Common Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

Dexibuprofen "Gebro" 200 mg powder for oral suspension
Dexibuprofen „Gebro" 300 mg powder for oral suspension
Dexibuprofen „Gebro" 400 mg powder for oral suspension

2. Qualitative and quantitative composition

Dexibuprofen „Gebro" 200 mg powder for oral suspension
Each sachet contains 200 mg of dexibuprofen.
Excipients: 1,2 g sucrose. For a full list of excipients, see section 6.1.

Dexibuprofen „Gebro" 300 mg powder for oral suspension
Each sachet contains 300 mg of dexibuprofen.
Excipients: 1,8 g sucrose. For a full list of excipients, see section 6.1.

Dexibuprofen „Gebro" 400 mg powder for oral suspension
Each sachet contains 400 mg of dexibuprofen.
Excipients: 2,4 g sucrose. For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Dexibuprofen „Gebro" 200 mg powder for oral suspension
Yellowish powder for oral suspension

Dexibuprofen „Gebro" 300 mg powder for oral suspension
Yellowish powder for oral suspension

Dexibuprofen „Gebro" 400 mg powder for oral suspension
Yellowish powder for oral suspension

4. Clinical particulars

4.1. Therapeutic indications
Symptomatic treatment for the relief of pain and inflammation associated with osteoarthritis.
Acute symptomatic treatment of pain during menstrual bleeding (primary dysmenorrhoea).
Symptomatic treatment of mild to moderate pain, such as muscular-skeletal pain, or dental pain.

4.2. Posology and method of administration
The dosage should be adjusted to the severity of the disorder and the complaints of the patient. Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

The maximum single dose is 400 mg, the maximum daily dose is 1200 mg dexibuprofen.

For individual dosage sachets with 200, 300 and 400 mg dexibuprofen are available. The 400 mg sachet is available as full dose in one sachet or as 400 mg sachet which is divided into two compartments with halve doses of 200 mg dexibuprofen each.

The duration of treatment should not exceed 2 weeks. Alternative products, e.g. Dexibuprofen film-coated tablets, are recommended if longer treatment is necessary.

Osteoarthritis
The recommended dose is 600 to 900 mg dexibuprofen daily, divided in up to three single doses, for example 400 mg twice a day or 300 mg two to three times a day. The dose may be increased up to 1200 mg dexibuprofen per day in patients with acute conditions or exacerbations.

Mild to moderate pain
The recommended dose is 600 mg dexibuprofen daily, divided in up to three single doses.
If clearly needed in patients with acute pain conditions (e.g. in surgical extraction of teeth) the dose may be transiently increased up to 1200 mg dexibuprofen per day.

Dysmenorrhoea
The recommended dose is 600 to 900 mg dexibuprofen daily, divided in up to three single doses, for example 400 mg twice a day or 300 mg two to three times a day.

Children and adolescents
Dexibuprofen has not been studied in children and adolescents (< 18 years): Safety and efficacy have not been established and therefore it is not recommended in these age groups.

Elderly
No special dosage modifications are required in the elderly. However, individual dose reduction and assessment has to be considered due to increased susceptibility to GI adverse reactions in the elderly (see section 4.4).

Hepatic dysfunction
Patients with mild to moderate hepatic dysfunction should start therapy at reduced doses and be closely monitored. Dexibuprofen should not be used in patients with severe hepatic dysfunction (see section 4.3).

Renal dysfunction
The initial dose should be reduced in patients with mild to moderate impaired renal function. Dexibuprofen should not be used in patients with severe renal dysfunction (see section 4.3).

The powder should be suspended in a glass of water, approximately 200 ml and should be taken immediately after preparation.

The sachets can be taken with or without a meal (see section 5.2). In general NSAIDs (non-steroidal anti-inflammatory drugs) are preferably taken with a meal to reduce gastrointestinal irritation, particularly during chronic use. However, a later onset of action in some patients may be anticipated when taken with or directly after a meal.

4.3. Contraindications

Dexibuprofen must not be administered in patients:

- with hypersensitivity to dexibuprofen, to any other NSAID, or to any of the excipients of the product.
- in whom substances with a similar action (e.g. acetylsalicylic acid or other NSAIDs) precipitate attacks of asthma, bronchospasm, acute rhinitis, or cause nasal polyps, urticaria or angioneurotic oedema.
- with a history of gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- with active, or a history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- with cerebrovascular bleeding or other active bleedings.
- with active Crohn's disease or active ulcerative colitis.
- with severe heart failure.
- with severe renal dysfunction (GFR < 30 ml/min).
- with severely impaired hepatic function.
- from the beginning of 6th month of pregnancy (see section 4.6).

