

Advalgin®

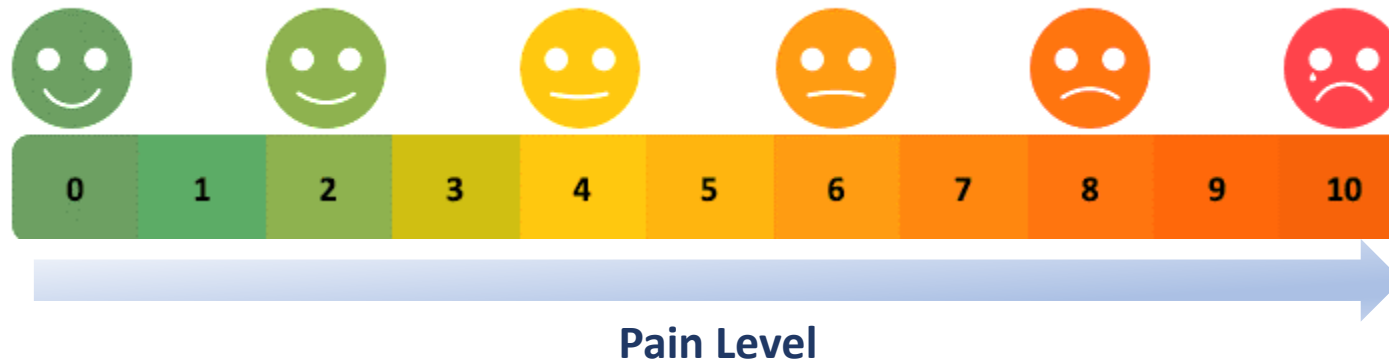
Ibuprofen Extended-Release **ER 600**



The Impact of Pain on Quality of Life

When it is ongoing and uncontrolled, has a detrimental, deteriorative effect on virtually every aspect of a patient's life.

- It produces **anxiety and emotional distress**
- Undermines well-being
- Interferes with functional capacity
- Hinders the ability to fulfill family, social, and vocational roles



