تم إعتماد النشرة من قبل لجنة الفارماكولوجيا
جامعة فيل
٢٠١٧/١١/١٦

MEGAFEN 200MG/ 325 MG TABLETS

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Megafen Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients: Each tablet contains ibuprofen 200 mg and paracetamol 325 mg
Inactive ingredients: Starch maize (dry), Povidone (P.V.P K30), Sodium lauryl sulphate, Croscarmellose sodium (Ac. Di-Sol), Colloidal anhydrous silica, Sunset yellow No. 6 (CI 15985) and Magnesium stearate

3 PHARMACEUTICAL FORM

Tablets

4 CLINICAL PARTICULARS

4.1Therapeutic indications

For the temporary relief of mild to moderate pain associated with migraine, headache, backache, period pain, dental pain, rheumatic and muscular pain, pain of non-serious arthritis, cold and flu symptoms, sore throat and fever. This product is especially suitable for pain, which requires stronger analgesia than ibuprofen or paracetamol alone.

4.2 Posology and method of administration

Posology

For short term-use only
Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.
The patient should consult a doctor if the symptoms persist or worsen or if the product is required for more than 3 days.
Adults: One tablet to be taken up to three times per day with water. Leave at least six hours between doses.
If the one tablet dose does not control symptoms, a maximum of two tablets may be taken up to three times a day. Leave at least six hours between doses.
Do not take more than six tablets (3000mg Paracetamol, 1200mg Ibuprofen) in any 24 hours period.
To minimize side effects, it is recommended that patients take Megafen with food.
Elderly: No special dosage modifications are required.
The elderly are at increased risk of the serious consequences of adverse reactions. If an
NSAID is considered necessary; the lowest effective dose should be used for the shortest possible duration. The patient should be monitored regularly for gastrointestinal bleeding during NSAID therapy.
Not for use by children under 18 years.

Method of Administration

For oral administration

4.3 Contraindications

This product is contraindicated:

- In patients with a known hypersensitivity to ibuprofen, paracetamol or any other excipients in the product.

- In concomitant use with other Paracetamol-containing products – increased risk of serious adverse effects.
- In patients with a history of hypersensitivity reactions (e.g. bronchospasm, angioedema, asthma, rhinitis, or urticaria) associated with acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).
- In patients with Active, or a history of recurrent peptic ulcer/hemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- In patients with a history of, or an existing gastrointestinal ulceration/perforation or bleeding, including that associated with NSAIDs.
- Patients with defects in coagulation.
- In patients with severe hepatic failure, severe renal failure or severe heart failure (NYHA Class IV).
- In concomitant use with other NSAID containing products, including cyclo-oxygenase-2 (COX-2) specific inhibitors and doses of acetylsalicylic acid above 75 mg daily – increased risk of adverse reactions.

During the last trimester of pregnancy due to risk of premature closure of the foetal ductus arteriosus with possible pulmonary hypertension .

4.4 Special warnings and precautions for use

Do not exceed the recommended dose.

If symptoms persist, consult your doctor.

Keep out of the sight and reach of children.

Paracetamol:

The hazards of paracetamol overdose are greater in patients with non-cirrhotic alcoholic liver disease. Immediate medical advice should be sought in the event of an overdose, even if the patient feels well, because of the risk of delayed, serious liver damage.

Ibuprofen:

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms and gastrointestinal and cardiovascular risks below) and by patients taking the dose with food.

Elderly:

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

Caution is required in patients with certain conditions:

- **Respiratory disorders:**

In patients suffering from, or with a history of, bronchial asthma or allergic disease NSAIDs have been reported to precipitate bronchospasm.

- **SLE and mixed connective tissue disease:**

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disease disorders there may be an increased risk of aseptic meningitis.

- **Cardiovascular and cerebrovascular effects:**

Appropriate monitoring and medical advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low

dose ibuprofen (e.g. ≤1200mg/day) is associated with an increased risk of arterial thrombotic events.
Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided. Careful consideration should be exercised before initiating long-term treatment for patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, and smoking) particularly if high doses of ibuprofen (2400 mg/day) are required.