4.4 Special warning and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 and GI and cardiovascular risks below).

The use of dexibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2).

Gastrointestinal bleeding, ulceration and perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID dose, in patients with a history of ulcers, particularly if complicated with haemorrhage or perforation (see section 4.3), alcoholism and in the elderly. 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 requiring concomitant low dose acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of GI toxicity particularly when elderly should report any abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.
Caution should be advised in patients receiving concomitant medication 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 acetylsalicylic acid (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving <TRADENAME>, the treatment should be withdrawn.

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).

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.

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

Dexibuprofen should only be given with care to patients with systemic lupus erythematosus and mixed connective tissue disease, because such patients may be predisposed to NSAID-induced renal and CNS side effects, including aseptic meningitis (see section 4.8).

Cardiovascular and cerebrovascular effects
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.
Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at a high dose (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). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg daily) is associated with an increased risk of myocardial infarction. There are insufficient data to exclude such a risk for dexibuprofen.
Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Caution is required in patients suffering hepatic and renal disease; the risk of fluid retention, oedema and a deterioration in renal function must be taken into account. If used in these patients, the dose of dexibuprofen should be kept as low as possible and renal function should be regularly monitored.

Caution is required in patients suffering from, or with a previous history of, bronchial asthma since NSAIDs can cause bronchospasm in such patients (see section 4.3).

NSAIDs may mask the symptoms of infections.

As with all NSAIDs, dexibuprofen can increase plasma urea nitrogen and creatinine. As with other NSAIDs, dexibuprofen can be associated with adverse effects on the renal system, which can lead to glomerular nephritis, interstitial nephritis, renal papillary necrosis, nephrotic syndrome and acute renal failure (see section 4.2, 4.3 and 4.5).

As with other NSAIDs, dexibuprofen can cause transient small increases in some liver parameters, and also significant increases in SGOT and SGPT. In case of a relevant increase in such parameters, therapy must be discontinued (see section 4.2 and 4.3).

In common with other NSAIDs dexibuprofen may reversibly inhibit platelet aggregation and function and prolong bleeding time. Caution should be exercised in patients with haemorrhagic diathesis and other coagulation disorders and when dexibuprofen is given concurrently with oral anticoagulants (see section 4.5).

Patients receiving long-term treatment with dexibuprofen should be monitored as a precautionary measure (renal, hepatic functions and haematologic function/blood counts).

During long-term, high dose, off-label treatment with analgesics, headaches can occur which must not be treated with higher doses of the medicinal product.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

In general the habitual use of analgesics, especially the combination of different analgesic drug substances, can lead to lasting renal lesions with the risk of renal failure (analgesic nephropathy). Thus combinations with ibuprofen or other NSAIDs (including OTC products and selective COX-2 inhibtors) should be avoided.

Drugs known to inhibit cyclooxygenase/prostaglandin synthesis may impair fertility reversibly and are not recommended in women attempting to conceive (see section 4.6).

Data from preclinical studies suggest that inhibition of platelet aggregation by low-dose acetylsalicylic acid may be impaired if NSAIDs such as dexibuprofen are administered concurrently. This interaction could reduce the cardiovascular-protective effect. Therefore if concomitant administration of low dose acetylsalicylic acid is indicated special precaution is required if duration of treatment exceeds short term use.

4.5. Interaction with other medicinal products and other forms of interaction
The information in this section is based upon previous experience with other NSAIDs. In general, NSAIDs should be used with caution with other drugs that can increase the risk of gastrointestinal ulceration or gastrointestinal bleeding or renal impairment.

Concomitant use not recommended:
Anticoagulants: NSAIDs may enhance the effect of anti-coagulants, such as warfarin (see section 4.4). Blood coagulation tests (INR, bleeding time) should be performed during the initiation of dexibuprofen treatment and the dosage of the anticoagulant should be adjusted if necessary.

Methotrexate used at doses of 15 mg/week or more: If NSAIDs and methotrexate are given within 24 hours of each other plasma levels of methotrexate may increase, via a reduction in its renal clearance thus increasing the potential for methotrexate toxicity. Therefore, in patients receiving high-dose treatment with methotrexate, the concomitant use of dexibuprofen is not recommended (see section 4.4).

Lithium: NSAIDs can increase the plasma levels of lithium, by reducing its renal clearance. The combination is not recommended (see section 4.4). Frequent lithium monitoring should be performed if the combination proves necessary. The possibility of reducing the dose of lithium should be considered.