Effect of Analgesic Therapy on Patient's Quality of Life

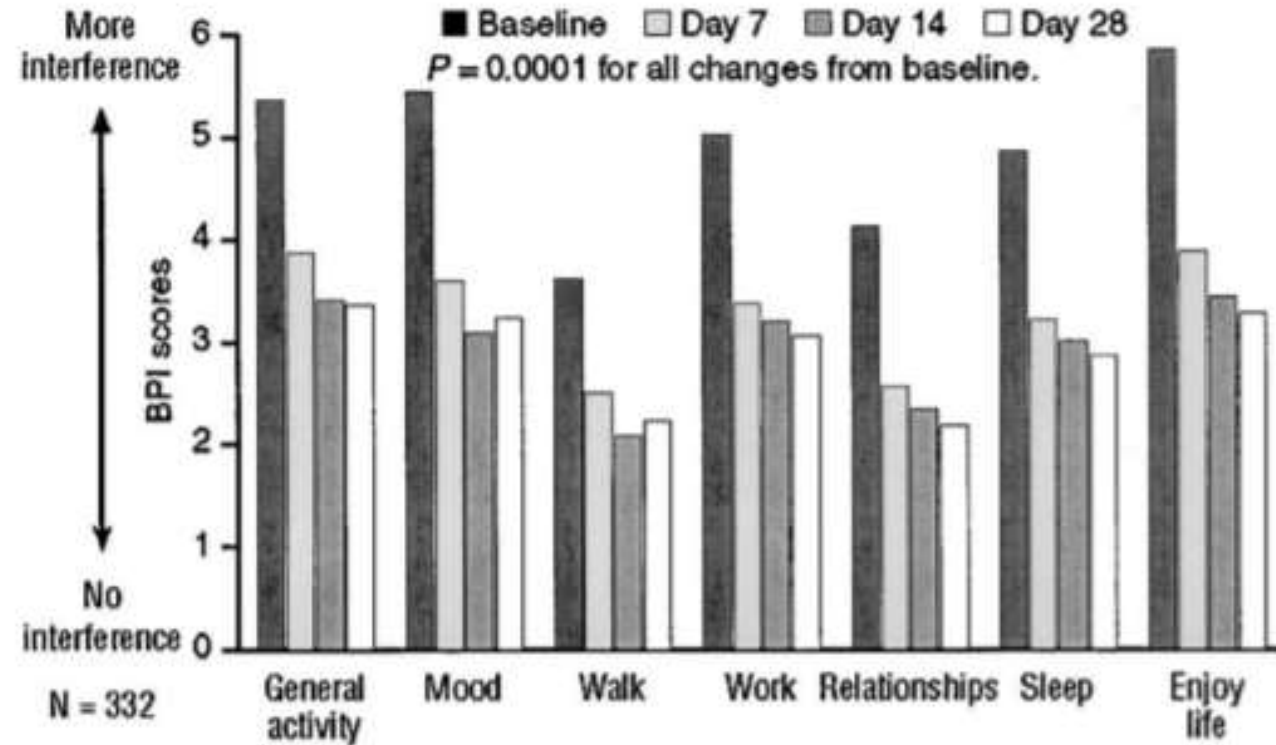


Fig. 3. Effect of analgesic therapy with lidocaine patch 5% on quality-of-life indicators in patients with postherpetic neuralgia.²⁶ BPI = Brief Pain Inventory. Adapted with permission from Ref. 26.

The Four Major Types of Pain

1. Nociceptive Pain

Typically the result of **tissue injury**. Common types of nociceptive pain are **arthritis pain**, **mechanical back pain** or post surgical pain.

2. Inflammatory Pain

An abnormal inflammation caused by an inappropriate response by the body's immune system. Conditions in this category include **gout and rheumatoid arthritis**.

3. Neuropathic Pain

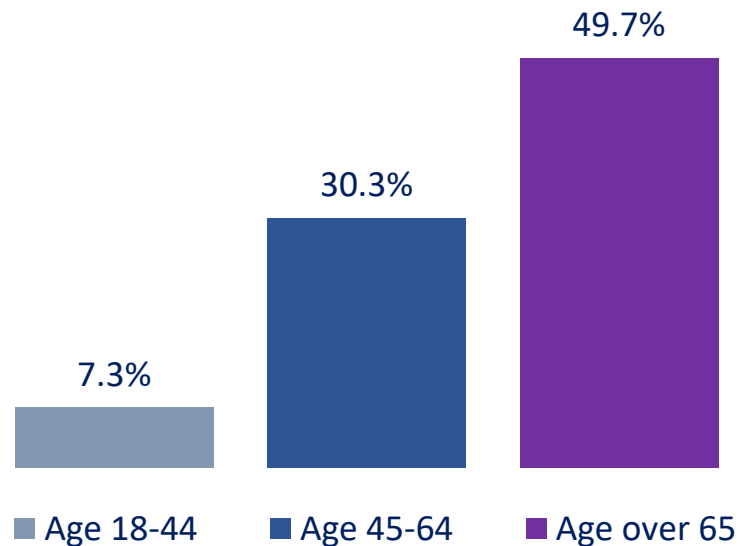
Pain caused by **nerve irritation**. This includes conditions such as neuropathy, **radicular pain** and **trigeminal neuralgia**.

4. Functional Pain

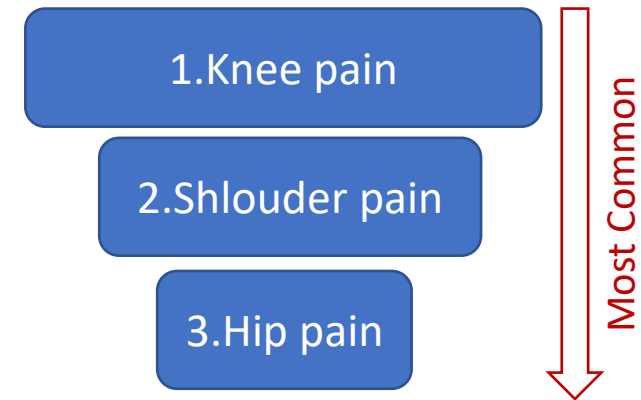
Pain **without obvious origin**, but can cause pain. Examples of such conditions are **fibromyalgia**.