- **Cardiovascular, renal and hepatic impairment:**

The administration of NSAIDs may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients.
NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. NSAIDs are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

- **Gastrointestinal effects:**

NSAIDS should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated.
Gastrointestinal (GI) bleeding, ulceration and 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 serious GI events.
The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation 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.
Patients with a history of GI toxicity, particularly the elderly, should report any unusualabdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.
Caution should be advised in 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 antiplatelet agents such as acetylsalicylic acid.
When GI bleeding or ulceration occurs in patients receiving ibuprofen containing products, the treatment should be withdrawn.
NSAIDs cause an increased risk of serious gastrointestinal adverse events including inflammation, bleeding, ulceration and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

- **Dermatological effects:**

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. 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. Use of this product should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

- **Impaired female fertility:**

There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may impair female fertility by an effect on ovulation and is not recommended in women attempting to conceive. This is reversible on withdrawal of treatment. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of the product should be considered.

4.5 Interaction with other medicinal products and other forms of interaction

This product (like any other paracetamol containing products) is contraindicated in combination with other paracetamol containing products – increased risk of serious adverse effects.

This product (like any other ibuprofen containing products and NSAIDs) is contraindicated in combination with:

- Acetylsalicylic acid: Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects, unless low-dose acetylsalicylic acid (not above 75 mg daily) has been advised by a doctor.
- Experimental data suggest that Ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.
- Other NSAIDs including cyclo-oxygenase-2 selective inhibitors as these may increase the risk of adverse effects

This product (like any other paracetamol containing products) should be used with caution in combination with:

- Cholestyramine: The speed of absorption of paracetamol is reduced by cholestyramine. Therefore, cholestyramine should not be taken within one hour if maximal analgesia is required.
- Metoclopramide and Domperidone: The absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.
- Warfarin: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

This product (like any other ibuprofen containing products and NSAIDs) should be used with caution in combination with:

- Anticoagulants: NSAIDs may enhance the effects of anticoagulants, i.e. warfarin.
- Antihypertensives (ACE inhibitors and Angiotensin II Antagonists) and diuretics: NSAIDs may reduce the effects of these drugs. 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 or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. These interactions should be considered in patients taking a coxib concomitantly with ACE inhibitors or angiotensin II antagonists. 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. Diuretics may increase the risk of nephrotoxicity of NSAID.

- Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.
- Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.
- Ciclosporin: Increased risk of nephrotoxicity.
- Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding.
- Lithium: Decreased elimination of lithium.
- Methotrexate: Decreased elimination of methotrexate.
- 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: Increased risk of haematological toxicity with NSAIDS are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

4.6 Pregnancy and lactation

Pregnancy:

There is no experience of use of this product in humans during pregnancy.

Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern.

In view of the known effects of NSAIDs on the fetal cardiovascular system (risk of closure of ductus arteriosus), use in the last trimester is contraindicated. The onset of labor may be delayed and duration increased with an increased bleeding tendency in both mother and child. NSAIDs should not be used during the first two trimesters of pregnancy or labor unless the potential benefit to the patient outweighs the potential risk to the fetus.

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol use at the recommended dosage. .

Therefore, if possible, the use of this product should be avoided in the first six months of pregnancy and contraindicated in the last three months of pregnancy.

Lactation:

Ibuprofen and its metabolites can pass in very small amounts (0.0008% of the maternal dose) into the breast milk. No harmful effects to infants are known.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breastfeeding.

Dr Maria 16/8/2021

A large amount of data on pregnant women indicate neither malformative nor feto/neonatal toxicity - Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results - If clinically needed, paracetamol can be used during pregnancy however it should be

Therefore, it is not necessary to interrupt breastfeeding for short-term treatment with the recommended dose of this product.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected patients should not drive or operate machinery.

4.8 Undesirable effects

Clinical trials with this product have not indicated any other undesirable effects other than those for ibuprofen or paracetamol alone.