Other NSAIDs and salicylates (acetylsalicylic acid at doses above those used as antiplatelet treatment, approximately 100 mg/day): The concomitant use with other NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided, since simultaneous administration of different NSAIDs can increase the risk of gastrointestinal ulceration and haemorrhage.

Precautions:
Acetylsalicylic acid:
Concomitant administration may impair inhibition of platelet aggregation by low-dose acetylsalicylic acid through competitive inhibition of the acetylation site of cyclooxygenase in the platelet (see section 4.4).

Antihypertensives:
NSAIDs may reduce the efficacy of beta-blockers, possibly due to inhibition of the formation of vasodilatory prostaglandins.
The concomitant use of NSAIDs and ACE inhibitors or angiotensin-II receptor antagonists may be associated with an increased risk of acute renal failure, especially in patients with pre-existing impairment of renal function. When given to the elderly and/or dehydrated patients, such a combination can lead to acute renal failure by acting directly on glomerular filtration. At the beginning of the treatment, a careful monitoring of renal function is recommended.
Furthermore, chronic administration of NSAIDs can theoretically reduce the antihypertensive effect of angiotensin-II receptor antagonists, as reported with ACE inhibitors. Therefore, caution is required when using such a combination and at the start of treatment, renal function should be carefully monitored (and patients should be encouraged to maintain adequate fluid intake).

Ciclosporin, tacrolimus, sirolimus and aminoglycoside antibiotics: Concomitant administration with NSAIDs may increase the risk of nephrotoxicity on account of reduced synthesis of prostaglandins in the kidney. During combination treatment renal function must be closely monitored, especially in the elderly.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (see section 4.4)

Digoxin: NSAIDs can increase the plasma levels of digoxin and increase the risk of digoxin toxicity.

Methotrexate used at doses lower than 15 mg/week: Dexibuprofen may increase methotrexate levels. If dexibuprofen is used in combination with low doses of methotrexate, then the patient's blood count should be monitored carefully, particularly during the first weeks of coadministration. An increased surveillance is required in the presence of even mildly impaired renal function, notably in the elderly, and renal function should be monitored to anticipate any reductions in the clearance of methotrexate.

Phenytoin: Some NSAIDs may displace phenytoin from protein-binding sites, possibly leading to increased phenytoin serum levels and toxicity. Although clinical evidence for this interaction is limited, phenytoin dosage adjustment, based on monitoring of plasma concentrations and/or observed signs of toxicity, is recommended.

Phenytoin, phenobarbital and rifampicin: Concomitant administration of CYP2C8 and CYP2C9 inducing agents may lower the effects of dexibuprofen.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):
Increased risk of gastrointestinal bleeding.

Thiazides, thiazide-related substances, loop diuretics and potassium-sparing diuretics:
Concurrent use of an NSAID and a diuretic may increase the risk of renal failure secondary to a reduction in renal blood flow.

Drugs increasing potassium plasma levels:
NSAIDs have been reported to increase serum potassium levels. Therefore, caution is required during concomitant treatment with other drugs that increase potassium plasma levels (such as potassium sparing diuretics, ACE inhibitors, angiotensin-II receptor antagonists, immunosuppressants like cyclosporin or tacrolimus, trimethoprim and heparins) and serum potassium levels should be monitored.

Thrombolytics, ticlopidine and other antiplatelet agents:
Dexibuprofen inhibits platelet aggregation via inhibition of platelet cyclooxygenase. Therefore, caution is required when dexibuprofen is combined with thrombolytics, ticlopidine and other antiplatelet agents, because of the risk of increased antiplatelet effect.

4.6. Pregnancy and lactation
Pregnancy:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development.
Data from epidemiological studies suggest an increased risk of miscarriage, cardiac malformation and gastroschisis 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 postimplantation loss and embryo-fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period (see section 5.3).
During the first and second trimester of pregnancy NSAIDs should not be given unless clearly necessary. If NSAIDs are used during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the fetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension),
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis, and may expose the mother and the neonate, at the end of pregnancy, to:
    - possible prolongation of bleeding time, an antiaggregating effect which may occur even at very low doses,
    - inhibition of uterine contractions resulting in delayed or prolonged labour.

Therefore, from the beginning of the 6th month of pregnancy onward dexibuprofen is contraindicated.

Lactation:
Ibuprofen is slightly excreted in human milk. Breast-feeding is possible with dexibuprofen if dosage is low and the treatment period is short.

