**Diclofenac potassium 12.5mg tablets**

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DICLOFENAC POTASSIUM 12.5MG TABLETS

PL 30306/0243

PL 30306/0244

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Marketing Authorisations (licences) for the medicinal product Diclofenac potassium 12.5mg tablets (product licence numbers: 30306/0243-0244). This medicine is only available on prescription.

Diclofenac potassium 12.5mg tablets belong to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDS), which are used to reduce pain and inflammation in the following conditions:

- Sprains, strains and other injuries
- Pain and inflammation following surgery
- Gout
- Other painful conditions affecting the joints and muscles, such as backache, rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and pyrophosphate arthropathy.

The tablets can also be used to relieve the symptoms associated with migraine attacks in adults.

Diclofenac potassium 12.5mg tablets raised no clinically significant safety concerns and it was, therefore, judged that the benefits of using this product outweigh the risks; hence Marketing Authorisations have been granted.
DICLOFENAC POTASSIUM 12.5MG TABLETS

PL 30306/0243

PL 30306/0244

SCIENTIFIC DISCUSSION

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Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations for the medicinal product Diclofenac potassium 12.5mg tablets to Actavis Group PTC ehf on 3 March 2009.

These are abridged applications for Diclofenac potassium 12.5mg tablets submitted under Article 10(c) of EC Directive 2001/83, last paragraph. The applicant claims that this product is identical to Diclofenac potassium 12.5mg tablets (PL 24702/0072), which was licensed to Medis ehf on 4 June 2007 following a change of ownership from Caduceus Pharma Limited. The marketing authorisation for Diclofenac potassium 12.5mg tablets (PL 24668/0001) was granted to Caduceus Pharma Limited on 19 December 2006. The reference product cross refers to Voltarol Rapid 25mg and 50mg tablets (PL 00101/0481 and PL 00101/0482), marketed by Novartis Pharmaceuticals UK Ltd since 17 February 1998.

No new data were submitted, nor was it necessary for these simple applications, as the data are identical to those of the previously granted cross-reference product.

Diclofenac potassium tablets are indicated for the treatment of rheumatoid arthritis; osteoarthrosis; low back pain; migraine attacks; acute musculo-skeletal disorders and trauma such as periarthritis (especially frozen shoulder), tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations and relief of pain in fractures; ankylosing spondylitis; acute gout; control of pain and inflammation in orthopaedic, dental and other minor surgery; and pyrophosphate arthropathy and associated disorders.
**PHARMACEUTICAL ASSESSMENT**

**LETTERS OF ACCESS**
A letter confirming that the applicant is in possession of the dossier for the reference product is provided.

The finished product manufacturer has provided written confirmation that they are prepared to manufacture the product on the applicant’s behalf.

**TSE**
The applicant has declared that there are no materials of animal and/or human origin contained in, or used in the manufacturing process of, the medicinal product. This is in line with the reference product.

**ADDITIONAL DATA REQUIREMENTS**
The manufacturing processes, finished product specifications and active ingredient specifications are in line with the reference product and are satisfactory.

**EXPERT REPORTS**
Satisfactory expert reports in the form of quality, non-clinical and clinical overall summaries are provided, with signed declarations from each expert confirming that the applicant’s product is identical to the reference product in all particulars. Expert CVs are also submitted and are acceptable.

**PRODUCT LITERATURE**
The proposed SPC is identical to the reference product and is satisfactory. No mock-ups of the Patient Information Leaflets or product labelling are provided and details of user testing of the Patient Information Leaflet have not been submitted. This is satisfactory as the product is not currently being marketed. Full user testing and product artwork will be submitted prior to marketing of this product.

**ASSESSOR’S OVERALL CONCLUSIONS**
Product licences may be granted for this product.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none is required for an application of this type.
CLINICAL ASSESSMENT

OVERVIEW
A statement has been provided confirming that the clinical particulars for Diclofenac potassium 12.5mg tablets (PL 30306/0243-0244) are identical to those for the already licensed product; Diclofenac potassium 12.5mg tablets (PL 24702/0072). This is satisfactory.

BIOAVAILABILITY AND BIOEQUIVALENCE
No bioequivalence study has been performed to support these applications and none is needed.

PRODUCT LITERATURE
All product literature is medically satisfactory.

ASSESSOR’S OVERALL CONCLUSIONS
It is recommended that marketing authorisations can be granted.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
Diclofenac potassium 12.5mg tablets (PL 30306/0243-0244) are identical to the already licensed reference product. This product is, therefore, pharmaceutically satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
The efficacy of diclofenac potassium is well established. The SPCs, PILs and labelling are satisfactory and consistent with those for the cross-reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable, no significant preclinical or clinical safety concerns were identified, and benefit has been shown to be associated with diclofenac potassium. The risk benefit is therefore considered to be positive.
## STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
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<th>Description</th>
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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 15 January 2009</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 20 January 2009</td>
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<td>3</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Diclofenac potassium 12.5mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Tablet contains 12.5 mg of Diclofenac potassium.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film coated Tablet
White round, unscored biconvex film coated tablet, 5mm diameter, with 'I' marked on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Diclofenac potassium tablets are indicated for:

- Rheumatoid arthritis
- Osteoarthritis
- Low back pain
- Migraine attacks
- Acute musculo-skeletal disorders and trauma such as periarthritis (especially frozen shoulder), tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations; relief of pain in fractures
- Ankylosing spondylitis
- Acute gout
- Control of pain and inflammation in orthopaedic, dental and other minor surgery

Pyrophosphate arthropathy and associated disorders

4.2 Posology and method of administration
For oral administration.
To be taken preferably with or after food.
The tablets should be swallowed whole with liquid

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4)

Adults
The recommended daily dose is 100-150mg in two or three divided doses. For milder cases, 75-100 mg daily in two or three divided doses is usually sufficient.