Prevalence and Burden of Osteo-articular Disorders

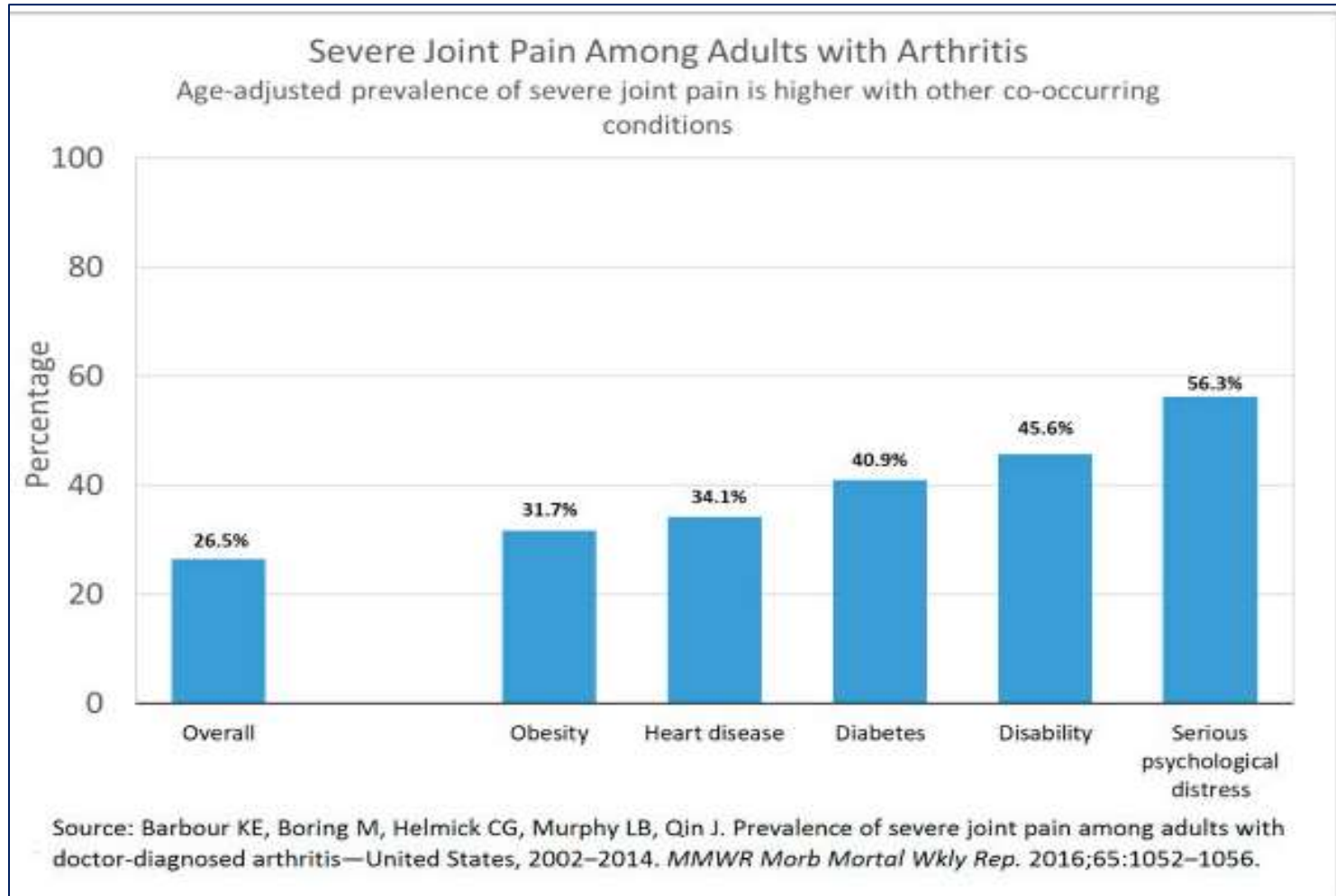
- More than **22%** of adults have **arthritis** or another **rheumatic condition** diagnosed by a doctor:



- About **one-third** of adults reported having joint pain within the past 30 days.



Thus, pain related to OA contribute to a **substantial socioeconomic burden.**



Severe joint pain is more common among adults with arthritis who also have other chronic conditions including:

- Diabetes (**40.9%**)
- Heart disease (**34.1%**)
- Obesity (**31.7%**)
- Adults with a disability (**45.6%**)

❑ Pain Pharmacotherapy

- Nociceptive pain usually is treated with **anti-inflammatory or analgesic medications**.
- Neuropathic pain typically is treated with medications that influence neurotransmitters (e.g., **antidepressants, antiepileptic drugs**), and treatment with **opioids** is reserved for patients with **refractory neuropathic pain**.

1. Acetaminophen
2. NSAIDs
3. Tricyclic antidepressants
4. SSRIs
5. Anticonvulsants
6. Opioids
7. Muscle relaxants



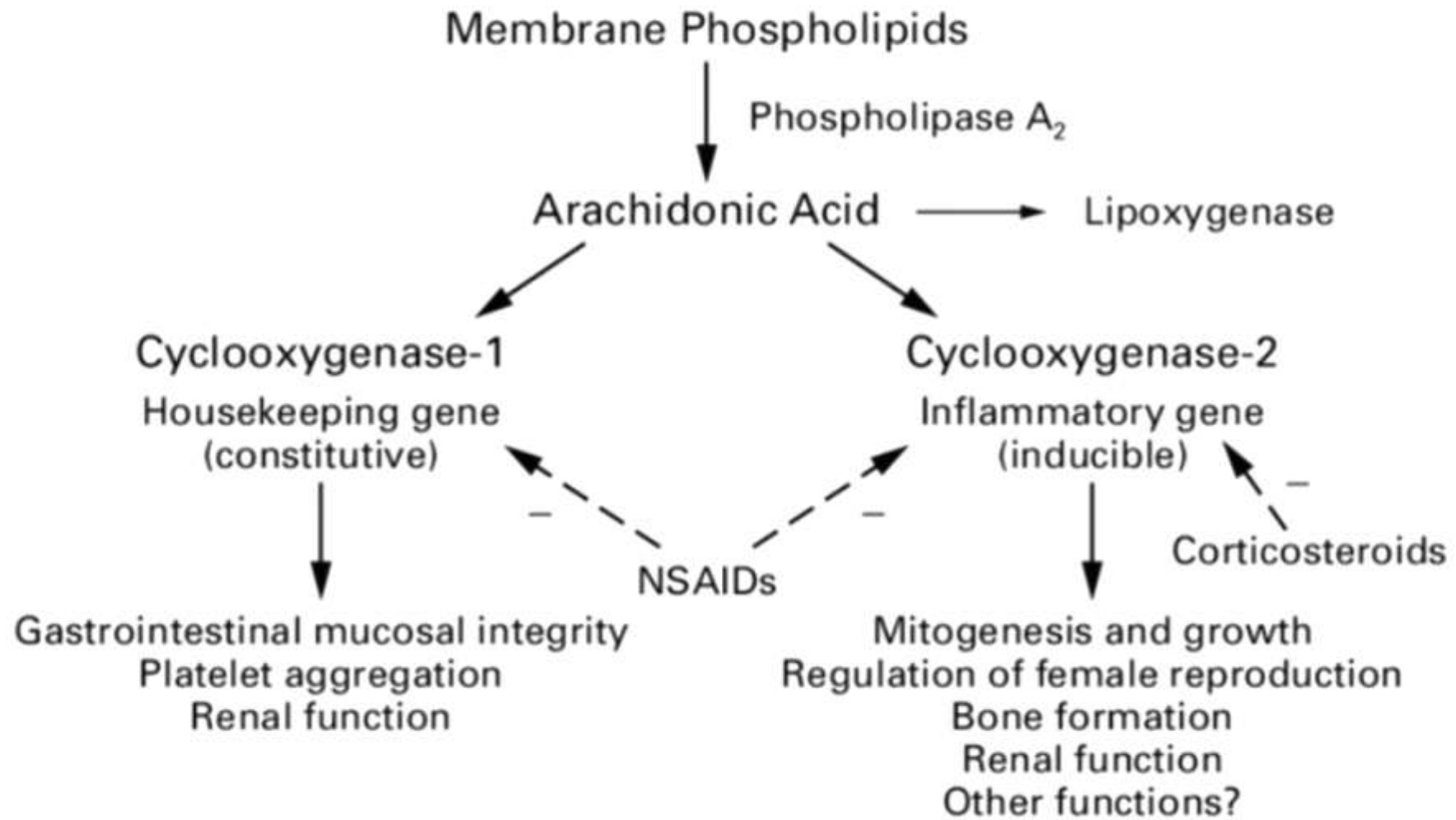
The main mechanism of action of Ibuprofen
(like other NSAIDs)