The following table lists adverse effects from pharmacovigilance data experienced by patients taking ibuprofen alone or paracetamol alone in short-term and long-term use. Adverse events which have been associated with Ibuprofen alone or Paracetamol alone are given below, tabulated by system organ class and frequency. Frequencies are defined as 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) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

Blood and Lymphatic System Disorders:

Very rare: Hematopoietic disorders

Immune System Disorders:

Uncommon: Hypersensitivity with urticarial and pruritus

Very rare: Severe hypersensitivity reactions, Symptoms can include facial, tongue and throat swelling, dyspnea tachycardia, hypotension (anaphylaxis angioedema or severe shock).

Psychiatric Disorders:

Very rare: Confusion, depression and hallucinations

Nervous System Disorders:

Uncommon: Headache and dizziness

Very rare: Aseptic meningitis[3], paraesthesia, optic, neuritis and somnolence,

Eye Disorders:

Very rare: Visual disturbance

Ear and Labyrinth Disorders:

Very rare: Tinnitus and vertigo

Cardiac Disorders:

Very rare: Cardiac failure and edema.

Vascular Disorders:

Very rare: Hypertension

Respiratory and thoracic and mediastinal disorders:

Very rare: Respiratory reactivity including: asthma, exacerbation of asthma, bronchospasm and dyspnoea

Gastrointestinal Disorders:

Common: Abdominal pain, vomiting, diarrhea, nausea, dyspepsia and abdominal discomfort

Uncommon: peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhag , melaena , haematemesis, mouth ulceration , exacerbation of colitis and crohn's disease gastritis, pancreatitis, flatulence and constipation

Hepatobiliary Disorders:
Very rare: Abnormal liver function, hepatitis and jaundice
Skin and Subcutaneous Tissue Disorders :
Common: Hyperhidrosis
Uncommon: Various skin rashes
Very rare: Bullous reactions including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis. Exfoliative dermatoses purpura, photosensitivity
Renal and urinary disorders:
Very rare: Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome, and acute and chronic renal failure
General Disorders and Administration site conditions:
Very rare: Alanine aminotransferase increased, gamma-glutamyltransferase increased and liver function tests abnormal with paracetamol. Blood creatinine increased, blood urea increased.
Uncommon: Aspartate aminotransferase increased, blood alkaline phosphatase increased, blood creatine phosphokinease increased, haemoglobin decreased and platelet count Increased.
Description of Selected Adverse Reactions
Examples include agranulocytosis, anaemia, aplastic anaemia, haemolytic anaemia, leucopenia, neutropenia, pancytopenia and thrombocytopenia.
First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising and nose bleeding.
Hypersensitivity reactions have been reported. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract activity, e.g. asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) various skin reactions, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including toxic epidermal necrolysis, Stevens-Johnson Syndrome and erythema multiforme).
The pathogenic mechanism of drug-Induced aseptic meningitis is not fully understood. However, the available data on NSAID-related aseptic meningitis points to a hypersensitivity reaction (due to a temporal relationship with drug intake, and disappearance of symptoms after drug discontinuation). Of note, Single cases of aseptic meningitis in patients with existing autoimmune disorders (such as systemic lupus erythematosus and mixed connective tissue disease) during treatment with Ibuprofen, with symptoms such as: stiff neck, headache, nausea, vomiting, fever or disorientation have been observed.
Clinical studies suggest that use of ibuprofen particularly at high a dose (2400mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).
The adverse events observed most often are gastrointestinal in nature.Sometimes fatal, particularly in the elderly.
In overdose Paracetamol can cause acute hepatic failure, hepatic failure, hepatic necrosis and liver injury.
Especially in long-term use, associated with increased serum urea and oedema.
Also includes papillary necrosis.

Reporting of Suspected Adverse Reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

Paracetamol
Liver damage is possible in adults who have taken 10 g (equivalent to 20 tablets) or more of paracetamol. Ingestion of 5 g (equivalent to 10 tablets) or more of paracetamol may lead to liver damage if the patient has one or more of the risk factors below:
a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
b) Regularly consumes alcohol in excess of recommended amounts.
c) Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Symptoms
Symptoms of paracetamol overdose in the first 24 hours include pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion as liver function tests become abnormal. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management
Immediate treatment is essential in the management of paracetamol overdose. Despite a lackof significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines.
Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable).
Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol however; the maximum protective effect is obtained up to 8 hours post ingestion. The effectiveness of the antidote declines sharply after this time.
If required the patient should be given intravenous-N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.
Patients who present with serious hepatic dysfunction beyond 24 hours from ingestion should be managed in accordance with established guidelines.

