Oruvail

1. NAME OF THE MEDICINAL PRODUCT

Oruvail 100
Oruvail 150
Oruvail 200

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ketoprofen 100mg
Ketoprofen 150mg
Ketoprofen 200mg

3. PHARMACEUTICAL FORM

Controlled release capsules

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oruvail is recommended in the management of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute articular and peri-articular disorders, (bursitis, capsulitis, synovitis, tendinitis), cervical spondylitis, low back pain (strain, lumbago, sciatica, fibrositis), painful musculo-skeletal conditions, acute gout, dysmenorrhoea and control of pain and inflammation following orthopaedic surgery.
Oruvail reduces joint pain and inflammation and facilitates increase in mobility and functional independence. As with other non-steroidal anti-inflammatory agents, it does not cure the underlying disease.

4.2 Posology and method of administration

Adults: 100 - 200mg once daily, depending on patient weight and on severity of symptoms.
Elderly: The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest dose should be used and the patient should be monitored for GI bleeding for 4 weeks following initiation of NSAID therapy.
Paediatric dosage not established.
Oruvail capsules are for oral administration. To be taken preferably with or after food.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

4.3 Contraindications

Active peptic ulceration, a history of recurrent peptic ulceration or chronic dyspepsia, severe renal dysfunction.
Oruvail should not be given to patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis or urticaria) in response to ketoprofen, any of the other ingredients contained, or to aspirin, ibuprofen or other non-steroidal anti-inflammatory agents. As with other non-steroidal anti-inflammatory agents, severe bronchospasm might be precipitated in these subjects, and in patients suffering from or with a history of, bronchial asthma or allergic disease.
Severe heart failure

4.4 Special warnings and precautions for use

Ketoprofen should be used with caution in patients with renal, hepatic or cardiac impairment. Inhibition of renal prostaglandin synthesis by non-steroidal anti-inflammatory agents may interfere with renal function especially in the presence of existing renal disease. The dose should be kept as low as possible and renal function should be monitored in these patients. NSAIDs should be given with care to patients with a history of heart failure or hypertension since oedema has been reported in association with NSAID administration.
Caution is required if NSAIDs are administered to patients suffering from, or with a previous history of, bronchial asthma, since NSAIDs have been reported to cause bronchospasm in such patients.
NSAIDs should only be given with care to patients with a history of gastrointestinal disease. Oruvail capsules should always be prescribed, "to be taken with food" to minimise gastric intolerance
Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration.
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).
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 some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for ketoprofen.
Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ketoprofen after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

4.5 Interaction with other medicinal products and other forms of interaction

Ketoprofen is highly protein bound, concomitant use of other protein-binding drugs e.g. anticoagulants, sulphonamides, hydantoins, might necessitate modification of dosage in order to avoid increased levels of such drugs resulting from competition for plasma protein-binding sites.
Similar acting drugs such as aspirin or other NSAIDS should not be administered concomitantly with ketoprofen as the potential for adverse reactions is increased.
Serious interactions have been recorded after the use of high dose methotrexate with non-steroidal anti-inflammatory agents, including ketoprofen. Decreased elimination of methotrexate has been reported.
NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Care should be taken in patients treated with any of the following drugs, as interactions with NSAIDs have been reported in some patients:
Antihpertensives: Reduced anti-hypertensive effect.
Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.
Lithium: Decreased elimination of lithium.
Cyclosporin: Increased risk of nephrotoxicity.
Corticosteroids: Increased risk of GI bleeding.
Anticoagulants: Enhanced anticoagulant effect.
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.

4.6 Pregnancy and lactation

No embryopathic effects have been demonstrated in animals and there is epidemiological evidence of the safety of ketoprofen in human pregnancy. Nevertheless, it is recommended to avoid ketoprofen unless considered essential in which case it should be discontinued within one week of expected confinement when NSAIDS might cause premature closure of the ductus arteriosus or persistent pulmonary hypertension in the neonate. They may also delay labour.
Trace amounts of ketoprofen are excreted in breast milk. Avoid use of ketoprofen unless it is considered essential

4.7 Effects on ability to drive and use machines

CNS side effects have been observed in some patients (see section 4.8). If affected patients should not drive or operate machinery.