Fertility
NSAIDs may impair fertility reversibly and are not recommended in women attempting to conceive; if treatment with NSAIDs is necessary, the lowest dose and the shortest duration of treatment possible should be chosen (see section 4.4).

4.7. Effects on ability to drive and use machines
During treatment with dexibuprofen the patient's reaction capacity may be reduced when dizziness or fatigue appear as side effects. This should be taken into consideration when increased alertness is required, e.g. when driving or operating machinery. For a single dose or short term use of dexibuprofen no special precautions are necessary.

4.8. Undesirable effects
Clinical experience has shown that the risk of undesirable effects induced by dexibuprofen is comparable to that of racemic ibuprofen. The most common adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4).
Clinical bridging and other studies with a duration of about 2 weeks show a frequency of about 8 to 20% of patients with mostly mild GI-events and a much lower frequency in low risk populations e.g. during short term use or if used occasionally.

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1000 to <1/100
Rare	≥1/10 000 to<1/1000
Very rare	<1/10 000, not known (cannot be estimated from the available data)

Infections and infestation
Very rare: Infection related inflammation may be aggravated (necrotising fascitis).

Blood and lymphatic system disorders
Bleeding time could be prolonged.
Rare: Cases of blood disorders including thrombocytopenia, leucopenia, granulocytopenia, pancytopenia, agranulocytosis, aplastic anemia or haemolytic anaemia.

Immune system disorders
Uncommon: Purpura (including allergic purpura), angiooedema.
Rare: Anaphylactic reaction.
Very rare: Generalized hypersensitivity reactions, including symptoms like fever with rash, abdominal pain, headache, nausea and vomiting, signs of liver injury, even aseptic meningitis. In the majority of cases in which aseptic meningitis has been reported with ibuprofen, some form of underlying auto-immune disease (such as systemic lupus erythematosus or other collagen diseases) was present as a risk factor. In the case of a severe generalized hypersensitivity reaction swelling of face, tongue and larynx, bronchospasm, asthma, tachycardia, hypotension and shock can occur.

Psychiatric disorders
Uncommon: Anxiety.
Rare: Psychotic reaction, depression, irritability.

Nervous system disorders
Common: Drowsiness, headache, dizziness, vertigo.
Uncommon: Insomnia, restlessness.
Rare: Disorientation, confusion, agitation.
Very rare: Aseptic meningitis (see immune system disorders).

Eye disorders
Uncommon: Visual disturbances.
Rare: Reversible toxic amblyopia.

Ear and labyrinth disorders
Uncommon: Tinnitus.
Rare: Impaired hearing.

Gastrointestinal disorders
Very common: Dyspepsia, abdominal pain.
Common: Diarrhoea, nausea, vomiting.
Uncommon: Gastrointestinal ulcers and bleeding, gastritis, ulcerative stomatitis, melaena. Local burning sensation in mouth or throat.
Rare: Gastrointestinal perforation, flatulence, constipation, esophagitis, esophageal strictures, exacerbation of diverticular disease, unspecific haemorrhagic colitis, ulcerative colitis or Crohn's disease. If gastrointestinal blood loss occurs, this may cause anaemia and haematemesis.

Skin and subcutaneous tissue disorders
Common: Rash.
Uncommon: Urticaria, pruritus.
Very rare: Erythema multiforme, epidermal necrolysis, systemic lupus erythematosus, alopecia, photosensitivity reactions, bullous reactions including Stevens-Johnson-Syndrome, acute toxic epidermal necrolysis (Lyell-Syndrome) and allergic vasculitis.

Respiratory, thoracic and mediastinal disorders
Uncommon: Rhinitis, bronchospasm.

Renal and urinary disorder
Very rare: Interstitial nephritis, nephrotic syndrome or renal failure.

Hepatobilary disorders
Rare: Abnormal liver function, hepatitis and jaundice.

General disorders
Common: Fatigue.
Fluid retention, patients with hypertension or renal impairment seem to be predisposed.

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 dose (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) (see section 4.4).

4.9. Overdose
Dexibuprofen has a low acute toxicity and patients have survived after single doses as high as 54 g of ibuprofen (equivalent to approximately 27 g of dexibuprofen). Most overdoses have been asymptomatic. There is a risk of symptoms at doses > 80 - 100 mg/kg ibuprofen.
The onset of symptoms usually occurs within 4 hours. Mild symptoms are most common, including abdominal pain, nausea, vomiting, lethargy, drowsiness, headache, nystagmus, tinnitus and ataxia. Rarely, moderate or severe symptoms include gastrointestinal bleeding, hypotension, hypothermia, metabolic acidosis, seizures, impaired kidney function, coma, adult respiratory distress syndrome and transient episodes of apnoea (in very young children following large ingestions).