Ibuprofen
In children ingestion of more than 400 mg/kg of Ibuprofen may cause symptoms. In adults the dose response effect is less clear cut.
The half-life in overdose is 1.5-3 hours.

Symptoms
Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning metabolic acidosis may occur and the prothrombin time / INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur if there is a co-incident of dehydration. Exacerbation of asthma is possible in asthmatics.

Management
Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Musculoskeletal system, anti-inflammatory and antirheumatic products, non-steroids, propionic acid derivatives. Ibuprofen combinations.
The pharmacological actions of ibuprofen and paracetamol differ in their site and mode of action. These complementary modes of action are synergistic which results in greater antinociception and antipyresis than the single actives alone.
Ibuprofen is an NSAID that has demonstrated its efficacy in the common animal experimental inflammation models by inhibition of prostaglandin synthesis. Prostaglandins sensitise nociceptive afferent nerve terminals to mediators such as bradykinin. Ibuprofen therefore elicits an analgesic effect through peripheral inhibition of the cycloxygenase-2 (COX-2)
isoenzyme with a subsequent reduction in sensitisation of nociceptive nerve terminals. Ibuprofen has also been shown to inhibit induced-leucocyte migration into inflamed areas. Ibuprofen has a pronounced action within the spinal cord due, in part, to the inhibition of COX. Ibuprofen's antipyretic effects are produced by the central inhibition of prostaglandinsin the hypothalamus. Ibuprofen reversibly inhibits platelet aggregation. In humans, ibuprofen reduces inflammatory pain, swellings and fever.
Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the
cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.
Paracetamol's exact mechanism of action is still not completely defined; however, there is considerable evidence to support the hypothesis of a central antinociceptive effect. Various

biochemical studies point to inhibition of central COX-2 activity. Paracetamol may also stimulate the activity of descending 5-hydroxytryptamine (serotonin) pathways that inhibit nociceptive signal transmission in the spinal cord. Evidence has shown that paracetamol is a very weak inhibitor of peripheral COX-1 and 2 isoenzymes.
The clinical efficacy of ibuprofen and paracetamol has been demonstrated in pain associated with headache, toothache and dysmenorrhoea, and fever; furthermore, efficacy has been shown in patients with pain and fever associated with cold and influenza and in pain models such as sore throat, muscular pain or soft tissue injury and backache.
This product is especially suitable for pain, which requires stronger pain relief than ibuprofen 400 mg or paracetamol 1000 mg alone, and faster pain relief than ibuprofen.

5.2 Pharmacokinetic properties

Ibuprofen is well absorbed from the gastrointestinal tract and is extensively bound to plasma proteins. Ibuprofen diffuses into the synovial fluid. Plasma levels of ibuprofen from this product are detected from 5 minutes with peak plasma concentrations achieved within 1-2 hours after ingestion on an empty stomach. When this product was taken with food peak ibuprofen plasma levels were lower and delayed by a median of 25 minutes, but overall extent of absorption was equivalent.
Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete. The elimination half-life is approximately 2 hours.
In limited studies, ibuprofen appears in the breast milk in very low concentrations.
No significant differences in ibuprofen pharmacokinetic profile are observed in the elderly.
Paracetamol is readily absorbed from the gastrointestinal tract. Plasma protein binding is negligible at usual therapeutic concentrations, although this is dose-dependent. Plasma levels of paracetamol from this product are detected from 5 minutes with peak plasma concentrations occurring at 0.5-0.67 hours after ingestion on an empty stomach. When this product was taken with food peak paracetamol plasma levels were lower and delayed by a median of 55 minutes, but overall extent of absorption was equivalent.
Paracetamol is metabolized in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates, with about 10% as glutathione conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life is approximately 3 hours.
A minor hydroxylated metabolite, which is usually produced in very small amounts by mixed function oxidases in the liver and detoxified by conjugation with liver glutathione, may accumulate following paracetamol overdose and cause liver damage.
No significant differences in the paracetamol pharmacokinetic profile are observed in the elderly.
The bioavailability and pharmacokinetic profiles of ibuprofen and paracetamol taken as this product are not altered when taken in combination as a single or repeat dose.
This product is formulated using a technology which releases both Ibuprofen and Paracetamol simultaneously, so that the active ingredients deliver a combination effect.