In migraine an initial dose of 50 mg should be taken at the first signs of an impending attack. In cases where relief 2 hours after the first dose is not sufficient, a further dose of 50 mg may be taken. If needed, further doses of 50 mg may be taken at intervals of 4-6 hours, not exceeding a total dose of 200 mg per day.

**Children**

For children over 14 years of age, the recommended daily dose is 75-100 mg in two or three divided doses. Diclofenac potassium tablets are not recommended for children under 14 years of age.

The use of Diclofenac potassium in migraine attacks has not been established in children.

**Elderly**

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 and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

### 4.3 Contraindications

- Hypersensitivity to diclofenac or any of the excipients.
- Active, or history of recurrent peptic ulcer / haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- NSAIDs are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs.
- Severe heart failure, hepatic failure and renal failure (see section 4.4).
- During the last trimester of pregnancy (see section 4.6).
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

This product contains soya. If you are allergic to peanut or soya, do not use this medicinal product.

### 4.4 Special warnings 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 Diclofenac with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

**Elderly:**

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:**
GI 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 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 (see section 4.3), 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 aspirin, 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 unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving diclofenac potassium, 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 these conditions may be exacerbated (see section 4.8).

**Hepatic:**
Close medical surveillance is imperative in patients suffering from severe impairment of hepatic function.

**Hypersensitivity reactions:**
As with other non-steroidal anti-inflammatory drugs, allergic reactions, including anaphylactic/anaphylactoid reactions, can occur without earlier exposure to the drug.
Like other NSAIDs, Diclofenac Potassium may mask the signs and symptoms of infection due to its pharmacodynamic properties.

**SLE and mixed connective tissue disease:**
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

**Precautions**

**Cardiovascular, Renal and Hepatic Impairment:**
The administration of an NSAID 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 (see also section 4.3).

**Hepatic:**
If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), Diclofenac Potassium should be discontinued. Hepatitis may occur without prodromal symptoms.
Use of Diclofenac Potassium in patients with hepatic porphyria may trigger an attack.

**Haematological:**
Diclofenac Potassium may reversibly inhibit platelet aggregation (see “Interactions”). Patients with defects of haemostasis should be carefully monitored.

**Long term treatment:**
All patients who are receiving long term treatment with non-steroidal, anti-inflammatory agents should be monitored as a precautionary measure e.g. renal function, hepatic function (elevation of liver enzymes may occur) and blood counts.

**Respiratory disorders:**
Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

**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 diclofenac, particularly at high dose (150 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).
Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should be treated with diclofenac 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).

**Dermatological:**
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 appear to be at highest risk for 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. Diclofenac potassium should be discontinued at the
first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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

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

**Other analgesics including cyclooxygenase-2 selective inhibitors:** Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects (see section 4.4).

**Anti-hypertensives:** 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

**Methotrexate:** Decreased elimination of methotrexate.

**Ciclosporin:** Increased risk of nephrotoxicity.

**Mifepristone:** NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

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

**Anti-coagulants:** NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4).

**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.

**Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):** Increased risk of gastrointestinal bleeding (see section 4.4).

**Tacrolimus:** Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

**Zidovudine:** Increased risk of haematological toxicity when 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.

Antidiabetic agents: Clinical studies have shown that Diclofenac Potassium can be given together with oral antidiabetic agents without influencing their clinical effect. However there have been isolated reports of hypoglycaemic and hyperglycaemic effects which have required adjustment to the dosage of hypoglycaemic agents.

4.6 Pregnancy and lactation

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 foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child (see section 4.3). NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus.

Lactation:
In limited studies so far available, NSAIDs can appear in breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

See section 4.4 Special warnings and precautions for use, regarding female fertility.

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

If serious side-effects occur, Diclofenac Potassium should be withdrawn.

Clinical Trial and epidemiological data suggest that use of diclofenac, particularly at high doses (150 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).

Gastrointestinal: The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (See section 4.4) have been reported following administration. Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely.
**Hypersensitivity:** Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Other adverse reactions reported less commonly include:

**Renal:** Nephrotoxicity in various forms, including interstitial nephritis, nephritic syndrome and renal failure.

**Hepatic:** abnormal liver function, hepatitis and jaundice.

**Neurological and special senses:** Visual disturbances, optic neuritis, headaches, paraesthesia, reports of aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (See section 4.4) , depression, confusion, hallucinations, tinnitus, vertigo, dizziness, malaise, fatigue and drowsiness.

**Haematological:** Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.

**Dermatological:** Bullous reactions including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis (very rare). Photosensitivity.

**Cardiovascular system:** In isolated cases, palpitations, chest pain, hypertension, congestive heart failure.

**Other organ systems:** Impotence (very rare).

### 4.9 Overdose

a) Symptoms
Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible

b) Therapeutic measure
Patients should be treated symptomatically as required.
Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.
Good urine output should be ensured.
Renal and liver function should be closely monitored.
Patients should be observed for at least four hours after ingestion of potentially toxic amounts. Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: NSAID, ATC code: {M01 AB 05}

Diclofenac potassium tablets contain the potassium salt of diclofenac, a non-steroidal compound with pronounced and clinically demonstrable analgesic, anti-inflammatory and anti-pyretic properties. Diclofenac is a potent inhibitor of prostaglandin bio-synthesis and modulator of arachidonic acid release and uptake. Diclofenac potassium tablets have a rapid onset of action and are, therefore, suitable for the treatment of acute episodes of pain and inflammation. In migraine attacks Diclofenac potassium has been shown to be effective in relieving the headache and in improving the accompanying symptom of nausea. Diclofenac in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

5.2 Pharmacokinetic properties
Absorption
Diclofenac is rapidly and completely absorbed from sugar-coated tablets. Food intake does not affect absorption. Peak plasma concentration after one 12.5 mg tablet was 0.944 µmol/l after 54 minutes. The plasma concentrations show a linear relationship to the size of the dose. Diclofenac undergoes first-pass metabolism and is extensively metabolised.

