Public Assessment Report

Diclofenac Potassium 25mg Tablets
Diclofenac Potassium 50mg Tablets

Diclofenac potassium

PL 18866/0033
PL 18866/0034

Rockspring Healthcare Ltd

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Lay Summary

The MHRA granted marketing authorisations (licences) to Rockspring Healthcare Ltd for the medicinal products Diclofenac potassium 25mg and 50mg Tablets on 25/02/2009 (PL 18866/0033-4). The market authorisations were then transferred to Gentian Generics Ltd (PL 33217/0010-1) on the 14/04/2009.

Diclofenac potassium is a non-steroidal anti-inflammatory drug and is used in the treatment of 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 fracture, ankylosing spondylitis, acute gout and relief of orthopaedic, dental and minor surgery, pyrophosphate anthropathy and associated disorders.

These products are prescription only medicines.
Scientific Discussion

INTRODUCTION

The MHRA granted marketing authorisations (licences) to Rockspring Healthcare Ltd for the medicinal products Diclofenac potassium 25mg and 50mg Tablets on 25/02/2009 (PL 18866/0033-4). The market authorisations were then transferred to Gentian Generics Ltd (PL 33217/0010-1) on the 14/04/2009.

Diclofenac potassium is a non steroidal anti-inflammatory drug of the phenylacetic acid class and an inhibitor of cyclo-oxygenase. It is used for the treatment of 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 fracture, ankylosing spondylitis, acute gout and relief of orthopaedic, dental and minor surgery, pyrophosphate anthrhopathy and associated disorders.

The drug products were demonstrated to be generic medical products of Voltaren T 25mg and 50mg tablets respectively, authorised to Novartis in Sweden 19/10/1990, which contain the same amount of active substance under Article 10.1 of EC directive 2001/83/EC,. The reference products in UK are Cataflam tablets 25mg and 50mg, PL 00030 / 0054 and PL 00030 / 0055, authorised to Novartis on 25/11/1992.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Active trimethoprim is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been generated supporting a retest period of 60 months, with no specific storage instructions.
DRUG PRODUCT

Other Ingredients

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

Tablet Coating:
Polyvinyl alcohol partially hydrolysed
Titanium dioxide E171
Talc
Lecithin Soya E322
Iron Oxide red E172
Iron Oxide yellow E172
Xanthan gum E415

All excipients used comply with their respective European Pharmacopoeial monograph. Magnesium stearate is of animal origin and an acceptable TSE Certificate of Suitability was provided.

Dissolution and impurity profiles
Dissolution and impurity profiles for both strengths of drug product were found to be similar to those for the reference products.

Manufacture
A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of each strength. The results are satisfactory.

Finished product specification
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System
Blister strips made from polyamide/aluminium/PVC (25um/45um/60um) film coupled with 20um aluminium lidding by polyvalent thermal lacquer. The specifications and COA are satisfactory.
PP-containers (Securitainer)
The container is white, tubular, made from polypropylene and the cap is white LDPE, both comply with Ph Eur Section 3.2.2 (Plastic Containers and Closures). Supplier’s data confirm compliance with EU food contact regulations, E.C. Directive 90/128, FDA, and BGA. It also contains desiccant (silica gel) in HDPE canister, complying with FDA food contact requirements. The specifications and COA are satisfactory.

**Stability**
Satisfactory stability data that met current requirements were provided supporting a shelf-life of 3 years with no specific storage instructions.

**ASSESSOR’S OVERALL CONCLUSIONS ON QUALITY AND ADVICE**
Marketing Authorisations were granted.
PRE-CLINICAL ASSESSMENT

No pre-clinical data were submitted with this application and none were required,
MEDICAL ASSESSMENT

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS

Diclofenac is a phenylacetic acid derivative, one of the group of non-steroidal anti-inflammatory drugs whose action is mediated by inhibition of enzymes of the cyclooxygenase type which are essential for the production of prostaglandins. Reduced prostaglandin synthesis is believed to be responsible for the anti-inflammatory and analgesic activities.

As with other NSAIDs diclofenac has been found to be an effective analgesic across the range of musculo-skeletal pathologies.

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 biosynthesis and a 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 tablets have been shown to be effective in relieving the headache and in improving the accompanying symptom of nausea.

PHARMACOKINETICS

Absorption

Diclofenac is rapidly and completely absorbed from sugar-coated tablets. Food intake does not affect absorption.

Peak plasma concentration after one 50 mg sugar-coated tablet was 3.9 µmol/l after 20-60 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 tablets for 8 days in daily doses of 50 mg t.d.s 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

**Bioequivalence Study**

A comparative bioavailability study (EC/BE/00.02) was performed comparing the plasma levels of Diclofenac Potassium after administration of the two products: 2x Diclofenac Potassium 50mg Tablets, batch No 56288 (Delta) and 2xVoltaren Rapid 50mg Tablets.