4.8 Undesirable effects

Adverse effects: minor adverse effects, frequently transient, consist for the most part of gastrointestinal effects such as indigestion, dyspepsia, nausea, vomiting, constipation, diarrhoea, heartburn and various types of abdominal discomfort. Other minor effects, such as, headache, dizziness, mild confusion, vertigo, drowsiness, oedema, mood change and insomnia may occur less commonly.
Major gastrointestinal adverse effects such as ulcerative stomatitis, melaena, haematemesis, peptic ulceration, gastrointestinal haemorrhage, or perforation, gastritis, duodenal ulcer, gastric ulcer may rarely occur.
Less commonly reported major adverse effects involving other organ systems include:
Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of non-specific allergic reactions and anaphylaxis; respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or
dyspnoea; or skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, less commonly, bullous dermatoses (including epidermal necrolysis and erythema multiforme, and exfoliative dermatitis).
Renal: Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome and renal failure.
Hepatic: Abnormal liver function, hepatitis and jaundice.
Neurological and special senses: Hallucinations, visual disturbances, optic neuritis, tinnitus, paraesthesia, malaise, fatigue, depression
Haematological: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.
Dermatological: Photosensitivity
As with other NSAIDs, rare cases of colitis, proctitis and ulcerative colitis have been reported. In such an event, all

NSAID drugs, including ketoprofen, should be discontinued.
In all cases of major effects Oruvail should be withdrawn at once.
Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment.
Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

4.9 Overdose

Like other propionic acid derivatives, ketoprofen is of low toxicity in overdosage; symptoms after acute ketoprofen intoxication are largely limited to drowsiness, abdominal pain and vomiting, but adverse effects seen after overdosage with propionic acid derivatives such as hypotension, bronchospasm and gastro-intestinal haemorrhage should be anticipated.
Owing to the slow release characteristics of Oruvail, it should be expected that ketoprofen will continue to be absorbed for up to 16 hours after ingestion.
Gastric lavage, aimed at recovering pellets that may still be in the stomach should be performed if the patient is seen soon after ingestion. It should be possible to identify the pellets in the gastric contents. Correction of severe electrolyte abnormalities may need to be considered. Treatment is otherwise supportive and symptomatic.
Administration of activated charcoal in an attempt to reduce absorption of slowly-released ketoprofen should be considered

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ketoprofen overall has the properties of a potent non-steroidal anti- inflammatory agent. It has the following pharmacological effects:
Anti-inflammatory
It inhibits the development of carageenan-induced abscesses in rats at 1mg/kg, UV-radiation induced erythema in guinea pigs at 6mg/kg. It is also a potent inhibitor of PGE_2 and PFG_2 synthesis in guinea pig and human chopped lung preparations.
Analgesic
Ketoprofen effectively reduced visceral pain in mice caused by phenyl benzoquinone or by bradykinin following p.o. Administration at about 6mg/kg.
Antipyretic
Ketoprofen (2 and 6mg/kg) inhibited hyperthermia caused by s.c injection of brewer's yeast in rats and, at 1mg/kg hyperthermia caused by i.v. administration of anticoagulant vaccine to rabbits.
Ketoprofen at 10mg/kg i.v. did not affect the cardiovascular, respiratory, central nervous system or autonomic nervous systems.

5.2 Pharmacokinetic properties

Ketoprofen is slowly but completely absorbed from Oruvail capsules. Maximum plasma concentration occurs after 6 - 8 hours. It declines thereafter with a half-life of about 8 hours. There is no accumulation on continued daily dosing. Ketoprofen is very highly bound to plasma protein

5.3 Preclinical safety data

No additional data of relevance to the prescriber

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pellets
Sugar spheres
Colloidal anhydrous silica
Shellac
Ethylcellulose
Talc
Capsule shell-body
Gelatin
Erythrosine (E127)
Capsule shell – cap
Gelatin
Titanium dioxide (E171)
Erythrosine (E127) – 100mg and 150mg only

Patent blue V (E131) – 100mg only

6.2 Incompatibilities

None stated

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 25°C in a dry place and protect from light.

6.5 Nature and contents of container

UPVC/Aluminium foil blister or UPVC coated with PVDC aluminium foil blister containing 28 capsules

6.6 Special precautions for disposal and other handling

None stated

7. MARKETING AUTHORISATION HOLDER

Sanofi-aventis
One Onslow Street
Guildford
Surrey
GU1 4YS
UK

8. MARKETING AUTHORISATION NUMBER(S)

100mg capsules: PL 04425/0597
150mg capsules : PL04425/0598
200mg capsules: PL 04425/0599

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

100mg capsules: 04 September 2006
150mg capsules: 09 January 2007
200mg capsules: 21 September 2006

10. DATE OF REVISION OF THE TEXT

Oruvail 150: 24 September 2007
Oruvail 100: March 2007
Oruvail 200: March 2007

11. LEGAL CLASSIFICATION

POM