6 PHARMACEUTICAL PARTICULARS

6.1 Shelf life

3 years

6.2 Special precautions for storage

Store at temperature not exceeding 30°C in a dry place

6.3 Package

Carton box containing 1,2 or 3 (Al/transparent PVC) blisters each of 10 tablets and an inner insert.

Manufactured by:

The Tenth of Ramadan for Pharmaceutical Industries & Diagnostics Reagents (Rameda)

6th Of October City – ARE

تم اعتماد النشرة من قبل الهيئة العامة للدواء
د/ منى فاضل
٢٠١٧/١١/١٦

ميجافين أقراص

إيبوبروفين وباراسيتامول

يُرجى قراءة النشرة كاملة لإحتوائها على معلومات هامة لك.

يجب عليك استعمال الدواء بعناية للحصول على النتائج المثلى.

- احتفظ بهذه النشرة فقد تحتاج إلى قراءتها مجددًا.
- للمزيد من المعلومات والاستفسارات، استشر الصيدلي.
- لا يجب عليك استعمال الدواء لأكثر من ثلاثة أيام.
- استشر الطبيب حال استمرار الأعراض المرضية أو تدهورها.
- يُرجى إعلام الطبيب أو الصيدلي حال تدهور أحد الآثار الجانبية أو ظهور آثار جانبية غير مذكورة بالنشرة.

في هذه النشرة:

١- ما هو ميجافين وفيما يستخدم

يسمى الدواء أقراص ميجافين بتركيز ٢٠٠ مجم/٣٢٥ مجم، وسيشار إليه بميجافين في بقية النشرة.

يحتوي ميجافين على المادتين الفعالتين (المسئولتين عن عمل الدواء). وهما الأيبوبروفين والباراسيتامول.

ينتمى الأيبوبروفين إلى المجموعة الدوائية مضادات الإلتهاب غير المحتوية على الستيرويد والتي تعمل على تسكين الألم وإزالة التورم وتخفيض درجة الحرارة.

بينما يعمل مسكن الألم الباراسيتامول بطريقة مختلفة عن الأيبوبروفين لتسكين الألم وعلاج الحمى. يعمل ميجافين على تسكين الألم ذو الدرجة البسيطة إلى المتوسطة المصاحب للصداع النصفي ،الصداع ،ألم الظهر ،ألم الدورة الشهرية ،ألم الأسنان ،آلام العضلات ،الروماتيزم ،آلام إلتهاب المفاصل غير الخطيرة ،أعراض نزلات البرد ،آلام الحلق والحمى.

٢- قبل بدء استعمال ميجافين

لا تستعمل ميجافين في الحالات التالية:

- إذا كنت تستعمل أحد المنتجات الدوائية المحتوية على الباراسيتامول.
- إذا كنت تستعمل أي مسكن يحتوي على الإيبوبروفين وجرعة عالية من الأسبيرين (فوق تركيز ٧٥ مجم يوميًا) أو أي دواء آخر مضاد للإلتهاب غير محتوٍ على الستيرويد بما يشمل مثبطات السايكلوأكسيجيناز-٢ النوعية.
- إذا كنت تعاني من الحساسية تجاه الأيبوبروفين والباراسيتامول أو أي من المكونات الأخرى للميجافين.
- إذا كنت تعاني من الحساسية تجاه الأسبيرين أو مضادات الإلتهاب غير المحتوية على الستيرويد.
- إذا كنت تعاني من القرحة أو النزف من المعدة أو الاثنا عشر (الأمعاء الدقيقة).
- إذا كنت تعاني من اضطراب تخثر الدم.
- إذا كنت تعاني من فشل القلب أو الكبد أو الكلى.
- في آخر ثلاثة أشهر من الحمل.
- إذا كان عمرك أصغر من ١٨ عامًا

