / capsule
Ibuprofen	USP Current Edition	400.00	400.00

'For full list of excipients, see section 6.1

3. Product description

Clear Colurless, oily, liquid filled in 20 minim, oblong, green, Transparent soft gelatin shell capsules.

4. Clinical Particulars

4.1 Therapeutic Indications

- Temporarily relief of minor aches and pain associated with the common cold, headache, toothache, muscular aches, backache, minor pain of arthritis, pain of menstrual cramps (dysmenorrhea).
- Temporarily reduces fever.

4.2 Posology and method of administration

Adults and children over 12 years: Take 1 capsule every 4-6 hours while symptoms occur.

Method of Administration: Oral

4.3 Contraindications

- Contraindicated in person with known hypersensitivity to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs).
- Ibuprofen may cause a severe allergic reaction which may include hives, facial swelling, asthma or shock.

4.4 Special Warnings and Precautions for Use

- Should not be administered with other nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin due to potentiate adverse gastrointestinal effect.
- Should not take with alcoholic drink.
- Use with caution in person with peptic ulcer disease.
- Stop taking Ibuprofen and consult physician if fever persist more than 3 days and/ or pain persist more than 10 days.

4.5 Interaction with other medicinal products and other forms of interaction

None reported.

4.6 Fertility, pregnancy and lactation

Not recommended in lactating women and during pregnancy (especially during the last trimester) or during labor and delivery.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable Effects

The most frequent adverse effects of Ibuprofen involve the irritation of gastrointestinal tract.

4.9 Overdose

Not applicable.

5. Pharmacological properties

5.1 Pharmacodynamic Properties

Pharmacology of Ibuprofen

Mechanism of Action of Ibuprofen [8,9]

Ibuprofen possesses analgesic, antipyretic and anti-inflammatory properties, similar to other non-steroidal anti-inflammatory drugs (NSAIDs). Its mechanism of action is unknown, but is thought to be throough peripheral inhibition of cyclooxygenases and subsequent prostaglandin synthetase inhibition.

NSAIDs inhibit cyclooxygenases (COX) – the enzyme responsible for the transformation of arachidonic acid into prostaglandins and thromboxanes, which are substances generically referred to as eicosanoids because their precursors contain 20 carbon atoms. Arachidonic acid is fundamentally found in the cell membrance, where it is bound to phospholipids. Physical, chemical or mechanical stimuli (tissue damage, hypoxia, immune processes, etc.) induce arachidonic acid release and metabolization. The resulting metabolites (prostaglandins and thromboxanes) exert effects on practically alll body organs and tissues. In relation to inflammation, the prostaglandins generally exert potent vasodilating action, resulting in increased vascular permeability, with the extravasation of fluids and white blood cells – all these phenomena contributing to inflammation. Consequently, the inhibition of cyclooxygenase synthesis exerts a clear anti-inflammatory effect.

NSAIDs and Prostaglandin (PG) Synthesis inhibition

In 1971 Vane and coworkers made the landmark observation that aspirin and some NSAIDs blocked PG generation. This is now considered to be the major mechanism of action of NSAIDs. Prostaglandins, prostacyclin (PG I_2) and thromboxane A_2 (TXA_2) are produced from arachidonic acid by the enzyme cycloxygenase which exists in a constitutive (COX-1) and an inducible (COX-2) isoforms; the former serves physiological 'house keeping' functions, while the latter, normally present in minute quantities, is induced by cytokines and other signal molecules at the site of inflammation generation of PGs locally which mediate many of the inflammatory changes. Most NSAIDs inhibit COX-1 and COX-2 nonselectively, but now some selective COX-2 inhibitors have been produced.

Aspirin inhibits COX irreversibly by acetylating one of its serine residues; return of COX activity depends on synthesis of fresh enzyme. Other NSAIDs are competitive and reversible inhibitors of COX, return of activity depends on their dissociation from the enzyme which in turn is governed by the pharmacokinetic characteristics of the compound.

Beneficial action due to PG Synthesis inhibition

- Analgesia: prevention of pain nerve ending sensitization
- Antipyresis
- Antiinflammatory
- Antithrombotic
- Closure of ductus arteriosus

Shared toxicities due to PG synthesis inhibition

- Gastric mucosal damage
- Bleeding: inhibition of platelet function
- Limitation of renal blood flow ; Na^+ and water retention
- Delay/prolongation of labour
- Asthma and anaphylactoid reactions in susceptible individuals

Analgesia (Pain)

PGs induce hyperalgesia by affecting the transducing property of free nerve endings—stimuli that normally donot elicit pain are able to do so. NSAIDs do not affect the tenderness induced by direct application of PGs, but block the pain sensitizing mechanism induced by bradykinin, TNFα interleukins (ILs) and other analgesic substances. They are therefore more effective against inflammation associated pain.