Decreasing prostaglandin biosynthesis

Prostaglandins are naturally-occurring fatty acid derivatives that are widely distributed in the tissues. They are believed to be a common factor in the production of **pain, fever, and inflammation.**





Formulation and delivery strategies of ibuprofen

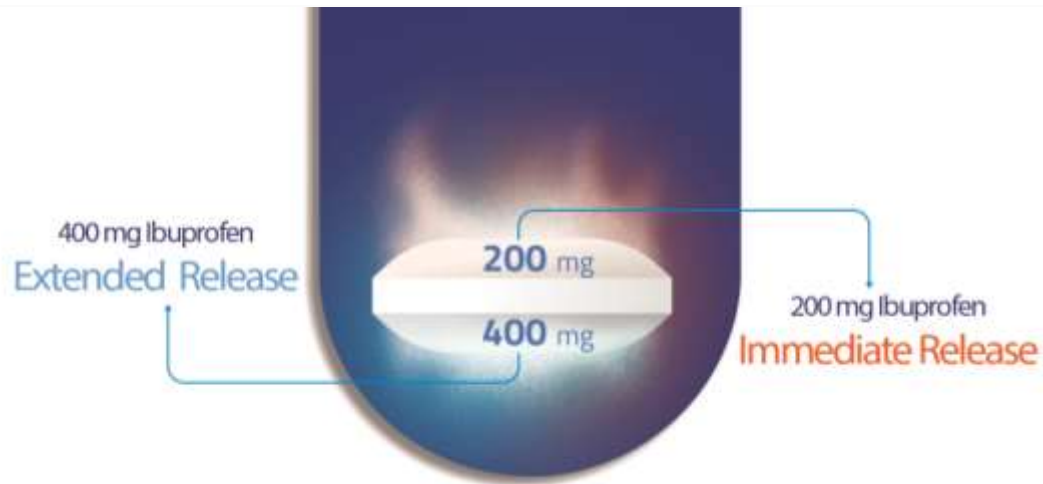
- ✓ It is **poorly soluble** in aqueous media.
- ✓ The **rate of dissolution** from the currently available solid dosage forms is limited.
- ✓ This leads to **poor bioavailability** at high doses after oral administration
- ✓ Thereby increasing the **risk of unwanted adverse effects**.