يجب أخذ الاحتياطات اللازمة واستشارة الطبيب أو الصيدلي في الحالات التالية

- كبار السن
- إذا كنت تعاني أو عانيت مسبقًا من أزمات الربو
- إذا كنت تعاني من مشاكل في الكبد والقلب والكلى والقولون.
- إذا كنت تعاني من الذئبة الحمراء- في هذه الحالة، يؤثر جهاز المناعة على الأنسجة الضامة مما يؤدي إلى آلام المفاصل وتغيرات في الجلد واضطراب الأعضاء الأخرى أو اضطراب الأنسجة الضامة المختلط.
- إذا كنت تعاني من اضطراب في الجهاز الهضمي أو إلتهاب الأمعاء المزمن (مثل إلتهاب القولون المتقرح أو مرض كرون).
- إذا كنت تخططين للحمل
- قد يزيد خطر الإصابة بنوبة أو سكتة قلبية مع الأدوية المسكنة للآلام/المضادة للإلتهاب مثل الأيبوبروفين، خاصة مع التركيزات المرتفعة. لا تتعدى الجرعة الموصى بها أو تتعدى الفترة العلاجية للدواء.
- يجب عليك مناقشة علاجك مع الطبيب أو الصيدلي قبل استعمال ميجافين في الحالات التالية:

- إذا كنت تعاني من أمراض في القلب مثل فشل القلب والذبحة (ألم الصدر) أو إذا تعرضت إلى نوبة قلبية أو أجريت عملية تركيب مجازة أو تعاني من داء الشريان الطرفية (ضعف الدورة الدموية في الساقين والقدمين نتيجة تضيق وانسداد الشرايين)، أو أي نوع من السكتات بما يشمل السكتات الصغيرة والنوبات الإقفارية المؤقتة.
- إذا كنت تعاني من ارتفاع ضغط الدم أو داء السكري أو ارتفاع الكوليسترول أو تاريخ أسري لأمراض القلب أو السكتات، أو إذا كنت مدخنًا.
- من المحتمل أن تؤدي مضادات للإلتهاب غير الإستيرويدية إلي زيادة مخاطر تخثر القلب و الأوعية الدموية, احتشاء عضلة القلب ، والسكتة الدماغية ، والتي يمكن أن تؤدي إلي الوفاة و تزداد إحتمالية هذه المخاطر مع طول فترة الإستخدام، كما تزداد هذه المخاطر مع مرضي القلب و الأوعية الدموية أو المرضي ذوي القابلية للإصابة بأمراض القلب و الأوعية الدموية. يمنع إستخدام مضادات الإلتهاب غير الإستيرودية في علاج ألم ما قبل عملية تحويل مسار الشرايين التاجية.
- مضادات الإلتهاب غير الستيرودية تزيد من مخاطر حدوث أعراض جانبية خطيرة بالجهاز الهضمي متضمنة: إلتهاب و نزيف و تقرح و إنثقاب المعدة و الأمعاء و التي من الممكن أن تؤدي إلي الوفاة، و قد تحدث هذه الأعراض في أي وقت أثناء العلاج بدون أي أعراض تحذيرية ، و تزداد هذه المخاطر في المرضي كبار السن

- **استعمال ميجافين مع الأدوية الأخرى**

لا تستعمل ميجافين مع الأدوية التالية:

- المنتجات الدوائية الأخرى المحتوية على الباراسيتامول
- مضادات الإلتهاب غير المحتوية على الستيرويد مثل الأسبيرين والإيبوبروفين.

