

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Teva Cold Relief 200 mg/30 mg Film-coated Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains 200 mg ibuprofen and 30 mg pseudoephedrine hydrochloride equivalent to 24.6 mg pseudoephedrine

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Film-coated tablets

Yellow coloured, oval shaped, biconvex film-coated tablet (dimension: approx. 15.6 mm x 7.7 mm).

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Symptomatic relief of nasal/sinus congestion with headache, fever and pain associated with the common cold and influenza.

Teva Cold Relief 200 mg/30 mg Film-coated Tablets are indicated in adults and adolescents aged 15 and over.

### 4.2 Posology and method of administration

#### Posology

Adults and adolescents aged 15 and over:

1 tablet (equivalent to 200 mg ibuprofen and 30 mg pseudoephedrine hydrochloride) every 4-6 hours if necessary. For more severe symptoms, 2 tablets (equivalent to 400 mg ibuprofen and 60 mg pseudoephedrine hydrochloride) every 6-8 hours if necessary, to a maximum total daily dose.

The maximum total daily dose of 6 tablets (equivalent to 1200 mg ibuprofen and 180 mg pseudoephedrine hydrochloride) must not be exceeded.

Treatment should not be continued for more than 5 days.

This combination product should be used where both, the decongestant action of Pseudoephedrine hydrochloride and the analgesic and/or anti-inflammatory action of Ibuprofen, are required. If one symptom (*either* nasal congestion *or* headache and/or fever) predominates, single-agent therapy is preferable.

If in adolescents this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

In older people and patients with a history of ulcers, particularly if complicated by haemorrhage or perforation (see section 4.3), start with lowest dose possible as the risk of gastrointestinal haemorrhage, ulceration or perforation is higher with increased doses of NSAIDs.

The concomitant use of protective agents (misoprostol or proton pump inhibitors) should be considered for these patients or patients taking other drugs that can increase the risk of gastrointestinal events (see below and section 4.5).

For patients with kidney or liver disorders it is necessary to adapt the dosage to suit the individual.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms.

*Paediatric population*

Teva Cold Relief is contraindicated in children under 15 years old (see section 4.3).

Method of administration

For oral use.

Tablets should be swallowed with water, preferably on a full stomach. Do not break or crush the tablets.

**4.3 Contraindications**

- Hypersensitivity to ibuprofen, pseudoephedrine or to any of the excipients listed in section 6.1.
- Patients aged under 15 years
- Pregnancy and Lactation (see section 4.6)
- A history of hypersensitivity reactions (e.g. bronchospasm, asthma, nasal polyposis, rhinitis, or urticaria) associated with aspirin, other analgesics, antipyretics or other non steroidal anti inflammatory drugs (NSAIDs).
- Active peptic ulcer or history of recurrent ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- History of gastrointestinal bleeding or perforation, including that associated with NSAIDs.
- Cerebrovascular or other bleeding.
- Unexplained haematopoietic abnormalities.
- Severe renal failure.
- Severe hepatic failure.
- Severe heart failure.
- Severe cardiovascular disorders, coronary artery disease (heart disease, hypertension, angina pectoris), tachycardia, hyperthyroidism, diabetes, phaeochromocytoma,
- History of stroke or presence of risk factors for stroke (because of the  $\alpha$ -sympathomimetic activity of pseudoephedrine hydrochloride).
- Risk of closed-angle glaucoma.
- Risk of urinary retention related to urethroprostatic disorders.
- History of myocardial infarction.
- History of seizures.
- Disseminated lupus erythematosus.
- Concomitant use of other vasoconstrictor agents used as nasal decongestants, whether administered orally or nasally (e.g. phenylpropanolamine, phenylephrine and ephedrine), and methylphenidate (see section 4.5)
- Concomitant use of NSAIDs or aspirin with a daily dose above 75 mg, analgesics and COX 2 selective inhibitors (see section 4.5).
- Concomitant or prior use of monoamine oxidase inhibitors (MAOIs) in the preceding 2 weeks (see section 4.5).

**4.4 Special warnings and precautions for use**

Concomitant use of Teva Cold Relief with other NSAIDs containing cyclo-oxygenase (COX)-2 inhibitors should be avoided.

Undesirable effects may be reduced by using the minimum effective dose for the shortest duration necessary to control symptoms (see "Gastro-intestinal effects" and "Cardiovascular and cerebrovascular effects" below).