Antipyresis (Fever)

Some NSAIDs such as ibuprofen, aspirin, mefenamic acid etc. reduce body temperature in fever, but do not cause hypothermia in normothermic individuals. Fever during infection is produced through the generation of pyrogen, ILs, TNFα, interferons which induce PG production in hypothalamus—raise its temperature set point. NSAIDs block the action of pyrogens but not that of PGE_2 injected into the hypothalamus. However, fever can occur through non-PG mediated mechanisms also; inhibition of COX does not entirely explain the antipyretic action of NSAIDs.

Antiinflammatory (Inflammation)

The most important mechanism of anti-inflammatory action of NSAIDs is considered to be inhibition of PG synthesis at the site of injury. The anti-inflammatory potency of different compounds roughly corresponds with their potency to inhibit COX. However, nimesulide is a potent anti-inflammatory but relatively weak COX inhibitor. PGs are only one of the mediators of inflammation; inhibition of COX does not depress the production of other mediators like LTs, PAF, cytokines etc. Inflammation is the result of concerted participation of a large number of vasoactive, chemotactic and proliferative factors at different stages, and there are many targets for anti-inflammatory action.

Activated endothelial cells express adhesion molecules (ECAM-1, ICAM-1) on their surface and play a key role in directing circulating leukocytes to the site of inflammation. Similarly inflammatory cells express *selectins* and *integrins*. Certain NSAIDs may act by additional mechanisms including inhibition of expression/activity of some of these molecules. Growth factors like GM-CSF, IL-6 and lymphocyte transformation factors may also be affected. Stabilization of leukocyte lysosomal membrane and antagonism of certain actions of kinins may be contributing to NSAIDs action.

5.2 Pharmacokinetic Properties

Ibuprofen is rapidly absorbed after oral administration in man, and peak concentrations in plasma are observed after 1 to 2 hours. The half-life in plasma is about 2 hours. Absorption is also efficient, although slower, from suppositories.

Ibuprofen is extensively (99%) bound to plasma proteins, but the drug occupies only a fraction of the total drug-binding sites at usual concentrations. Ibuprofen passes slowly into the synovial spaces and may remain there in higher concentration as the concentrations in plasma decline. In experimental animals, ibuprofen and its metabolites pass easily across the placenta.

The excretion of ibuprofen is rapid and complete. More than 90% of an ingested dose is excreted in the urine as metabolites or their conjugates; and no ibuprofen *per se* is found in the urine. The major metabolites are a hydroxylated and a carboxylated compound.

Table 1. Pharmacokinetic profile of Ibuprofen in human

Drug	BA* (%)	Half-life (hr)	Vol.** Dist. (L/kg)	Clearance (L/hr)	Peak (hr)	Protein-bound (%)	Urinary excretion (%)	Fecal excretion (%)
Ibuprofen	> 80	1.8-2	0.15	3-3.5	1-2	99%	45-79	-

* Bioavailability

5.3 Preclinical Safety Data

Not applicable.

6. Pharmaceutical Particulars

6.1 List of Excipients

Inactive :

Polyethylene Glycol 600

Potassium hydroxide

Purified water

Capsule shell :

Gelatin

Sorbitol 70% solution

Purified Water

FD & Green no. 3

6.2 Incompatibilities

None.

6.3 Shelf Life

24 months

6.4 Special Precautions for Storage

Store below 30°C in a dry place, away from direct sunlight.

6.5 Nature and Contents of Container

Unit carton containing 6x10 capsules blister packed.

Aluminium foil:	Printed aluminium foil Blister film: PVC/PVDC film
Outer Carton:	Printed cardboard carton

6.6 Special precaution for disposal and other handling

No special requirements.

7. Marketing Authorization Holder and Manufacturing Site Addresses

MEGA LIFESCIENCES Public Company Limited

384 Moo 4, Soi 6, Bangpoo Industrial Estate,

Pattana 3 Road, Phraeksa, Mueang,
Samutprakarn 10280, Thailand.

8. Marketing Authorization Number: N/A

9. Date of first Registration/ Renewal of the Registration

N/A

10. Date of revision of the text: February 2023