Different Approaches to Enhance the Solubility of Ibuprofen

- ✓ Mechanical micronization (The submicron size of pharmaceutical particles offers the opportunity to deliver poorly soluble drugs, like Ibuprofen.)
- ✓ Solid dispersion
- ✓ Self-emulsifying drug delivery system
- ✓ Using surfactants
- ✓ Block copolymers

Bilayer tablet is a new concept for **the successful development of controlled release formulation** along with various features to provide a way of **successful drug delivery system**.



- ✓ Bilayer tablets can be a primary option to **avoid chemical incompatibilities** between Active Pharmaceutical Ingredient (API) by physical separation and to **enable the development of different drug release profiles-immediate release with extended release**.

The Advantages of Modified Release Oral Dosage Forms

The ability to control the rate of drug release, makes clinical objectives that cannot be achieved using conventional dosage forms:

Modified-release (MR) drug delivery advantages

MR
Drugs

MR oral dosage forms can **improve efficacy** and **prevent adverse events** as well as, **increase convenience and patient compliance**.

MR pellet technology allows to **modify the rate of release** as well as **reduce the number of doses** required per day which is ultimately more efficient for the patient.

Bi-Layer technology with 12 hours pain relief

composition

- 600mg Ibuprofen per tablet:
 - 200 mg Ibuprofen Immediate release
 - 400 mg Ibuprofen Extended release (**Provides long lasting pain relief**)

Indications

- Chronic pain such as OA, musculoskeletal pain, joint pain

Administration

- One tablet every 12 hours for patients older than 12 years of age.



Relief of minor aches and pains in

- Muscles
- Bones and joints
- Body pain
- Backache
- Muscle sprains and strains

Pain from inflammation associated with conditions including:

- Arthritis
- Headache pain
- Menstrual pain
- Toothache (dental pain);
- Aches and pains due to the common cold and flu



Advantages of Advalgin ER



- 1 Less side effects
- 2 Provides sustained plasma drug levels over an extended duration of time
- 3 Bioequivalent to ibuprofen 200 mg IR q4h
- 4 Provides more consistent pain relief
- 5 Less frequent dosing may also be more convenient for patients
- 6 Reduces the need for rescue medication

Proportion of Patients Able to Carry out Normal Activities

4 Weeks
treatment with
Ibuprofen ER*

Patients suffering from **chronic** and mostly **moderate-to severe osteoarthritic pain** reported significant improvements in day and night pain, reduced symptom severity of joint tenderness/stiffness and increased ability to carry out normal activities.

In multiple-dose studies, ibuprofen 1200 mg/day has been found to be at least as effective as acetaminophen **3000–4000 mg/day** in **relieving pain** associated with osteoarthritis.