This study was a single dose (2x50mg), randomised, two-way cross-over study, performed on minimum of 24 health volunteers (male and females). A total of 26 volunteers entered the study and 26 completed the study. The wash period was one week (accepted, given t½ is 1.8 hours). The blood samples were taken at 0, 0.166, 0.333, 0.5, 0.75, 1, 2, 3, 4, 6, 8, 10, after the drug intake. The ratio AUCt / AUC∞ is not estimated as the data do not include AUCt.

The samples were analysed by the validated [for selectivity, linearity (20-3000ng/ml, R² >0.9947), accuracy (CV<1.91%), specificity and LOQ of 20ng/ml)] HPLC analysis at UV detection at 280nm, after drug precipitation and extraction from the biological sample with methanol/water (50:50) mixture.

Pharmacokinetic parameters of Diclofenac Potassium 50mg Tablets vs Voltaren Rapid 50 mg tablets are presented below:

<table>
<thead>
<tr>
<th>Pharmacokinetic parameters</th>
<th>Diclofenac potassium 50mg (Delta) Test</th>
<th>Voltaren Rapid 50mg (Novartis) Reference</th>
<th>Ratio* Test/Ref</th>
<th>Ratio at 90% CI of the ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC (h.ng/ml)</td>
<td>3653</td>
<td>3780</td>
<td>0.98</td>
<td>0.93-1.03</td>
</tr>
<tr>
<td>C max (ng/ml)</td>
<td>3274</td>
<td>3347</td>
<td>0.98</td>
<td>0.79-1.21</td>
</tr>
<tr>
<td>Tmax** (h)</td>
<td>0.54</td>
<td>0.71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T / h (h)</td>
<td>1.8</td>
<td>1.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The ratio and the 90% confidence interval for the ratio are found after logarithmic transformation.
** Non-parametic median

The results from the statistical analysis show that the AUC ratio between 0.93-1.03 (90%CI) comply with the NfG (CPMP.EWP/QWP/1401/98) requirement of 0.80-1.25% (90% CI). The Cmax value of 0.79-1.21 is just outside the 0.80-125% acceptance criteria but within the 0.70-1.45 criteria in the protocol. This may be accepted with the medical justification.

From the data obtained it is concluded that two formulations are bioequivalent with respect to the rate and extent of absorption.
Safety and Efficacy
The clinical expert report satisfactorily reviewed the bibliographic data on safety and efficacy of diclofenac potassium and was written by a suitably qualified person.

Summary of Product Characteristics
Satisfactory summary of product characteristics were arrived at during the assessment of these applications.

Patient Information Leaflet and Labels
The patient information leaflet and labels are acceptable.

Medical Conclusion
The applicant appears to have demonstrated bioequivalence. Marketing authorisations should be granted for these products.
Overall Conclusion and Risk/Benefit Analysis

Quality
The important quality characteristics of diclofenac potassium are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

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

Clinical
Bioequivalence has been demonstrated between the applicant’s product and the reference product. No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for the reference product.

Risk/Benefit Analysis
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. The risk benefit is, therefore, considered to be positive.
### Steps Taken During Assessment

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the application on 26/06/2003.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 19/09/2003</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information from the applicant regarding the quality assessment on 07/12/2004 and 28/11/2006.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant provided further information in regard to the quality assessment on 07/02/2005, 22/04/2005 and 24/07/2007.</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 25/02/2009.</td>
</tr>
</tbody>
</table>
Steps Taken after Assessment

The Market Authorisations were transferred to Gentian Generics Ltd on 14/04/2009 (PL 33217/0010-1).
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Diclofenac Potassium 25 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 25 mg of diclofenac potassium

Also contains Lecithin Soya E322.

This medicine contains 0.075 mmol (2.92mg) potassium per 25mg tablet.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablets

Pink, circular, coated, biconvex tablets, diameter 6mm

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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 100-150 mg 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 25 mg tablets are not recommended for children under 14 years of age.
The use of Diclofenac Potassium 25 mg tablets 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.

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

- 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).
- History of gastro-intestinal bleeding or perforation, relating to previous NSAID therapy.
- During the last trimester of pregnancy (see section 4.6)
- 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

Warnings

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 potassium with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

Elderly:

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

Gastrointestinal:

Close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders, with a history suggestive of gastric or intestinal ulceration, with ulcerative colitis, or with Crohn's disease as these conditions may be exacerbated (see section 4.8 Undesirable effects). Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding).
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 (see section 4.8). Like other NSAIDs, Diclofenac Potassium tablets may mask the signs and symptoms of infection due to their 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 tablets should be discontinued. Hepatitis may occur without prodromal symptoms. Use of Diclofenac Potassium tablets in patients with hepatic porphyria may trigger an attack.

