**AUSTRALIAN PRODUCT INFORMATION**

# BRUFEN® PAIN

*(ibuprofen) tablets*

## 1 NAME OF THE MEDICINE

Ibuprofen.

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 400 mg of ibuprofen as the active ingredient.

Excipients with known effect: lactose.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

## 3 PHARMACEUTICAL FORM

White to off-white, pillow-shaped, film coated tablets, plain on both sides.

## 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

For the temporary relief of pain and/or inflammation associated with headache, migraine headache, tension headache, sinus pain, toothache, dental procedures, backache, muscular aches and pains, period pain, sore throat, tennis elbow, arthritis, rheumatic pain and aches and pains associated with colds and flu. Reduces fever.

### 4.2 DOSE AND METHOD OF ADMINISTRATION

#### Adults and children 12 years and over

The recommended dose is one tablet to be taken every 4 to 6 hours as necessary (maximum 3 tablets in 24 hours).

Do not exceed the recommended dose.

#### Pregnancy

See Section 4.3 CONTRAINDICATIONS and Section 4.6 FERTILITY, PREGNANCY AND LACTATION.

#### Children under 12 years

BRUFEN PAIN should not be administered to children aged less than 12 years.

This product should not be used for more than 3 days at a time except on medical advice, in which case the patient should be reviewed regularly with regards to efficacy, risk factors and ongoing need for treatment. Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage.

### 4.3 CONTRAINDICATIONS

Ibuprofen is contraindicated for use in patients with:

- known hypersensitivity or idiosyncratic reaction to ibuprofen (or any of the inactive ingredients)
- known hypersitivity to aspirin and other NSAIDs
- asthma that is aspirin or NSAID sensitive
- active gastrointestinal bleeding or peptic ulceration
- renal impairment
- heart failure
- severe liver impairment

- undergoing treatment of perioperative pain in a setting of coronary artery bypass surgery (CABG)

Use of ibuprofen is contraindicated during the third trimester of pregnancy (see Section 4.6 FERTILITY, PREGNANCY AND LACTATION).

Ibuprofen should not be taken with other products containing ibuprofen or with other anti-inflammatory medicines.

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Ibuprofen should be used with caution in patients with:

- Previous history of gastrointestinal haemorrhage or ulcers
- Asthma who have not previously taken NSAIDs
- Hepatic, or cardiac impairment

Ibuprofen should be used with caution in:

- Pregnancy (See Section 4.6 FERTILITY, PREGNANCY AND LACTATION)
- Elderly patients (See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE, USE IN ELDERLY)

Ibuprofen should be taken with caution with other products containing aspirin or salicylates.

As with other NSAIDs, excessive use of ibuprofen may increase the risk of heart attack, stroke or liver damage in both patients with predisposing cardiovascular risk factors and in normal patients.

Refer to Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS, for additional information.

### Cardiovascular and cerebrovascular effects

Observational studies have indicated that NSAIDs may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke, which may increase with dose or duration of use.

Patients with cardiovascular disease, history of atherosclerotic cardiovascular disease or cardiovascular risk factors may also be at greater risk.

Patients should be advised to remain alert for such cardiovascular events, even in the absence of previous cardiovascular symptoms. Patients should be informed about signs and/or symptoms of serious cardiovascular toxicity and the steps to take if they occur.

Fluid retention, hypertension and oedema have been reported in association with NSAID therapy. Patients taking antihypertensives with NSAIDs may have an impaired antihypertensive response.

BRUFEN PAIN tablets should be used with caution in patients with hypertension (see also Section 4.3 CONTRAINDICATIONS – HEART FAILURE).

### Gastrointestinal (GI)

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (See Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)).

Gastrointestinal GI bleeding, ulceration and perforation which can be fatal, have been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. The frequency of such events may increase with dose or duration of use. Patients at most risk of developing these types of GI complications with NSAIDs are the elderly, patients using concomitant aspirin,

patients with a history of, or active GI disease (e.g. ulceration, GI bleeding or inflammatory conditions) and patients with a history of smoking and alcoholism.

Ibuprofen should be used only under medical advice in:

- Patients with previous history of GI haemorrhage or ulcers (see also Section 4.3 CONTRAINDICATIONS – ACTIVE GI BLEEDING OR PEPTIC ULCERATION). Patients should report any new or unusual abdominal symptoms during treatment. If GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn immediately. Appropriate clinical evaluation and treatment should be considered.

- Patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin or other NSAIDs including cyclooxygenase-2 (COX-2) selective inhibitors.

## Respiratory

Ibuprofen should be used only under medical advice in patients with, or a previous history of, bronchial asthma or allergic disease because bronchospasm may be precipitated in these patients.