Distribution
Diclofenac is highly bound to plasma proteins (99.7%), chiefly albumin (99.4%)

Elimination
The total systemic clearance of diclofenac in plasma is 263 ± 56 ml/min (mean ± SD). The terminal half-life in plasma is 1-2 hours. Repeated oral administration of Diclofenac Potassium for 8 days in daily doses of 50 mg t i d does not lead to accumulation of diclofenac in the plasma. Approx. 60% of the dose administered is excreted in the urine in the form of metabolites, and less than 1% as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

Biotransformation
The biotransformation of diclofenac involves partly glucuronidation of the intact molecule but mainly single and multiple hydroxylation followed by glucuronidation.

**Characteristics in patients**
The age of the patient has no influence on the absorption, metabolism, or excretion of diclofenac.
In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of <10 ml/min the theoretical steady-state plasma levels of metabolites are about four times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.
In the presence of impaired hepatic function (chronic hepatitis, non-decompensated cirrhosis) the kinetics and metabolism are the same as for patients without liver disease.

5.3 Preclinical safety data
Relevant information on the safety of Diclofenac potassium is included in other sections of the Summary of Product Characteristics.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**
*Tablet core:*
Silica colloidal anhydrous
Sodium starch glycollate
Povidone
Starch maize
Calcium hydrogen phosphate anhydrous
Magnesium stearate

*Film coating:*
Polyvinyl alcohol partially hydrolysed
Titanium dioxide E171
Talc
Lecithin soya E322
Xanthan gum E415

6.2 **Incompatibilities**
Not applicable.

6.3 **Shelf life**
36 months

6.4 **Special precautions for storage**
Do not store above 25 °C
6.5 Nature and contents of container
Blister pack. Pack sizes: 7, 10, 14, 28, 30, 50, 56, 98 and 100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements

7 MARKETING AUTHORISATION HOLDER
Actavis Group PTC ehf
Reykjavikurvegi 76-78
220 Hafnarfjordur
Iceland.

8 MARKETING AUTHORISATION NUMBER(S)
PL 30306/0243

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
03/03/2009

10 DATE OF REVISION OF THE TEXT
03/03/2009

1 NAME OF THE MEDICINAL PRODUCT
Diclofenac potassium 12.5mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Tablet contains 12.5 mg of Diclofenac potassium.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film coated Tablet
White round, unscored biconvex film coated tablet, 5mm diameter, with 'I'
marked on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Diclofenac potassium tablets are indicated for:
- Rheumatoid arthritis
- Osteoarthritis
- Low back pain
- Migraine attacks
- Acute musculo-skeletal disorders and trauma such as periarthritis (especially frozen shoulder), tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations; relief of pain in fractures
- Ankylosing spondylitis
- Acute gout
- Control of pain and inflammation in orthopaedic, dental and other minor surgery

Pyrophosphate arthropathy and associated disorders

4.2 Posology and method of administration
For oral administration.
To be taken preferably with or after food.
The tablets should be swallowed whole with liquid

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4)

Adults
The recommended daily dose is 100-150mg in two or three divided doses. For milder cases, 75-100 mg daily in two or three divided doses is usually sufficient.
In migraine an initial dose of 50 mg should be taken at the first signs of an impending attack. In cases where relief 2 hours after the first dose is not sufficient, a further dose of 50 mg may be taken. If needed, further doses of 50 mg may be taken at intervals of 4-6 hours, not exceeding a total dose of 200 mg per day.

Children
For children over 14 years of age, the recommended daily dose is 75-100 mg in two or three divided doses. Diclofenac potassium tablets are not recommended for children under 14 years of age.
The use of Diclofenac potassium in migraine attacks has not been established in children.

Elderly
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 and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

4.3 Contraindications
- Hypersensitivity to diclofenac or any of the excipients.
- Active, or history of recurrent peptic ulcer / haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- NSAIDs are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria)
in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs.

- Severe heart failure, hepatic failure and renal failure (see section 4.4).
- During the last trimester of pregnancy (see section 4.6).
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

This product contains soya. If you are allergic to peanut or soya, do not use this medicinal product.

4.4 Special warnings 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 Diclofenac with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

_Elderly:_

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:_

GI 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 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 (see section 4.3), 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 aspirin, 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 unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving diclofenac potassium, 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 these conditions may be exacerbated (see section 4.8).
Hepatic:
Close medical surveillance is imperative in patients suffering from severe impairment of hepatic function.

Hypersensitivity reactions:
As with other non-steroidal anti-inflammatory drugs, allergic reactions, including anaphylactic/anaphylactoid reactions, can occur without earlier exposure to the drug.
Like other NSAIDs, Diclofenac Potassium may mask the signs and symptoms of infection due to its pharmacodynamic properties.

SLE and mixed connective tissue disease:
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

Precautions
Cardiovascular, Renal and Hepatic Impairment:
The administration of an NSAID 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 (see also section 4.3).

Hepatic:
If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), Diclofenac Potassium should be discontinued. Hepatitis may occur without prodromal symptoms.
Use of Diclofenac Potassium in patients with hepatic porphyria may trigger an attack.