Haematological

Diclofenac Potassium tablets may reversibly inhibit platelet aggregation (see section 4.5 “Interactions”). Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities 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 eg renal function, hepatic function (elevation of liver enzymes may occur) and blood counts. This is particularly important in the elderly.

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 (150mg 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 only 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, and 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, including Diclofenac Potassium (see section 4.8 Undesirable effects). Patients appear to be at the 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. Diclofenac Potassium tablets should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

*Impaired female fertility:

The use of Diclofenac Potassium tablets may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Diclofenac Potassium tablets 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 tablets 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

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 tablets 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. Pancreatititis 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, tinnitus, fainting, occasionally convulsions. In rare 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:** Non-steroidal anti-inflammatory drug (NSAID).

**ATC code:** M01A B05

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 biosynthesis and a 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 tablets have 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 50 mg sugar-coated tablet was 3.9 µmol/l after 20–60 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 tablets for 8 days in daily doses of 50 mg t.d.s does not lead to accumulation of diclofenac in the plasma. Approximately 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 Tablets is included in previous sections of this Summary of Product Characteristics.

### 6 PHARMACEUTICAL PARTICULARS

#### 6.1 List of excipients

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

*Tablet Coating:*  
Polyvinyl alcohol partially hydrolysed  
Titanium dioxide E171  
Talc  
Lecithin Soya E322  
Iron Oxide red E172  
Iron Oxide yellow E172  
Xanthan gum E415
6.2 **Incompatibilities**

Not applicable

6.3 **Shelf life**

36 months

6.4 **Special precautions for storage**

No special storage precautions

6.5 **Nature and contents of container**

7,12,21,28,30,50,56,60,84,100 in Al/Al, OPA/Al/PVC blister
100 or 500 tablets in PP Tablet Container with LDPE Cap

*Not all pack sizes may be marketed*

6.6 **Special precautions for disposal**

Not applicable.

7 **MARKETING AUTHORISATION HOLDER**

Rockspring Healthcare Limited
38/40 Chamberlayne Road
London
NW10 3JE
8 MARKETING AUTHORISATION NUMBER(S)

PL 18866/0033

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25/02/2009

10 DATE OF REVISION OF THE TEXT

25/02/2009
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Diclofenac Potassium 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 50 mg of diclofenac potassium

Also contains Lecithin Soya E322.

This medicine contains 0.150 mmol (5.85mg) potassium per 50mg tablet.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablets

Reddish brown, circular, coated, biconvex tablets, diameter 9 mm

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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
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 – 150 mg 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 50 mg tablets are not recommended for children under 14 years of age.  
The use of Diclofenac Potassium 50 mg tablets 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.

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
• 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).
• History of gastro-intestinal bleeding or perforation, relating to previous NSAID therapy.
• During the last trimester of pregnancy (see section 4.6).
• 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

Warnings

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 potassium with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

Elderly:

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

Gastrointestinal:

Close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders, with a history suggestive of gastric or intestinal ulceration, with ulcerative colitis, or with Crohn's disease as these conditions may be exacerbated (see section 4.8 Undesirable effects). Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding).

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 (see section 4.8). Like other NSAIDs, Diclofenac Potassium tablets may mask the signs and symptoms of infection due to their 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 tablets should be discontinued. Hepatitis may occur without prodromal symptoms. Use of Diclofenac Potassium tablets in patients with hepatic porphyria may trigger an attack.

Haematological

Diclofenac Potassium tablets may reversibly inhibit platelet aggregation (see section 4.5 “Interactions”). Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities 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 eg renal function, hepatic function (elevation of liver enzymes may occur) and blood counts. This is particularly important in the elderly.

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 (150mg 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 only 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, and 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 tablets may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Diclofenac Potassium tablets 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 tablets 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

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 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 tablets 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, tinnitus, fainting, occasionally convulsions. In rare 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:** Non-steroidal anti-inflammatory drug (NSAID).
**ATC code:** M01A B05

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 biosynthesis and a 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 tablets have 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 50 mg sugar-coated tablet was 3.9 µmol/l after 20-60 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 tablets for 8 days in daily doses of 50 mg t.d.s 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 preclinical safety of Diclofenac Potassium Tablets is included in previous sections of this Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

Tablet Coating:
Polyvinyl alcohol partially hydrolysed
Titanium dioxide E171
Talc
Lecithin Soya E322
Iron Oxide red E172
Iron Oxide yellow E172
Xanthan gum E415

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
No special storage precautions