قد يؤثر أو يتأثر ميجافين على بعض الأدوية مثل:

- أقراص الكورتيكوسيترويد
- المضادات الحيوية (مثل الكلورامفينيكول والكينولون)
- الأدوية المضادة للقيء (مثل الميتاكلوبراميد والدومبيريدون)
- الأدوية المضادة لتخثر الدم (أدوية تخفيف الدم/الواقية من التجلط) مثل الأسبيرين وحمض الأسيتيل سالسيليك والوارفارين والتيكلوبيدين.
- محفزات القلب (مثل الجليكوسيدات)
- الأدوية المعالجة لارتفاع الكوليسترول (مثل الكوليستيرامين)
- مدرات البول (المساعدة لإدرار البول)

- الأدوية المخفضة لارتفاع ضغط الدم (مثل مثبطات الإنزيم المحول للأنجيوتنسين مثل الكابتوبريل وحاجبات بيتا مثل أدوية الأتينولول ومضادات مستقبل أنجيوتنسين-٢ مثل اللوسارتان).
- الأدوية المثبطة لجهاز المناعة (مثل الميثوتريكسات والسايكلوسبورين والتاكرولايماس)
- أدوية الهوس والاكتئاب (مثل الليثيوم ومثبطات إعادة امتصاص السيروتونين الاختيارية)
- الميفيبريستون (لإنهاء الحمل)
- أدوية فيروس عوز المناعة الإنساني (مثل الزايدوفيودين).

قد تتأثر بعض الأدوية الأخرى أو تؤثر على عمل ميجافين، لذا يجب عليك استشارة الطبيب دائمًا قبل بدء استعمال ميجافين مع الأدوية الأخرى.

استعمال ميجافين مع الطعام:

يمكنك استعمال ميجافين أثناء تناول الطعام لتخفيض الآثار الجانبية.

الحمل والرضاعة الطبيعية:

استشيري الطبيب دائمًا قبل استعمال أي دواء. ولا تستعملي الدواء خلال آخر ٣ أشهر من الحمل. واتبعي الاحتياطات اللازمة إذا كنت في أول ٦ أشهر من الحمل. واذا لزم الأمر عكن استخدامه أثناء الحمل بعد استشارة الطبيب

قد يصعب الحمل أثناء استعمال ميجافين. وينمتي إيبوبروفين للمجموعة الدوائية التي تؤثر على خصوبة المرأة. وهذا الأثر عكسي عند وقف استعماله ولذا يجب عليك إعلام الطبيب حال رغبتك بالحمل أو إذا كنت تعانين من صعوبة في الحمل.

٣- كيفية استعمال ميجافين

للاستعمال الفموي ولمدة قصيرة فقط.

استعمل أقل تركيز فعال لأقصر مدة علاجية لازمة لتسكين الألم. لا يجب عليك استعمال ميجافين لأكثر من ٣ أيام. واستشر الطبيب حال استمرار أعراضك المرضية أو تدهورها.

تناول قرص واحد مع الطعام أو الماء لثلاث مرات يوميًا ولكن افصل بين الجرعات بست ساعات على الأقل.

إذا لم يتحكم قرص واحد بأعراضك المرضية، يمكنك تناول قرصين لحد أقصى ثلاث مرات يوميًا. لا تتناول أكثر من ٦ أقراص خلال ٢٤ ساعة (والتي تعادل ٣٠٠٠ مجم من الباراسيتامول و١٢٠٠ مجم من الإيبوبروفين في يوم واحد).

لا يجب استعماله مع الأطفال دون الثامنة عشر.

إذا أفرطت في استعمال ميجافين:

استشر الطبيب على الفور حال إفراطك في استعمال ميجافين حتى إذا لم تكن تشعر بأي أعراض وذلك لأن الإفراط من الباراسيتامول قد يسبب تلف شديد ومتأخر في الكبد.

إذا نسيت استعمال ميجافين:

لا تتناول جرعة مزدوجة للتعويض عن جرعة منسية. إذا نسيت تناول أحد الجرعات، تناولها فور تذكرها وتناول الجرعة التالية بعد ٦ ساعات على الأقل.