***Special warnings related to pseudoephedrine hydrochloride:***

- The dosage, the recommended maximum duration of treatment (5 days) and the contraindications must be strictly adhered to (see section 4.8).
- Patients should be informed that treatment must be discontinued if they develop hypertension, tachycardia, palpitations, cardiac arrhythmias, nausea or any neurological signs such as onset or worsening of headache.

Before using this product, patients should consult their doctor in case of:

- Hypertension, heart disease, hyperthyroidism, psychosis or diabetes.
- Concomitant administration of antimigraine agents, especially ergot alkaloid vasoconstrictors (because of the  $\alpha$ -sympathomimetic activity of pseudoephedrine).
- SLE and mixed connective tissue disease: Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).
- Neurological symptoms such as seizures, hallucinations, behavioural disturbances, agitation and insomnia have been described after systemic administration of vasoconstrictors, especially during febrile episodes or on overdose. These symptoms have been more commonly reported in paediatric population.

As a result, it is advisable:

- to avoid administration of (Invented name) either in combination with medicines which can lower the epileptogenic threshold, such as terpene derivatives, clobutinol, atropine-like substances and local anaesthetics, or where there is a history of seizures;
- to adhere strictly to the recommended dosage in all cases and to inform the patients about the risks of overdose if (Invented name) is taken concomitantly with other medicines containing vasoconstrictors.

Patients with urethroprostatic disorders are more prone to develop symptoms like dysuria and urinary retention.

Elderly patients may be more sensitive to the effects on the central nervous system (CNS).

***Precautions for use related to pseudoephedrine hydrochloride:***

- In patients undergoing scheduled surgery in which volatile halogenated anaesthetics are to be used, it is preferable to discontinue treatment with (Invented name) several days before surgery in view of the risk of acute hypertension (see section 4.5).
- Athletes should be informed that treatment with pseudoephedrine hydrochloride can lead to positive results in doping tests.

**Interference with serological testing**

Pseudoephedrine has the potential to reduce iobenguane i-131 uptake in neuroendocrine tumors, thus interfering with scintigraphy.

***Special warnings related to ibuprofen:***

Bronchospasm may be precipitated in patients suffering from, or with a history of bronchial asthma or allergic disease. The product should not be taken with cases of asthma without prior consultation with a doctor (see section 4.3).

Patients who have asthma associated with chronic rhinitis, chronic sinusitis and/or nasal polyposis have a higher risk of allergic reactions when taking acetylsalicylic acid and/or NSAIDs. Administration of (Invented name) may precipitate an acute asthma attack; particularly in some patients who are allergic to acetylsalicylic acid or an NSAID (see section 4.3).

There is a risk of renal impairment in dehydrated adolescents.

***Gastro-intestinal effects:***

Gastro-intestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of gastrointestinal events.

The risk of gastro-intestinal bleeding, ulceration or perforation, which can be fatal, is higher with increasing NSAID doses, in patients with a history of ulcer (particularly if complicated with bleeding or perforation (see section 4.3) and in patients older than 60 years of age. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients and also for patients taking concomitant low-dose acetylsalicylic acid or other medicinal drug products likely to increase gastro-intestinal risk (see below and section 4.5).

Patients with a history of gastrointestinal toxicity, especially elderly patients, may present with unusual abdominal symptoms (especially gastrointestinal bleeding) in the initial stages of treatment.

Particular caution is advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding such as oral corticosteroids, anticoagulants such as warfarin, SSRIs or antiplatelet agents such as acetylsalicylic acid (see section 4.5).

Treatment with Teva Cold Relief should be discontinued immediately if gastro-intestinal bleeding or ulceration occurs. NSAIDs should be given with care to patients with a history of gastro-intestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (see section 4.8).

Through concomitant consumption of alcohol, active substance-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

*Cardiovascular and cerebrovascular effects:*  
Clinical trials and epidemiological data suggest that use of ibuprofen, particularly at high doses (above 2400 mg daily) and in long-term treatment, may be associated with a small increased risk of arterial thrombotic events such as myocardial infarction or stroke. Overall, epidemiological studies do not suggest that low-dose ibuprofen (below 1200 mg daily) is associated with an increased risk of myocardial infarction.

Caution is required in patients with a history of hypertension and/or heart failure as fluid retention, hypertension or oedema have been observed in association with previous NSAID therapy; advice from a doctor and/or pharmacist must be sought prior to starting treatment under these circumstances.