Haematological:
Diclofenac Potassium may reversibly inhibit platelet aggregation (see “Interactions”). Patients with defects of haemostasis should be carefully monitored.

Long term treatment:
All patients who are receiving long term treatment with non-steroidal, anti-inflammatory agents should be monitored as a precautionary measure e.g. renal function, hepatic function (elevation of liver enzymes may occur) and blood counts.

Respiratory disorders:
Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

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 diclofenac, particularly at high dose (150 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)

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should be treated with diclofenac after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipideamia, diabetes mellitus, smoking)

**Dermatological:**
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 appear to be at highest risk for 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. Diclofenac potassium should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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

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

**Other analgesics including cyclooxygenase-2 selective inhibitors:** Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects (see section 4.4).

**Anti-hypertensives:** 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

**Methotrexate:** Decreased elimination of methotrexate.

**Ciclosporin:** Increased risk of nephrotoxicity.
**Mifepristone:** NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

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

**Anti-coagulants:** NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4).

**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.

**Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):** Increased risk of gastrointestinal bleeding (see section 4.4).

**Tacrolimus:** Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

**Zidovudine:** Increased risk of haematological toxicity when 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.

**Antidiabetic agents:** Clinical studies have shown that Diclofenac Potassium can be given together with oral antidiabetic agents without influencing their clinical effect. However there have been isolated reports of hypoglycaemic and hyperglycaemic effects which have required adjustment to the dosage of hypoglycaemic agents.

### 4.6 Pregnancy and lactation

**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 foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child (see section 4.3). NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus.

**Lactation:**
In limited studies so far available, NSAIDs can appear in breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

See section 4.4 Special warnings and precautions for use, regarding female fertility.
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
If serious side-effects occur, Diclofenac Potassium should be withdrawn.

Clinical Trial and epidemiological data suggest that use of diclofenac, particularly at high doses (150 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)

Gastrointestinal: The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemeses, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (See section 4.4) have been reported following administration. Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely.

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Other adverse reactions reported less commonly include:

Renal: Nephrotoxicity in various forms, including interstitial nephritis, nephritic syndrome and renal failure.

Hepatic: abnormal liver function, hepatitis and jaundice.

Neurological and special senses: Visual disturbances, optic neuritis, headaches, paraesthesia, reports of aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (See section 4.4), depression, confusion, hallucinations, tinnitus, vertigo, dizziness, malaise, fatigue and drowsiness.

Haematological: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.

Dermatological: Bullous reactions including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis (very rare). Photosensitivity.
Cardiovascular system: In isolated cases, palpitations, chest pain, hypertension, congestive heart failure.

Other organ systems: Impotence (very rare).

4.9 Overdose
a) Symptoms
Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.

b) Therapeutic measure
Patients should be treated symptomatically as required.
Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.
Good urine output should be ensured.
Renal and liver function should be closely monitored.
Patients should be observed for at least four hours after ingestion of potentially toxic amounts.
Frequent or prolonged convulsions should be treated with intravenous diazepam.
Other measures may be indicated by the patient's clinical condition.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: NSAID, ATC code: {M01 AB 05}

Diclofenac potassium tablets contain the potassium salt of diclofenac, a non-steroidal compound with pronounced and clinically demonstrable analgesic, anti-inflammatory and anti-pyretic properties.
Diclofenac is a potent inhibitor of prostaglandin bio-synthesis and modulator of arachidonic acid release and uptake.
Diclofenac potassium tablets have a rapid onset of action and are, therefore, suitable for the treatment of acute episodes of pain and inflammation.
In migraine attacks Diclofenac potassium has been shown to be effective in relieving the headache and in improving the accompanying symptom of nausea.
Diclofenac in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

5.2 Pharmacokinetic properties
Absorption
Diclofenac is rapidly and completely absorbed from sugar-coated tablets. Food intake does not affect absorption.
Peak plasma concentration after one 12.5 mg tablet was 0.944 µmol/l after 54 minutes. The plasma concentrations show a linear relationship to the size of the dose. Diclofenac undergoes first-pass metabolism and is extensively metabolised.

**Distribution**

Diclofenac is highly bound to plasma proteins (99.7%), chiefly albumin (99.4%).

**Elimination**

The total systemic clearance of diclofenac in plasma is 263 ± 56 ml/min (mean ± SD). The terminal half-life in plasma is 1-2 hours. Repeated oral administration of Diclofenac Potassium for 8 days in daily doses of 50 mg t i d does not lead to accumulation of diclofenac in the plasma. Approx. 60% of the dose administered is excreted in the urine in the form of metabolites, and less than 1% as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

**Biotransformation**

The biotransformation of diclofenac involves partly glucuronidation of the intact molecule but mainly single and multiple hydroxylation followed by glucuronidation.

**Characteristics in patients**

The age of the patient has no influence on the absorption, metabolism, or excretion of diclofenac. In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of <10 ml/min the theoretical steady-state plasma levels of metabolites are about four times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile. In the presence of impaired hepatic function (chronic hepatitis, non-decompensated cirrhosis) the kinetics and metabolism are the same as for patients without liver disease.