Clinical Pharmacology in Drug Development 2017, 6(3) 302–312

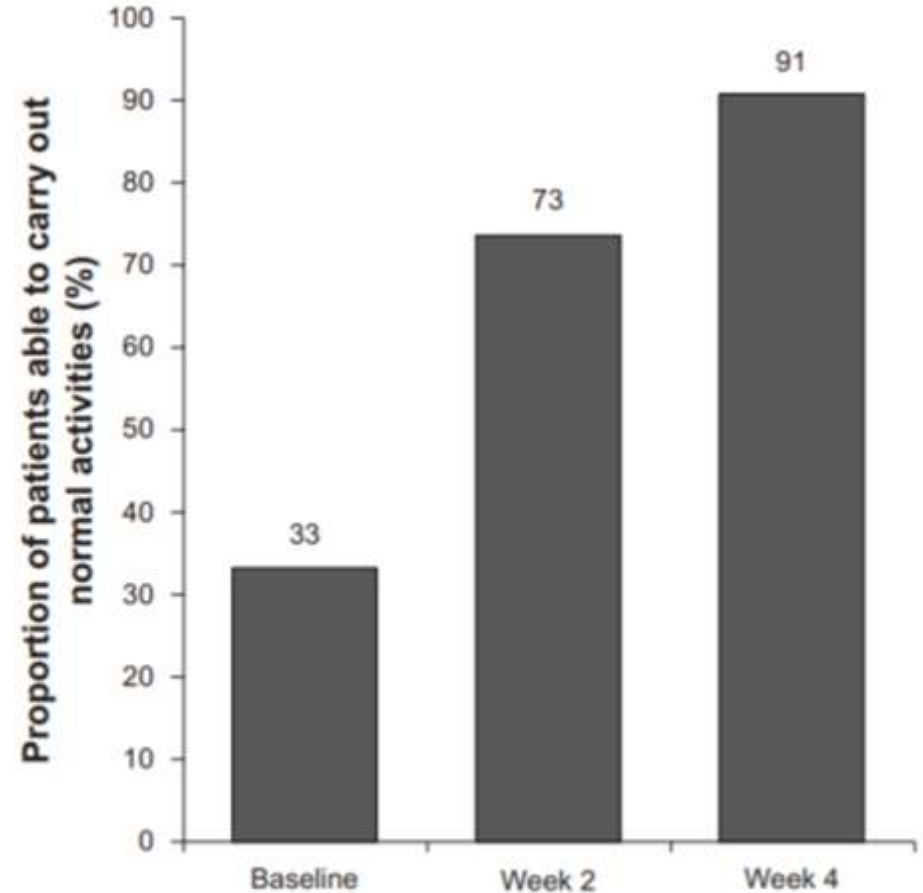


Figure 2 Ability to carry out normal activities before (baseline) and after 2 and 4 weeks of treatment.

ANNEX



Use with Caution

- In patients with heart failure, hypertension or other conditions predisposing to fluid retention.
- Patients with impaired renal function, heart failure, liver dysfunction,
- Patients taking diuretics
- Elderlies
- If urinary symptoms occur (such as blood in the urine or inflammation of the bladder), the drug should be stopped immediately.

CONTRAINDICATIONS



1-Active **peptic ulcer**

2- Known or suspected **hypersensitivity** to ibuprofen or other NSAIDs.

3- In patients with **nasal polyps**, or in whom **asthma, anaphylaxis, urticarial/angioedema**, rhinitis or other allergic conditions.

4- Significant **hepatic impairment** or active liver disease.

5- Severely **impaired or deteriorating renal function**

6- Ibuprofen should not be used during **pregnancy** or by **nursing mothers**.

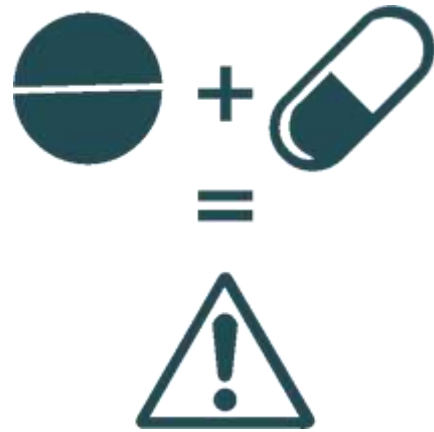
7- Ibuprofen should not be used right **before or after heart surgery**.



Adverse Events Occurring in $\geq 2\%$ Subjects



- Gastrointestinal disorders
- Nausea
- Vomiting
- Nervous system disorders
- Dizziness
- Headache
- Vascular disorders
- Flushing



With acetaminophen (may increase the risk of adverse renal effect)

With acetylsalicylic acid (ASA) or other NSAIDs, may result in possible additive side effects

With anticoagulants may increase the risk of GI adverse events (e.g., ulceration and bleeding).

With antihypertensives

With diuretics

With hypoglycemic agents

With methotrexate

Pharmaceutical Technology

Complex Bilayer Process

In conclusion, ibuprofen 600 mg IR/ER provides a twice-daily over-the-counter analgesic option that is **bioequivalent to standard ibuprofen 200 mg IR (every 4 hours)** with regard to both the rate (C_{max}) and the extent (AUC) of absorption.



Thanks
for Your Attention