*Skin reactions:*  
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients are 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. Teva Cold Relief should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

**Precautions for use related to ibuprofen:**

- Elderly: The pharmacokinetics of ibuprofen is not modified by age, no dose adjustments is necessary in the elderly. However, elderly patients should be carefully monitored as they are more sensitive to NSAID-related undesirable effects, particularly gastro-intestinal bleeding and perforation, which can be fatal.
- Caution and special monitoring is required when administering ibuprofen to patients with a history of gastro-intestinal disease (such as peptic ulcer, hiatus hernia or gastrointestinal bleeding).
- In the initial stages of treatment, careful monitoring of urine output and renal function is required in patients with heart failure, patients with chronically impaired renal or hepatic function, patients taking diuretics, patients who are hypovolaemic as a result of major surgery and, in particular, elderly patients. Renal function in these patients may be adversely influenced by treatment with NSAIDs.
- If visual disturbances occur during the course of treatment, a full ophthalmological examination should be carried out.

If symptoms persist or worsen, the patient should consult a doctor.

Teva Cold Relief contains 0.28 mg sodium per tablet.

**4.5 Interaction with other medicinal products and other forms of interaction**

Combination of pseudoephedrine with:	Possible Reaction
Non-selective monoamine oxidase inhibitors (MAOIs):	Teva Cold Relief 200 mg/30 mg Film-coated Tablets must not be taken by patients taking

	monoamine oxidase inhibitors (MAOIs) currently or in the last two weeks, since there is a risk of hypertensive episodes as paroxysmal hypertension and hyperthermia, which can be fatal (see section 4.3).
Other indirectly-acting, orally or nasally administered sympathomimetics or vasoconstrictor agents, $\alpha$ -sympathomimetic drugs, phenylpropanolamine, phenylephrine, ephedrine, methylphenidate:	Pseudoephedrine may potentiate the effect of other sympathomimetic (vasoconstrictor) and lead to risk of vasoconstriction and/or hypertensive crises.
Reversible inhibitors of monoamine oxidase A (RIMAs), linezolid, dopaminergic ergot alkaloids, vasoconstrictor ergot alkaloids:	Risk of vasoconstriction and/or hypertensive crises.
Volatile halogenated anaesthetics:	Perioperative acute hypertension. In scheduled surgery, discontinue treatment with Teva Cold Relief 200 mg/30 mg Film-coated Tablets several days before.
Guanethidine, reserpine and methyl dopa:	Effect of pseudoephedrine may be diminished.
Tricyclic antidepressants:	Effect of pseudoephedrine may be diminished or enhanced.
Digitalis, chinidine or tricyclic antidepressants:	Increased frequency of arrhythmia.

Concomitant use of ibuprofen with :	Possible Reaction
Other NSAIDs, salicylates, analgesics, antipyretics and COX 2:	The concomitant administration of several NSAIDs, analgesics, antipyretics and COX 2 selective inhibitors may increase the risk of adverse reactions as gastrointestinal ulcers and bleeding due to a synergistic effect. The concomitant use of with these products should therefore be avoided (see section 4.4).
Cardiac glycosides (as digoxin):	The concomitant use with digoxin preparations may increase serum levels cardiac glycosides (digoxin). A check of serum-digoxin is not as a rule required on correct use (maximum over 5 days).
Corticosteroids:	Corticosteroids as these may increase the risk of adverse reactions, especially of the gastrointestinal tract (gastrointestinal; ulceration or bleeding) (see section 4.3).
Anti-platelet agents:	Increased risk of gastrointestinal bleeding (see section 4.4).
Acetylsalicylic acid (low dose):	The concomitant administration of acetylsalicylic acid with a daily dose above 75 mg should be avoided due to increased risk of adverse reactions (see section 4.3).
Anticoagulants: (e.g.: warfarin, ticlopidine, clopidogrel, tirofiban, eptifibatide, abciximab, iloprost)	Increased risk of gastrointestinal bleeding as NSAIDs as ibuprofen may enhance the effect of anti-coagulants (see section 4.4)