5.3 Preclinical safety data

Relevant information on the safety of Diclofenac potassium is included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

*Tablet core:*

- Silica colloidal anhydrous
- Sodium starch glycollate
- Povidone
- Starch maize
Calcium hydrogen phosphate anhydrous
Magnesium stearate

Film coating:
Polyvinyl alcohol partially hydrolysed
Titanium dioxide E171
Talc
Lecithin soya E322
Xanthan gum E415

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months

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

6.5 Nature and contents of container
Blister pack. Pack sizes: 7, 10, 14, 28, 30, 50, 56, 98 and 100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements

7 MARKETING AUTHORISATION HOLDER
Actavis Group PTC ehf
Reykjavikurvegi 76-78
220 Hafnarfjordur
Iceland.

8 MARKETING AUTHORISATION NUMBER(S)
PL 30306/0244

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
03/03/2009

10 DATE OF REVISION OF THE TEXT
03/03/2009
Diclofenac potassium 12.5mg tablets
PATIENT INFORMATION LEAFLET

Read all of this leaflet carefully before you start taking this medicine.
• Keep this leaflet. You may need to read it again.
• If you have further questions, please ask your doctor or your pharmacist.
• This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If you have any of the side effects, or if you notice any not listed, please tell your doctor or pharmacist.

In this leaflet:
1. What Diclofenac potassium 12.5mg Tablets are and what they are used for
2. Before you take Diclofenac potassium 12.5mg Tablets
3. How to take Diclofenac potassium 12.5mg Tablets
4. Possible side effects
5. How to store Diclofenac potassium 12.5mg Tablets
6. Further Information

1. What Diclofenac potassium 12.5mg tablets are and what they are used for

Diclofenac potassium belongs to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs), which are used to reduce pain and inflammation in the following conditions:
• Sprains, strains and other injuries
• Pain and inflammation following surgery
• Gout
• Other painful conditions affecting the joints and muscles such as backache, rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and pyrophosphate arthropathy.

The tablets can also be used to relieve the symptoms associated with migraine attacks in adults.

Before you take Diclofenac potassium 12.5mg tablets

Do not take Diclofenac potassium 12.5mg Tablets if you:
• are allergic (hypersensitive) to diclofenac potassium or any of the other ingredients in the tablet (see section 4)
• have a peptic ulcer (ulcer in your stomach or duodenum) or bleeding in your stomach, or have had two or more episodes of peptic ulcers, stomach bleeding or perforation
• suffer from asthma, hay fever or a cold caused by an allergy to salicylates (e.g. aspirin) or other non-steroidal pain killers.

Check with your doctor or pharmacist before taking Diclofenac potassium 12.5mg tablets if you:
• have a history of gastrointestinal disease e.g. ulcerative colitis or Crohn's disease
• have reduced heart, kidney, or liver function
• suffer from any blood clotting disorder
• have or have had asthma
• suffer from liver porphyria (disorder of the red blood pigment)
• have had or need to have surgery.

Medicines such as diclofenac may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke. Any risk is more likely with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment.

If you have heart problems, have had a previous stroke or think that you might be at risk of these conditions (for example if you have high blood pressure, diabetes or high cholesterol or are a smoker) you should discuss your treatment with your doctor or pharmacist.

Whilst you are taking these tablets, your doctor may want to give you a check-up from time to time.

Diclofenac potassium tablets are not recommended for children under the age of 14.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Especially:
• medicines to treat diabetes - a dose adjustment of these medicines may be necessary as blood sugar may drop too low
• anticoagulants - increased risk of bleeding
• diuretics (water tablets) - effect may be decreased. Potassium-sparing diuretics may increase the potassium levels in the blood.
• Lithium (medicine to treat depression) or digoxin (medicine to treat impaired heart function) - may cause an increase in blood levels of these medicines
• Cytoxic medicines (e.g. methotrexate to treat cancers) - should not be taken less than 24 hours before or after Diclofenac potassium 12.5mg tablets - may cause an increase in blood levels of this medicine
• Cidofovir - may harm kidney function
• Quinolone (medicines to treat infections) - may cause convulsions (fits)
• Steroid tablets - increased risk of bleeding in the stomach
• Other NSAIDs such as aspirin - increase the risk of side effects
• Medicines to treat high blood pressure (ACE-inhibitors, beta blockers) - blood pressure lowering effect may be reduced
• Mefenamic acid (used to reduce pain) - effect of mefenamic acid may be reduced by NSAIDs
• Cardiac glycosides (used for some heart conditions) - may worsen heart failure.

Laboratory tests
Frequent liver and kidney function tests and monitoring of blood counts are necessary if taken for more than a few days.

Pregnancy and breastfeeding
Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy
You should not take Diclofenac during the first 6 months of pregnancy unless directed by your doctor and must not take Diclofenac during the last 3 months of pregnancy as damage to the foetus and reduced labour may occur.

Breastfeeding
You should only use Diclofenac whilst breastfeeding if advised by your doctor.

Female fertility
Diclofenac may make it more difficult to become pregnant. You should inform your doctor if you are planning to become pregnant or if you have problems becoming pregnant.

Driving and using machines
Some patients may experience side effects such as dizziness, drowsiness and visual disturbances, which may affect their ability to drive or operate machinery. Make sure you are not affected before driving or operating machinery.

Important information about some of the ingredients
If you are allergic to peanut or soya do not take this medicine, as it contains soya. This medicine contains 0.0374 mmol (1.48 mg) potassium per tablet. This should be taken into account if you have reduced kidney function or are on a controlled potassium diet.

How To Take Diclofenac potassium 12.5mg tablets
Always take Diclofenac potassium 12.5mg tablets exactly as your doctor has told you. If you are unsure, check with your doctor or pharmacist.

Diclofenac potassium 12.5mg tablets must not be taken long-term, blood tests should be carried out if taken for more than a few days. The tablets must be swallowed whole, with a glass of water, with or after food.