٤- الآثار الجانبية المحتملة:

قد يسبب ميجافين آثارًا جانبية كسائر الأدوية، ولكن ليس بالضرورة أن يصاب بها الجميع.\

توقف عن استعمال الدواء واستشر الطبيب في الحالات التالية:

- حرقة المعدة وعسر الهضم
- علامات نزف الجهاز الهضمي (ألم المعدة الشديد وقيء الدم أو السوائل التي تظهر كحبيبات القهوة أو الدم في البراز والبراز الأسود)
- علامات إلتهاب بطانة المخ مثل تيبس الرقبة والصداع والغثيان والقيء والحمى وعدم الإدراك.
- علامات التفاعل التحسسي الشديد (تورم الوجه واللسان والحلق وصعوبة التنفس وتدهور حالة أزمات الربو).
- التفاعلات الجلدية الشديدة مثل ظهور الحبوب
- ارتفاع ضغط الدم واحتباس الماء
- مشاكل الكبد (التي تسبب اصفرار الوجه وبياض العين)
- مشاكل الكلى (التي تسبب زيادة أو انخفاض التبول وتورم الساقين)

- فشل القلب (الذي يسبب صعوبة التنفس والتورم

الآثار الجانبية المحتملة الأخرى:

الآثار الجانبية الشائعة (تصيب أقل من شخص من بين ١٠ أشخاص):

- ألم واضطراب المعدة والغثيان والقيء والإسهال.
- ارتفاع نسب إنزيمات الكبد (في فحوصات الدم)
- فرط التعرق.

الآثار الجانبية غير الشائعة (تصيب أقل من شخص من بين ١٠٠ شخص)

- الدوار والصداع والغازات والإمساك والطفح الجلدي وتورم الوجه والحكة.
- انخفاض عدد كرات الدم الحمراء أو زيادة عدد الصفائح الدموية (الخلايا المسئولة عن تخثر الدم)

الآثار الجانبية النادرة جدًا (تصيب أقل من شخص من بين ١٠,٠٠٠ شخص)

- انخفاض عدد كرات الدم الحمراء (مما يسبب إلتهاب الحلق وقرح الفم وأعراض نزلات البرد والتعب الشديد والنزيف غير معروف السبب والكدمات ونزيف الأنف)
- اضطراب النظر وطنين الأذن والإحساس بالدوار.
- التشوش والإكتئاب والهلوسة
- التعب وعدم الشعور بالراحة

قد ترتبط بعض الأدوية مثل الميجافين بزيادة ضئيلة لخطر الإصابة بنوبات القلب (احتشاء عضلة القلب) أو السكتة (انظر القسم ٢).

الإبلاغ عن الآثار الجانبية المحتملة:

استشر الطبيب أو الصيدلي أو التمريض حال إصابتك بالآثار الجانبية. ويشمل ذلك الآثار الجانبية غير المذكورة بالنشرة، وقد تساعد في تقديم المزيد من المعلومات عن سلامة الدواء. عن طريق إبلاغك عن الآثار الجانبية.

٥- كيفية تخزين ميجافين

احتفظ به بعيدًا عن متناول وبصر الأطفال. لا يلزم اتباع أي شروط لتخزين هذا الدواء. لا تستخدم ميجافين بعد انتهاء فترة الصلاحية المدونة على الشريط والعبوة. ويشير تاريخ الصلاحية إلى آخر يوم في الشهر.

لا يجب التخلص من الأدوية عن طريق الصرف الصحي أو النفايات المنزلية. استشر الطبيب في كيفية التخلص من الأدوية التي لم تعد بحاجة إليها، وستساعد تلك المعايير في حماية البيئة.

٦. المعلومات الأخرى

يحيوط : ٢٠ دايم مدوبر عن مكان جاف

محتويات ميجافين

- المادة الفعالة: الإيبوبروفين والباراسيتامول. يحتوي كل قرص مغلف على ٢٠٠ مجم من الإيبوبروفين ٣٢٥ مجم من الباراسيتامول.
- المواد الغير فعالة : صوديوم الكروسكارميلوز والسليكا الرغوية اللامائية وستيارات المغنسيوم و الذرة النشا (الجافة)، البوفيدون (K30)، كبريتات لوريل الصوديوم، لون اصفر غروب .

كروس كارميلوز صودين

- العبوة : علبة كرتون تحتوي علي ١ ، ٢ أو ٣ شريط كل منه يحتوي علي ١٠ أقراص و نشرة داخلية .

صلاحية : ٢ سنوات

إنتاج:

العاشر من رمضان للصناعات الدوائية والمستحضرات التشخيصية (راميـــــدا)

مدينه السادس من أكتوبر - جمهورية مصر العربية