## SLE and mixed connective tissue disease

Ibuprofen should be used with caution in patients with systemic lupus erythematosus and mixed connective tissue disease as there is a risk of increased aseptic meningitis.

## Skin and Subcutaneous Tissue Disorders

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, Drug Reaction with Eosinophilia with Systemic Symptoms (see DRESS) and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see Adverse Effects). These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Ibuprofen use should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity and medical advice should be sought immediately.

*Severe skin reactions:* Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) may occur with ibuprofen- containing products. The acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localised on the skin folds, trunk and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of BRUFEN PAIN tablets should be discontinued, and appropriate measures taken if needed.

## Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS)

DRESS has been reported in patients using NSAIDs. Some of these events have been fatal or life threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue the NSAID and evaluate the patient immediately.

## Masking of symptoms of underlying infections

BRUFEN PAIN tablets can mask symptoms of infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When BRUFEN PAIN tablets are administered for fever or pain relief in relation infection, monitoring of infection is advised. In non-hospital settings the patient should consult a doctor if symptoms persist or worsen.

### Use in hepatic impairment

As with other NSAIDs elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may resolve with continued therapy. Meaningful elevations (three times the upper limit of normal) of ALT or AST occurred in controlled clinical trials in less than 1% of patients.

Ibuprofen has been reported to have a minor and transient effect on liver enzymes. Therefore, BRUFEN PAIN tablets should be used with caution in patients with hepatic dysfunction.

Patients should be advised to remain alert for hepatotoxicity and be informed about the signs and/or symptoms of hepatotoxicity (e.g. nausea, fatigue, lethargy, pruritus, jaundice, abdominal tenderness in the right upper quadrant and "flu-like" symptoms).

### Use in the elderly

Ibuprofen should not be taken by adults over the age of 65 without careful consideration of co-morbidities and co-medications because of an increased risk of adverse effects, in particular heart failure, gastro-intestinal ulceration and renal impairment (see also Section 4.3 CONTRAINDICATIONS – RENAL IMPAIRMENT, HEART FAILURE).

### Effects on laboratory tests

No data available.

## 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

The following interactions with ibuprofen have been noted:

- *Anticoagulant-including warfarin*: Ibuprofen interferes with the stability of INR and may increase the risk of severe bleeding and sometimes-fatal haemorrhage, especially from the gastrointestinal tract. Ibuprofen should only be used in patients taking warfarin if absolutely necessary and they must be closely monitored
- *Lithium*: Ibuprofen may decrease the renal clearance and increase plasma concentrations of lithium.
- *Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):* increased risk of gastrointestinal bleeding.
- *Cardiac glycosides*: Ibuprofen may exacerbate cardiac failure, reduce glomerular filtration rate (GFR) and may increase plasma glycoside levels.
- *Ciclosporin:* Increased risk of nephrotoxicity.
- *Corticosteroids*: An increased risk of gastrointestinal bleeding may occur with corticosteroids.
- *Methotrexate*: Ibuprofen reduces methotrexate clearance.
- *Mifepristone:* NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
- *Quinolone antibiotics:* Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.
- *Tacrolimus:* possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.
- *Zidovudine*: Concurrent administration with ibuprofen may prolong bleeding time in patients.
- *Antidiabetic medicines, Probenecid and phenytoin*: Interactions may also occur with probenecid and phenytoin.
- *ACE inhibitors, beta-blockers and diuretics*: Ibuprofen, like other NSAIDs may reduce the antihypertensive effect of ACE inhibitor and beta-blockers and diuretics and may cause natriuresis and hyperkalemia in patients under these treatments. Combination use of an ACE inhibitor or angiotensin receptor antagonist, and anti-inflammatory drug (NSAID or COX-2 inhibitor) and a diuretic increases the risk of renal impairment. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.
- *NSAIDs and aspirin*: Concurrent use of ibuprofen with aspirin or other NSAIDs can lead to increased gastrointestinal adverse effects.

### Lactose

This medicine contains lactose monohydrate. Patients with rare hereditary forms of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption syndrome should not take this medicine.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### Effects on fertility

The use of ibuprofen may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

### Use in pregnancy (Category C)

Ibuprofen inhibits prostaglandin synthesis and, when given during the latter part of pregnancy, may cause closure of the fetal ductus arteriosus, oligohydramnios, fetal renal impairment, inhibition of platelet aggregation and may delay labour and birth. Use of ibuprofen is thus contraindicated during the third trimester of pregnancy, including the last few days before expected birth.

Data from epidemiological studies suggest an increased risk of miscarriage after the use of a prostaglandin synthesis inhibitor in early pregnancy.