The usual dose is:
- To treat pain and inflammation
  - Adults - 75 mg (6 tablets) to 150 mg (12 tablets) a day in two or three doses.
  - Elderly patients - a lower dose may be used. If you are frail or have a low body weight, your doctor may ask you to go back to see him regularly for the first 4 weeks of treatment, to make sure that you are not experiencing any side effects.
  - Children over 14 years of age - 7.5 mg (6 tablets) to 15 mg (6 tablets) daily, in two or three doses.
- To treat the symptoms of migraine in adults
  - 50 mg (4 tablets) taken when the first signs of a migraine attack appear. Another 50 mg (4 tablets) taken 2 hours after the first dose if needed and then every 4 to 6 hours. You should not take more than 200 mg (16 tablets) in 24 hours.

These tablets are not suitable for the treatment of migraine in children.

If you take more Diclofenac potassium tablets than you should:
Contact your doctor, emergency room or pharmacist if you have taken more Diclofenac potassium tablets than stated in this leaflet or more than what your doctor has prescribed (and you feel unwell).

If you forget to take Diclofenac potassium tablets:
Do not take a double dose to make up for forgotten dose. Continue the treatment as advised by your doctor.

4. Possible side effects

Like all medicines, Diclofenac potassium 12.5mg tablets can cause side effects, although not everybody gets them.

If you suffer from any of the following at any time during your treatment, STOP TAKING the medicine and seek immediate medical help:
- pass blood in your stools (faeces / motions)
- pass black tarry stools
• vomit any blood or dark particles that look like coffee grounds
• an allergic reaction such as itching, low blood pressure, swelling of the face, lips, tongue, mouth and throat, which may cause shortness of breath or difficulty swallowing
• a form of meningitis (aseptic) causing a combination of symptoms such as headache, fever, stiff neck, tiredness, muscle pain, sore throat and disorientation
• yellowing of the skin or the whites of your eyes
• stomach pain, indigestion, heartburn, wind, nausea (feeling sick) or vomiting (being sick)

STOP TAKING the medicine and see your doctor if you experience:
• indigestion or heartburn
• Abdominal pain (pain in your stomach) or other abnormal stomach symptoms

Tell your doctor if you experience any of the following symptoms:

Common (occurs in less than 1 in 10 people):
headache, dizziness, nausea, stomach pain, diarrhea, stomach pain, wind, loss of weight or poor appetite, indigestion, nausea, vomiting

Rare (occurs in less than 1 in 1000 people):
nausea, vomiting, abdominal pain, abdominal swelling, loss of appetite, headache, dizziness, tiredness, backache, chest pain, heart problems, liver problems, kidney problems, skin problems, blood problems, allergic reactions, angina, blood in the urine, blood in the stools, blood in the urine, blood in the stools, blood in the urine, blood in the stools

Very rare (occurs in less than 1 in 10 000 people):
erythema nodosum, angina pectoris, angina, chest pain, backache, blood in the urine, blood in the stools, blood in the urine, blood in the stools, blood in the urine, blood in the stools

Medicines such as Diclofenac potassium 12.5mg tablets may be associated with a small increased risk of heart attack (myocardial infarction) or stroke. If you have any of the side effects, or if you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. How to store Diclofenac potassium 12.5mg tablets
Keep out of the reach and sight of children.
Do not store above 25°C.
Do not use after the expiry date stated on the carton. Unused tablets should be taken back to the pharmacist for safe disposal.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required.
These measures will help to protect the environment.

6. Further information
What Diclofenac potassium 12.5mg tablets contain
The active substance (the ingredient that makes the tablet work) is diclofenac. Each tablet contains 12.5mg Diclofenac potassium. The tablets also contain silica colloidal anhydrous, sodium starch glycolate, povidone, maize starch, calcium hydrogen phosphate anhydrous, magnesium stearate, polyvinyl alcohol partially hydrolysed, Titanium dioxide E171, tartar emetic, 2% and Xanthan gum E415.

What Diclofenac potassium 12.5mg tablets look like and contents of the pack
The tablets are white, round, uncoated, biconvex 12.5mg film coated tablets, with ‘F’ marked on one side.
Pack sizes 7, 10, 14, 28, 30, 50, 58, 80 and 98 and 100 film coated tablets.
(Not all pack sizes may be available)
Marketing Authorisation Holder
Actavis Group PTC elf Reykjavikurvegar 76-78, 220 Hafnarfjordur, Iceland.
Product Licence Number: PL 50306/0240
Manufacturer
Actavis hf, Reykjavikurvegar 78, PO Box 429, IS-222, Hafnarfjordur, Iceland.
This leaflet was last approved in (MM/YYYY).
Revision date.
Diclofenac potassium 12.5mg tablets
PATIENT INFORMATION LEAFLET

Read all of this leaflet carefully before you start taking this medicine.
• Keep this leaflet. You may need to read it again.
• If you have further questions, please ask your doctor or your pharmacist.
• This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If you have any of the side effects, or if you notice any not listed, please tell your doctor or pharmacist.

In this leaflet:
1. What Diclofenac potassium 12.5mg Tablets are and what they are used for
2. Before you take Diclofenac potassium 12.5mg Tablets
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4. Possible side effects
5. How to store Diclofenac potassium 12.5mg Tablets
6. Further information

1. What Diclofenac potassium 12.5mg tablets are and what they are used for

Diclofenac potassium belongs to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs), which are used to reduce pain and inflammation in the following conditions:
• Sprains, strains and other injuries
• Pain and inflammation following surgery
• Gout
• Other painful conditions affecting the joints and muscles such as backache, rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and pyrophosphate arthropathy.

The tablets can also be used to relieve the symptoms associated with migraine attacks in adults.