Phenytoin:	The concomitant use of Teva Cold Relief 200 mg/30 mg Film-coated Tablets with phenytoin preparations may increase serum levels of these medicinal products. A check of serum-phenytoin levels is not as a rule required on correct use (maximum over 5 days).
Selective serotonin reuptake inhibitors (SSRIs):	Increased risk of gastrointestinal bleeding (see section 4.4).
Lithium:	The concomitant use of Teva Cold Relief 200 mg/30 mg Film-coated Tablets with lithium preparations may increase serum levels of these medicinal products. A check of serum-lithium is not as a rule required on correct use (maximum over 5 days).
Probenecid and sulfinpyrazone:	Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of ibuprofen.
Diuretics, ACE inhibitors, betareceptor-blockers and angiotensin-II antagonists:	NSAIDs may reduce the effect of diuretics and other antihypertensive agents. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor, betareceptor-blockers or angiotensin-II antagonists and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.
Potassium sparing diuretics:	The concomitant administration of Teva Cold Relief 200 mg/30 mg Film-coated Tablets and potassium-sparing diuretics may lead to hyperkalaemia (check of serum potassium is recommended).
Methotrexate:	The administration of Teva Cold Relief 200 mg/30 mg Film-coated Tablets within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.
Ciclosporin:	The risk of a kidney-damaging effect due to ciclosporin is increased through the concomitant administration of certain nonsteroidal antiinflammatory drugs. This effect also cannot be ruled out for a combination of ciclosporin with ibuprofen.
Tacrolimus:	The risk of nephrotoxicity is increased if the two medicinal products are administered concomitantly.

Zidovudine:	There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.
Sulphonylureas:	Clinical investigations have shown interactions between nonsteroidal anti-inflammatory drugs and antidiabetics (sulphonylureas). Although interactions between ibuprofen and sulphonylureas have not been described to date, a check of blood-glucose values is recommended as a precaution on concomitant intake.
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.
Heparins; <i>Gingko biloba</i> :	Increased risk of bleeding.

4.6 Fertility, pregnancy and lactation

Pregnancy:

**Teva Cold Relief 200 mg/30 mg Film-coated Tablets is contraindicated during pregnancy** (see section 4.3).

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastrochisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1 % , up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- Cardiopulmanary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- Renal dysfunction, which may progress to renal failure with oligo hydroamniosis;

The mother and the neonate, at the end of pregnancy, to:

- Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- Inhibition of uterine contractions resulting in delayed or prolonged labour.

There is the possibility of an association between the occurrence of foetal abnormalities and the taking of pseudoephedrine in the 3<sup>rd</sup> trimester of pregnancy.

Breastfeeding

**Teva Cold Relief 200 mg/30 mg Film-coated Tablets are contraindicated during breast-feeding** (see section 4.3).

Ibuprofen/pseudoephedrine have been identified in breastfed newborns/infants of treated women. There is insufficient information on the effects of ibuprofen/ pseudoephedrine in newborns/ infants.

Fertility

The effects of this product on fertility have not been specifically investigated. The use of ibuprofen may impair 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.  
There are no adequate reproductive toxicology studies with pseudoephedrine.

4.7 Effects on ability to drive and use machines

Teva Cold Relief 200 mg/30 mg Film-coated Tablets have no known effects on the ability to drive and use machines. However, since dizziness or hallucinations may appear in exceptional cases, owing to the presence of pseudoephedrine, anyone intending to drive should take this possibility into account.

4.8 Undesirable effects

The most commonly-observed adverse events related to ibuprofen are gastrointestinal in nature. In general, the risk of development of adverse events (in particular the risk of development of serious gastrointestinal complications) increases with increasing dose and with increasing duration of treatment administration. Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of:

- (a) Non-specific allergic reaction and anaphylaxis
- (b) Respiratory tract reactivity comprising of asthma, aggravated asthma, bronchospasm or dyspnoea
- (c) Assorted skin disorders, including rashes of various types, pruritis, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)

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.

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 2400mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke), (see section 4.4).

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

Patients should be informed that they should stop taking Teva Cold Relief 200 mg/30 mg Film-coated Tablets immediately and consult a doctor if they experience a serious adverse drug reaction.

Adverse reaction frequency is defined using the following convention: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Infections and infestations	Ibuprofen	Very rare	Exacerbation of infectious inflammations (e.g. necrotizing fasciitis), Aseptic meningitis (stiffness of the neck, headache, nausea, vomiting, fever or disorientation in patients with pre-existent autoimmune diseases (SLE, mixed connective tissue disease)
Blood and lymphatic system disorders	Ibuprofen	Very rare	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis, neutropenia)
Immune system disorders	Ibuprofen	Uncommon	Hypersensitivity reactions with urticaria, pruritus, , skin rashes and asthma attacks (with drop in blood pressure)
	Ibuprofen and pseudoephedrine hydrochloride	Very rare	Severe generalised hypersensitivity reactions, signs may be facial oedema, angioedema, dyspnoea, bronchospasm, tachycardia, drop in blood pressure, anaphylactic shock
Psychiatric disorders	Ibuprofen	Very rare	Psychotic reactions, depression