Further, there is insufficient experience about the safety of use of ibuprofen in humans during pregnancy. BRUFEN PAIN tablets should therefore not be used during the first 6 months of pregnancy unless the potential benefits to the patient outweigh the possible risk to the fetus.

### Oligohydramnios and Neonatal Renal Impairment

Use of NSAIDs from about 20 weeks gestation may cause neonatal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment.

These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation.

Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some post-marketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If, after careful consideration of alternative treatment options for pain management, NSAID treatment is necessary from about 20 weeks, limit use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if treatment extends beyond 48 hours. Discontinue treatment with NSAIDs if oligohydramnios occurs.

### Use in Lactation

Ibuprofen appears in breast milk in very low concentrations and is unlikely to affect the breast fed infant adversely.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

## 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Adverse effects with non-prescription (OTC) or short-term use ibuprofen are rare and may include:

- Gastrointestinal-dyspepsia, heartburn, nausea, loss of appetite, stomach pain, diarrhoea.
- Central nervous system (CNS) –dizziness, fatigue, headache, nervousness.

- Hypersensitivity reactions – skin rashes and itching. Rarely exfoliative dermatitis and epidermal necrolysis have been reported with ibuprofen.
- Rare cases of photosensitivity.
- Cardiovascular fluid retention and in some cases oedema. These effects are rare at non-prescription doses.

The frequencies of adverse effects are defined as follows:

Very common: *>1/10*
Common: *>1/100, <1/10*
Uncommon: *>1/1,000, <1/100*
Rare: *>1/10,000, <1/1,000*
Very Rare: *<1/10,000,* including isolated reports.

Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of:

a) non-specific allergic reactions and anaphylaxis
b) respiratory tract reactivity e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
c) Assorted skin disorders, including rashes of various types, pruritius, urticaria, urpura, angioedema and more rarely bullous dermatoses (including epidermal necrolysis and erythema multiforme)

The following adverse effects relates to those experienced with ibuprofen at OTC doses, for short-term use. In the treatment of chronic conditions, under long term treatment, additional adverse effects may occur.

Allergic reactions such as skin rash, itching, swelling of the face or breathing difficulties may also occur. These are usually transient and reversible on cessation of treatment.

***Blood and Lymphatic System Disorders:***

Very rare: Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia and agranulocytosis).

***Hypersensitivity reactions:***

Uncommon: Hypersensitivity reactions with urticaria and pruritius.

Very rare: severe hypersensitivity reactions. Symptoms could be facial, tongue and larynx, swelling, dyspnoea, apnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock - syndrome may be characterised by abdominal pain, fever, shivering, nausea and vomiting. Exacerbation of asthma and bronchospasm.

Hepatotoxicity and aseptic meningitis which occur less frequently may also be hypersensitivity reactions.

Allergic reactions such as skin rash, itching, swelling of the face or breathing difficulties are usually transient and reversible on cessation of treatment.

***Gastrointestinal disorders:***

The most commonly observed adverse events are gastrointestinal in nature.

Uncommon: Abdominal pain, nausea, dyspepsia.

Rare: Diarrhoea, flatulence, heartburn, loss of appetite, constipation and vomiting.

Very rare: Peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis.

Exacerbation of ulcerative colitis and Crohn's, disease, Gastric pyrosis.

***Nervous System:***

Uncommon: Headache.

Very rare: Aseptic meningitis - single cases have been reported, Dizziness, nervousness, tinnitus, depression, drowsiness, insomnia, irritability, difficulty in concentrating, emotional instability, convulsions, auditory and visual problems.

Rare: Fatigue.

***Renal:***

Very rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

Ibuprofen may cause cystitis and haematuria, interstitial nephritis, nephrotic syndrome, oliguria, tubular necrosis, glomerulonephritis, alteration in the renal function test, polyuria.

***Liver:***

Very rare: Liver disorders, especially in long term treatment, including hepatotoxicity, hepatitis, jaundice, alterations of hepatic function tests, pancreatitis, duodenitis, oesophagitis, hepato-renal syndrome, hepatic necrosis, hepatic insufficiency.

***Haematological:***

Very rare: Haematopoietic disorders (anaemia, neutropenia, aplastic anaemia, haemolytic anaemia, eosinophilia, reduction of haemoglobin and haematocrit leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). Reversible platelet aggregation, alveolitis, pulmonary eosinophilia, pancreatitis.

***Skin and Subcutaneous Tissue Disorders:***

Uncommon: Various skin rashes.

Very rare: Severe forms of skin reactions such as bullous reactions including Stevens Johnson Syndrome, erythema multiform and toxic epidermal necrolysis can occur.

Rarely skin peeling, alopecia, exfoliative dermatitis, photosensitive dermatitis, maculopapular, rash.