2. Before you take Diclofenac potassium 12.5mg tablets

Do not take Diclofenac potassium 12.5mg Tablets if you:
• are allergic (hypersensitive) to diclofenac potassium or any of the other ingredients in the tablet (see section 6)
• have a peptic ulcer (ulcer in your stomach or duodenum) or bleeding in your stomach, or have had two or more episodes of peptic ulcers, stomach bleeding or perforation
• suffer from asthma, hives or a cold caused by an allergy to salicylates (e.g. aspirin) or other non-steroidal pain killers.

Check with your doctor or pharmacist before taking Diclofenac potassium 12.5mg tablets if you:
• have a history of gastrointestinal disease e.g. ulcerative colitis or Crohn's disease
• have reduced heart, kidney, or liver function
• suffer from any blood clotting disorder
• have or have had asthma
• suffer from liver porphyria (disorder of the red blood pigment)
• have had or need to have surgery.

Medicines such as diclofenac may be associated with a small increased risk of heart attack (myocardial infarction) or stroke. Any risk is more likely with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment.

If you have heart problems, have had a previous stroke or think that you might be at risk of these conditions (for example if you have high blood pressure, diabetes or high cholesterol or are a smoker) you should discuss your treatment with your doctor or pharmacist.

Whilst you are taking these tablets, your doctor may want to give you a check-up from time to time.

Diclofenac potassium tablets are not recommended for children under the age of 14.

3. How to take Diclofenac potassium 12.5mg Tablets

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Especially:
• medicines to treat diabetes - a dose adjustment of these medicines may be necessary as blood sugar may drop too low
• antiplatelet agents - increased risk of bleeding
• diuretics (water tablets) - effect may be decreased. Potassium-sparing diuretics may increase the potassium levels in the blood.
• Lithium (medicine to treat depression) or digoxin (medicine to treat impaired heart function) - may cause an increase in blood levels of these medicines.
• Cytotoxic medicines (e.g. methotrexate to treat cancers) - should not be taken less than 24 hours before or after Diclofenac potassium tablet.
• 12.5mg tablets - may cause an increase in blood levels of this medicine.
• Diazepam - may harm kidney function.
• Quinolones (medicines to treat infections) - may cause convulsions (fits).
• Steroid tablets - increased risk of bleeding in the stomach.
• Other NSAIDs such as aspirin - increase the risk of side effects.
• Medicines to treat high blood pressure (ACE inhibitors, beta blockers) - blood pressure-lowering effect may be reduced.
• Milrinone (used to induce abortion) - effect of milrinone may be reduced by NSAIDs.
• Cardiac glycosides (used for some heart conditions) - may worsen heart failure.

Laboratory tests
Frequent liver and kidney function tests are necessary if taken for more than a few days.

Pregnancy and breastfeeding
Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy
You should not take Diclofenac during the first 6 months of pregnancy unless directed by your doctor and must not take Diclofenac during the last 3 months of pregnancy as damage to the fetus and reduced labour may occur.

Breastfeeding
You should only use Diclofenac whilst breastfeeding if advised by your doctor.

Female fertility
Diclofenac may make it more difficult to become pregnant. You should inform your doctor if you are planning to become pregnant or if you have problems becoming pregnant.

Driving and using machines
Some patients may experience side effects such as dizziness, drowsiness and visual disturbances which may affect their ability to drive or operate machinery. Make sure you are not affected before driving or operating machinery.

Important information about some of the ingredients
If you are allergic to peanut or soy do not take this medicine as it contains soy. This medicine contains 0.0074 mmol (0.16mg) potassium per tablet. This should be taken into account if you have reduced kidney function or are on a controlled potassium diet.

How To Take Diclofenac potassium 12.5mg tablets
Always take Diclofenac potassium 12.5mg tablets exactly as your doctor has told you. If you are unsure check with your doctor or pharmacist.

Diclofenac potassium 12.5mg tablets must not be taken long-term, blood tests should be carried out if taken for more than a few days. The tablets must be swallowed whole with a glass of water, with or after food.

The usual dose is:
• To treat pain and inflammation:
  Adults - 75mg (6 tablets) to 150mg (12 tablets) a day in two or three doses.
  Elderly patients - a lower dose may be used. If you are frail or have a low body weight, your doctor may ask you to go back to see him regularly for the first 4 weeks of treatment, to make sure that you are not experiencing any side effects.
  Children over 14 years of age - 75mg (6 tablets) to 150mg (6 tablets) daily, in two or three doses.

• To treat the symptoms of migraine in adults:
  50mg (4 tablets) taken when the first signs of a migraine attack appear. Another 50mg (4 tablets) taken 2 hours after the first dose if needed and then every 4 to 6 hours. You should not take more than 200mg (16 tablets) in 24 hours.

These tablets are not suitable for the treatment of migraine in children.

If you take more Diclofenac potassium tablets than you should:
Contact your doctor, emergency room or pharmacist. If you have taken more Diclofenac potassium tablets than stated in this leaflet or more than what your doctor has prescribed (and you feel unwell)

If you forget to take Diclofenac potassium tablets:
Do not take a double dose to make up for forgotten dose. Continue the treatment as advised by your doctor.

4. Possible side effects
Like all medicines, Diclofenac potassium 12.5mg tablets can cause side effects, although not everybody gets them.