	Pseudoephedrine hydrochloride	Not known	Agitation, hallucination, anxiety, abnormal behaviour, insomnia
<b>Nervous system disorders</b>	Ibuprofen	Uncommon	Central nervous disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness
	Pseudoephedrine hydrochloride	Rare  Not known	Insomnia, nervousness anxiety, restlessness, tremor, hallucinations  Haemorrhagic stroke, ischemic stroke, convulsion, headache
<b>Eye disorders</b>	Ibuprofen	Uncommon	Visual disturbances
<b>Ear and labyrinth disorders</b>	Ibuprofen	Rare	Tinnitus
<b>Cardiac disorders</b>	Ibuprofen	Very rare	Oedema, hypertension, palpitations, heart failure, myocardial infarction
	Pseudoephedrine hydrochloride	Not known	Palpitations, tachycardia, chest pain, arrhythmia
<b>Vascular disorders</b>	Ibuprofen	Very rare	Arterial hypertension
	Pseudoephedrine hydrochloride	Not known	Hypertension
<b>Respiratory, thoracic and mediastinal disorders</b>	Pseudoephedrine hydrochloride	Rare	Exacerbation of asthma or hypersensitivity reaction with bronchospasm
<b>Gastrointestinal disorders</b>	Ibuprofen	Common	Gastrointestinal discomfort, dyspepsia, abdominal pain, nausea, vomiting, flatulence, diarrhoea, anorexia, constipation, minor gastrointestinal blood loss in rare cases leading to anaemia
	Ibuprofen	Uncommon	Peptic ulcer, perforation, or gastrointestinal haemorrhage (with melaena or haematemesis, gastritis, ulcerous stomatitis. Exacerbation of colitis and Crohn's disease (see section 4.4)
	Ibuprofen	Very rare	Oesophagitis, pancreatitis, intestinal diaphragm-like stricture
	Pseudoephedrine hydrochloride	Not known	Dry mouth, thirst, nausea, vomiting
<b>Hepatobiliary disorders</b>	Ibuprofen	Very rare	Hepatic dysfunction, hepatic damage, particularly in long-term therapy, hepatic failure, acute hepatitis
<b>Skin and subcutaneous tissue disorders</b>	Ibuprofen	Uncommon	Various skin rashes
	Ibuprofen	Very rare	Severe forms of skin reactions as exfoliative dermatitis or bullous exanthema such as Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis (Lyell syndrome), alopecia, severe skin

			infections, soft-tissue complications in a varicella infection
	Pseudoephedrine hydrochloride	Not known	Rash, urticaria, pruritus,, erythema, hyperhidrosis
<b>Renal and Urinary disorders</b>	Ibuprofen	Rare	Kidney-tissue damage (papillary necrosis) and elevated uric acid concentrations in the blood
	Ibuprofen	Very rare	Renal and hepatic disorders, increase in serum creatinine, liver disorders, oedemas (particularly in patients with arterial hypertension or renal insufficiency), nephrotic syndrome, interstitial nephritis, acute renal insufficiency
	Pseudoephedrine hydrochloride	Not known	Urinary retention in men with prostatic hypertrophy

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

**4.9 Overdose**

Symptoms

The most frequent manifestations of ibuprofen overdose are abdominal pain, nausea, vomiting, lethargy, thirst, muscle weakness, drowsiness, blurred vision and dizziness. Other effects including headache, tinnitus, CNS depression, convulsions, hypotension, bradycardia, tachycardia, supraventricular and ventricular arrhythmias, and atrial fibrillation, may occur. Metabolic acidosis, coma, acute renal failure, hyperkalaemia, apnoea (mainly in young children), respiratory depression, and respiratory failure have been reported rarely. Exacerbation of asthma is possible in asthmatics.

Symptoms and signs of pseudoephedrine overdose include irritability, insomnia, fever, sweating, anxiety, restlessness, tremor, convulsions, palpitations (sinus arrhythmia), hypertension, dry mouth, and difficulty in urination. Hallucinations have been reported (more likely in children).

Treatment

Treatment of overdose is supportive. Gastric lavage and activated charcoal may be of benefit within 1 hour of ingestion of a potentially toxic amount, and if necessary, correction of serum electrolytes.