Treatment is symptomatic, and there is no specific antidote. Amounts not likely to produce symptoms (less than 50 mg/kg dexibuprofen) may be diluted with water to minimize gastrointestinal upset. In case of ingestion of a significant amount, activated charcoal should be administered.

Emptying of the stomach by emesis may only be considered if the procedure can be undertaken within 60 minutes of ingestion. Gastric lavage should not be considered unless a patient has ingested a potentially life-threatening amount of the drug and the procedure can be undertaken within 60 minutes of ingestion. Forced diuresis, hemodialysis or hemoperfusion are unlikely to be of assistance because dexibuprofen is strongly bound to plasma proteins.

5. Pharmacological properties

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Antiinflammatory and antirheumatic products, non-steroids, propionic acid derivatives.
ATC code: M01AE14

Dexibuprofen (= S(+)-ibuprofen) is the pharmacologically active enantiomer of ibuprofen, a non-selective NSAID. Its mechanism of action is thought to be due to inhibition of prostaglandin synthesis. In humans it reduces pain, inflammation and fever and reversibly inhibits ADP- and collagen- stimulated platelet aggregation.
Bridging clinical studies in order to compare the efficacy of racemic ibuprofen and dexibuprofen in osteoarthritis over a treatment period of 15 days, in dysmenorrhea, including symptoms of pain and in dental pain have demonstrated at least non-inferiority of dexibuprofen versus racemic ibuprofen at the recommended 1:2 dose ratio.

5.2. Pharmacokinetic properties
Following oral administration dexibuprofen is well absorbed primarily from the small intestine. After metabolic transformation in the liver (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely excreted, mainly by the kidneys (90%), but also in the bile. The elimination half-life is 1.8 – 3.5 hours; the plasma protein binding is about 99 %. Maximum plasma levels are reached about 2 hours after oral administration. The administration of 400 mg dexibuprofen as prepared suspension with a high fat meal prolongs the time to reach maximum concentrations slightly (from 2.5

hours after a high fat meal to 2.0 hours after fasting conditions) and decreases the maximum plasma concentrations (from 22 to 15 µg/ml), but has no effect on the extent of absorption.

Pharmacokinetic studies with ibuprofen in patients with renal failure suggest a dosage reduction in these patients. Caution is also required due to inhibition of renal prostaglandin synthesis (see section 4.2 and 4.4).
Elimination of dexibuprofen is slightly lower in patients with liver cirrhosis.

5.3. Preclinical safety data
Bridging studies on single and repeated dose toxicity, reproduction toxicity and mutagenicity have shown that the toxicological profile of dexibuprofen is comparable to that of ibuprofen and reveal no other specific toxicological or carcinogenic hazards for humans.
Ibuprofen inhibited ovulation in the rabbit and impaired implantation in different animal species (rabbit, rat, mouse). Administration of prostaglandin synthesis inhibitors including ibuprofen (mostly in doses higher than used therapeutically) to pregnant animals has been shown to result in increased pre- and postimplantation loss, embryo-fetal lethality and increased incidences of malformations.

6. Pharmaceutical particulars

6.1. List of excipients
Sucrose,
Citric acid,
Orange flavour,
Saccharin,
Silica,
Sodium laurilsulfate.

6.2. Incompatibilities
Not applicable.

6.3. Shelf life
Dexibuprofen „Gebro" 200 mg powder for oral suspension
3 years

Dexibuprofen „Gebro" 300 mg powder for oral suspension
3 years

Dexibuprofen „Gebro" 400 mg powder for oral suspension
Sachets: 3 years
Bipartite sachets: 18 month

6.4. Special precautions for storage
Do not store above 25 °C.

6.5. Nature and contents of container
Dexibuprofen „Gebro" 200 mg powder for oral suspension
Yellowish Powder in 10 sachets per box.

Dexibuprofen „Gebro" 300 mg powder for oral suspension
Yellowish Powder in 30 sachets per box.

Dexibuprofen „Gebro" 400 mg powder for oral suspension
Yellowish Powder in 10, 30, and 40, sachets per box.
or
Yellowish Powder in 10, 30, and 40, bipartite sachets per box.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7. Marketing authorisation holder

8. Marketing authorisation number(s):

9. Date of first authorisation / renewal of the authorisation:

10. Date of revision of the text
May 2008