Unknown: Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS), Acute generalized exanthematous pustulosis (AGEP), photosensitivity reactions, fixed eruption.

***Immune System:***

In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed.

***Cardiovascular and Cerebrovascular:***

Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment.

Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2400 mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Rarely: Cerebrovascular accidents, hypotension, congestive cardiac insufficiency in patients with compromised cardiac function, palpitations.

***Ocular:***

Very rare: Blurred vision, changes in visual colour perception, toxic amblyopia, episodes of ocular alteration with consequent visual disorders.

***Other:***

Effect on the endocrine system and on the metabolism, reduction in appetite.

Rarely: Dryness of the eyes and mouth, gingival ulcers, rhinitis, hearing disturbances.

***Pregnancy, puerperium and perinatal conditions:***

Unknown: Oligohydramnios, neonatal renal impairment.

### Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

## 4.9 OVERDOSE

Symptoms include nausea, abdominal pain and vomiting, dizziness, convulsion and rarely, loss of consciousness. Clinical features of overdose with ibuprofen which may result are depression of the central nervous system and the respiratory system.

There is no specific antidote to ibuprofen.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 PHARMACODYNAMIC PROPERTIES

### Mechanism of Action

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

Ibuprofen has shown anti-inflammatory, analgesic and antipyretic activity in both animal and human studies. These properties provide symptomatic relief of inflammation and pain in rheumatoid arthritis, osteoarthritis and allied conditions.

### Clinical Trials

This information is not available.

## 5.2 PHARMACOKINETIC PROPERTIES

### Absorption

Ibuprofen is well absorbed from the gastrointestinal tract.

### Metabolism

It is highly bound (90-99%) to plasma proteins and is extensively metabolized to inactive compounds in the liver, mainly by glucuronidation.

### Excretion

Both inactive metabolites and a small amount of unchanged ibuprofen are excreted rapidly and completely by the kidney, with 95% of the administered dose eliminated in the urine within four hours of ingestion. The elimination half-life of ibuprofen is in the range of 1.9 to 2.2 hours.

## 5.3 PRECLINICAL SAFETY DATA

### Genotoxicity

No data available.

### Carcinogenicity

No data available.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 LIST OF EXCIPIENTS

Excipients: Lactose monohydrate, microcrystalline cellulose, povidone, croscarmellose sodium, sodium lauryl sulfate, colloidal anhydrous silica, stearic acid, macrogol 6000, hypromellose, titanium dioxide and purified talc.

## 6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

## 6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

## 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

## 6.5 NATURE AND CONTENTS OF CONTAINER

Available in cartons with PVC/Aluminium blister packs containing 10, 28, 50* tablets.

* Not all pack sizes may be marketed.

### Australian Register of Therapeutic Goods (ARTG)

AUST R 401754 – BRUFEN® PAIN ibuprofen 400 mg film-coated tablet blister pack

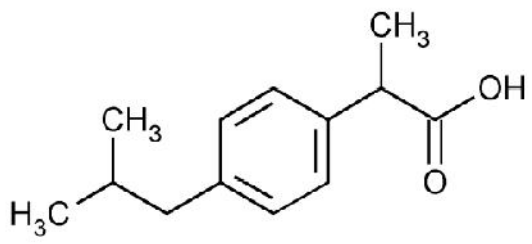
## 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

## 6.7 PHYSICOCHEMICAL PROPERTIES

Ibuprofen is a (±)-2-(*p*-isobutylphenyl) propionic acid. Ibuprofen is a white crystalline solid with a melting point of 74 – 77°C and is practically insoluble in water (< 0.1 mg/mL) and readily soluble in organic solvents such as ethanol and acetone.

Chemical structure:



Chemical formula: $C_{13}H_{18}O_2$

Molecular weight: 206.3

CAS Number: 15687-27-1

# 7 MEDICINE SCHEDULE (POISONS STANDARD)

S2 – Pharmacy Medicine (10 tablet pack sizes)

S3 – Pharmacist Only Medicine (28 & 50 tablet pack sizes)

# 8 SPONSOR

**Viatris Pty Ltd**

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Millers Point NSW 2000

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Phone: 1800 274 276

# 9 DATE OF FIRST APPROVAL

03/01/2023

# 10 DATE OF REVISION

14/04/2025

### Summary Table of Changes

| Section Changed | Summary of New Information |
|---|---|
| **All** | Minor editorial changes |
| **4.8** | Addition of ADR fixed eruption with the frequency unknown under 'Skin and Subcutaneous Tissue Disorders' |



**BRUFEN PAIN_pi\Apr25/00 (CCDS 15-Jan-2025)**