Symptomatic and supportive treatment should be undertaken, particularly with regard to the cardiovascular and respiratory systems. For example, severe hypertension may need to be treated with an alpha-receptor blocking drug, whilst a beta-receptor blocking drug may be required to control cardiac arrhythmias. Convulsions may be controlled with intravenous diazepam, while chlorpromazine may be used to control marked excitement and hallucinations.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other cold combination preparations; nasal decongestants for systemic use, sympathomimetics, pseudoephedrine combinations.  
ATC code: R05X; R01BA52

Teva Cold Relief 200 mg/30 mg Film-coated Tablets are a medicine consisting of a combination of two active substances: ibuprofen and pseudoephedrine.

Pseudoephedrine is a sympathomimetic agent with direct and indirect effects on adrenergic receptors. It has alpha and beta stimulant adrenergic stimulant activity and some stimulant effect on the central nervous system.

The sympathomimetic effect of pseudoephedrine produces vasoconstriction which relieves nasal congestion.

Ibuprofen is an anti-inflammatory analgesic and antipyretic drug belonging to the group of non-steroidal anti-inflammatory drugs.

In humans it has been shown to be effective in reducing the symptoms (pain, fever and swelling) associated with inflammation and influenza.

The therapeutic effects of the drug are the result of an inhibitory activity on the prostaglandin synthesis.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400 mg was taken within 8 h before or within 30 min after immediate release aspirin dosing (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

### 5.2 Pharmacokinetic properties

#### Ibuprofen

Ibuprofen is rapidly absorbed from the gastrointestinal tract, and its plasma concentrations reach a maximum peak level about 2 hours after administration. Elimination half-life is approximately 2 hours.

Ibuprofen is metabolised in the liver into two major inactive metabolites and these together with unchanged ibuprofen are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete.

Ibuprofen is extensively bound to plasma proteins.

#### Pseudoephedrine

Pseudoephedrine is absorbed in the gastrointestinal tract and is largely excreted in the urine unchanged, together with small amounts of a hepatic metabolite.

It has an elimination half-life of several hours, which may be reduced by acidifying the urine.

### 5.3 Preclinical safety data

Only limited toxicity data are available with the drug combination ibuprofen and pseudoephedrine hydrochloride.

Based on different mechanisms of action of ibuprofen (non-steroidal anti-inflammatory) and pseudoephedrine

hydrochloride (sympathomimetic), a compound-specific toxicity profile related to the pharmacodynamic activity of the mono-compounds was seen in non-clinical toxicity tests following overdosing (pseudoephedrine human data). Accordingly, there were different toxicological target organs, e.g. gastrointestinal lesions for ibuprofen and hemodynamic as well as CNS-effects for pseudoephedrine hydrochloride. Co-administration of ibuprofen and pseudoephedrine hydrochloride did not result in any clinically significant interaction. Therefore, no additive, synergistic and potentiating effects will be expected for the fixed-dose combination (FDC) ibuprofen/pseudoephedrine hydrochloride (200 mg/30 mg) in animals and men at equipotent doses. This is also supported by the absence of competitive metabolic pathways. There is no scientific evidence that the safety margins for the individual drugs will be different for the drug combination.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

#### Tablet Core

Microcrystalline cellulose  
Pregelatinised starch (maize)  
Povidone K-30  
Colloidal anhydrous silica  
Stearic acid 95  
Crosscarmellose sodium  
Sodium laurilsulfate

#### Film coating:

Polyvinyl Alcohol – Part. Hydrolyzed  
Talc (E553b)  
Macrogol 3350  
MICA-Based Pearlescent Pigment  
(Mixture of: Potassium aluminium silicate (E555)-[mica] and titanium dioxide (E171))  
Polysorbate 80 (E433)  
Hypromellose  
Titanium dioxide (E 171)  
Macrogol 400  
Yellow iron oxide (E 172)  
Red iron oxide (E 172)  
Black Iron oxide (E 172)

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

3 years

### 6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

### 6.5 Nature and contents of container

Blister packs containing either 10 or 12 tablets and consisting of a Polyvinylchloride (PVC) / Aclar (Polychlorotrifluoroethylene (PCTFE) film and aluminium foil (25µm), packed in cardboard cartons.

Pack sizes: 12, 20, 24 film-coated tablets

Not all pack sizes may be marketed.

## **6.6 Special precautions for disposal**

Any unused product or waste material should be disposed of in accordance with local requirements.

## **7 MARKETING AUTHORISATION HOLDER**

Procter & Gamble (Health & Beauty Care) Ltd  
The Heights  
Brooklands  
Weybridge  
Surrey  
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## **8 MARKETING AUTHORISATION NUMBER**

PA0441/045/001

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

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