If you suffer from any of the following at any time during your treatment, STOP TAKING the medicine and seek immediate medical help:
• pass blood in your stools (faeces) (stools / motions)
• pass black tarry stools:
• vomit any blood or dark particles that look like coffee grounds
• an allergic reaction such as itching, low blood pressure, swelling of the face, lips, tongue, mouth and throat, which may cause shortness of breath or difficulty swallowing
• a form of meningitis (septic) causing a combination of symptoms such as headache, fever, stiff neck, tiredness, muscle pain, sore throat, and disorientation
• yellowing of the skin or the whites of your eyes
• stomach pain, indigestion, heartburn, wind, nausea (feeling sick) or vomiting (being sick)

STOP TAKING the medicine and tell your doctor if you experience:
• indigestion or heartburn
• abdominal pain (pain in your stomach) or other abnormal stomach symptoms

Tell your doctor if you experience any of the following symptoms:

Common (occurs in less than 1 in 10 people):
headache, dizziness, 'spinning' sensation, feeling or being sick, diarrhoea, stomach pain, wind, loss of weight or poor appetite, heartburn, abnormal liver function tests, skin rashes

Rare (in less than 1 in 1000 people):
dizziness, tiredness, stomach ulcers or bleeding, hepatitis, jaundice (causing yellowing of the skin and whites of the eyes), itching, fluid retention (symptoms of which include swollen ankles)

Very rare (occur in less than 1 in 10 000 people):
nausea and headache, tremor, blurred or double vision, hearing loss or impairment, dizziness (including feeling faint), difficulty sleeping, nightmares, depression, irritability, anxiety, psychoses, hallucinations, loss of memory, fits, numbness, sensitivity to light, taste disturbance, constipation, inflammation of the tongue, mouth ulcers, ulcers of the gullet, lower gut disorders (including inflammation of the colon causing diarrhoea and stomach pain), palpitations (fast or irregular heart beat), chest pain, high blood pressure, inflammation of blood vessels (vasculitis), inflammation of the lung (pneumonitis), congestive heart failure, blood disorders (including anaemia), making you tired and more prone to minor infections or bleeding), kidney or liver disorders, presence of blood or protein in the urine, skin rash, itching, skin eruptions, eczema, lichenoid urticaria (round red patches on the skin), Stevens-Johnson syndrome (severe skin rash with blistering, fever, blisters and ulcers), or Lyell's Syndrome (severe rash with reddening, peeling and swelling of skin that looks like severe burns), hair loss, pancreatitis (inflammation of the pancreas), worsening of ulcerative colitis or Crohn's disease, impotence (difficulty getting an erection).

Medicines such as Diclofenac potassium 12.5mg tablets may be associated with a small increased risk of heart attack ('myocardial infarction') or stroke. If you have any of the side effects, or if you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. How to store Diclofenac potassium 12.5mg tablets
Keep out of the reach and sight of children
Do not store above 25 °C
Do not use after the expiry date stated on the carton. Unused tablets should be taken back to the pharmacist for safe disposal.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information
What Diclofenac potassium 12.5mg tablets contain
The active substance in the ingredients that make up the tablet work) is diclofenac. Each tablet contains 12.5mg Diclofenac potassium. The tablets also contain silica colloidal anhydrous, sodium starch glycolate, povidone, maize starch, calcium hydrogen phosphate anhydrous, magnesium stearate, polyvinyl alcohol partly hydrolysed. Titanium dioxide E171, talc, lecithin soya E322 and Xanthan gum E415.

What Diclofenac potassium 12.5mg tablets look like and contents of the pack
The tablets are white, round, uncoated, bisconex 5mm film coated tablets, with 1 marked on one side.
Pack sizes 7, 10, 14, 28, 30, 50, 98 and 120 film coated tablets. (Not all pack sizes are available)

Marketing Authorisation Holder
Actavis Group PTC c/o Reykjavikurveg 76-78, 220 Hafnarfjordur, Iceland.

Product Licence Number: PL 30306/0244

Manufacturer
Actavis hf, Reykjavikurveg 78, PO Box 420, IS-122, Hafnarfjordur, Iceland.

This leaflet was last approved in (MM/YYYY).
Revision date:
LABELLING

PL 30306/0243

Foil:

Foil text Diclofenac potassium 12.5mg Tablets

Diclofenac potassium 12.5mg Tablets
MA Holder: Actavis Group PTC ehf
Actavis logo
BN:
EXP:
(The Batch Number and Expiry Date will be embossed on to the actual blister pack)
Carton:

Carton text Diclofenac potassium 12.5mg Tablets

Back panel

Place Dispensing Label here

Actavis Logo
Marketing Authorisation holder:
Actavis Group PTC ehf Reykjavikurvegi 76-78, 220 Hafnarfjordur, Iceland.

PL 30306/0243
POM
Barcode

Flap
Batch no:
Expiry Date:
(The Batch Number and Expiry Date will be embossed on to the actual cartons).

Side

For oral administration only.
To be taken as directed by your doctor.
Please read the enclosed Patient Information Leaflet before use.
Keep out of the reach and sight of children.
Do not store above 25 °C
Actavis logo

Front panel

Diclofenac potassium 12.5mg Tablets
* Tablets
Each film coated tablet contains 12.5mg
Diclofenac potassium
Also contains E322
Braille (diclofenac potassium 12.5mg tablets)
Actavis logo

Side

Diclofenac potassium 12.5mg Tablets
*Tablets
Actavis logo
Foil:

Foil text *Diclofenac potassium 12.5mg Tablets*

(Diclofenac potassium 12.5mg Tablets
MA Holder: Actavis Group PTC ehf
Actavis logo
BN: EXP:)
(The Batch Number and Expiry Date will be embossed on to the actual blister pack)
Carton:

Carton text Diclofenac potassium 12.5mg Tablets

Back panel

Place Dispensing Label here

Actavis Logo
Marketing Authorisation holder:
Actavis Group PTC ehf Reykjavikurvegi 76-78, 220 Hafnarfjordur, Iceland.

PL 30306/0244

Barcode

Flap
Batch no:
Expiry Date:
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