6.5 Nature and contents of container
7,12,21,28,30,50,56,60,84,100 in Al/Al, OPA/Al/PVC blister
100 or 500 tablets in PP Tablet Container with LDPE Cap
*Not all pack sizes may be marketed*

6.6 Special precautions for disposal
Not applicable.

7 MARKETING AUTHORISATION HOLDER
Rockspring Healthcare Limited
38/40 Chamberlayne Road
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8 MARKETING AUTHORISATION NUMBER(S)

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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25/02/2009

10 DATE OF REVISION OF THE TEXT

25/02/2009
Labels and Leaflets
Diclofenac potassium 25mg & 50mg 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 any further questions, please ask your doctor or 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 tablets are and what they are used for
2. Before you take Diclofenac potassium tablets
3. How to take Diclofenac potassium tablets
4. Possible side effects
5. How to store Diclofenac potassium tablets
6. Further information

1. What Diclofenac potassium 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
- Joint pain
- 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 tablets

Do not take Diclofenac potassium 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.
- have previously had a reaction (asthma, hives or a cold) caused by an allergy to sulphonamides (e.g. aspirin) or other non-steroidal painkillers.
- have ever had a kidney, heart or liver failure.
- are pregnant, and in the last three months (last trimester) of pregnancy.

Check with your doctor or pharmacist before taking Diclofenac potassium 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 (disorders of the red blood pigment).
- have had or need to have surgery.
- are elderly (over 65).
- if you are being treated with diuretics (water tablets) or COX-2 inhibitors such as celecoxib.

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 (e.g. warfarin) - these may increase the risk of bleeding.
- diuretics (water tablets) - the effect of these may be decreased
- lithium (medicine to treat depression) - the level of this medicine may be increased if taken with Diclofenac.
- corticosteroids (e.g. methylprednisolone to treat cancers) - should not be taken in more than 24 hours before or while taking Diclofenac potassium tablets. The blood levels of these medicines may be increased if taken with Diclofenac.
- ciclosporin - this may harm kidney function.
- quinolones (to treat infections, e.g. ciprofloxacin and levofloxacin) - these may cause convulsions (fits).
- steroid tablets - these may increase the risk of bleeding in the stomach.
- other NSAIDs (e.g. aspirin) - these may increase the risk of side effects.
- medicines to treat high blood pressure (ACE inhibitors, beta blockers) - the blood pressure lowering effect may be reduced.
- milnacipran (used to induce abortion) - the effect of milnacipran may be reduced by NSAIDs.
- cardiac glycosides (e.g. digitoxin) used to treat heart failure. Use with Diclofenac may worsen heart failure or increase blood levels of these medicines.
- Tacrolimus (an immunosuppressant) - these may increase the risk of kidney damage.
- Zidovudine (an antiretroviral drug used to treat HIV) - combination with Diclofenac may increase the risk of blood disorders.

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

It is not recommended that you take Diclofenac during the first 6 months of pregnancy. However, your doctor may prescribe Diclofenac for you during the first few months of pregnancy if he/she feels that the benefit to you outweighs the risk. You must not however take Diclofenac for 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.

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UKPAR Rockspring Healthcare, Diclofenac Potassium 25 and 50mg Tablets 40
Driving and using machines
Some people 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 0.075mmol (2.59 mg) potassium per 25mg tablet and 0.150mmol (5.16 mg) potassium per 50mg tablet. This should be taken into account if you have reduced kidney function or are on a controlled potassium diet.

3. How To Take Diclofenac potassium tablets
Always take Diclofenac potassium tablets exactly as your doctor has told you. If you are unsure check with your doctor or pharmacist. Diclofenac potassium tablets must not be taken long-term, blood tests should be carried out if taken for more than a few days. To minimise side effects, you should take the lowest effective dose for the shortest time necessary to relieve your symptoms. 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 to 150 mg 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 to 100mg daily, in two or three doses.
- To treat the symptoms of migraine in adults
  50mg taken when the first signs of a migraine attack appear. Another 50mg taken 2 hours after the first dose if needed and then every 4 to 6 hours. You should not take more than 200mg 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 rooms 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 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) or 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, diarrhoea and disorders of the skin
- yellowing of the skin or the whites of your eyes
- stomach pain, indigestion, heartburn, wind, nausea (feeling sick), vomiting (being sick) or other abnormal stomach symptoms

STOP TAKING the medicine and tell your doctor if you experience:
- Any type of fit or seizure
- An unexpected change in the amount of urine produced and/or its appearance
- Tell your doctor if you experience any of the following symptoms:

Common (occurs in less than 1 in 10 people):
- headache, dizziness, ‘spinning’ sensation, diarrhoea, loss of weight or poor appetite, abnormal liver function tests, skin rashes

Rare (occurs in less than 1 in 1000 people):
- drowsiness, tiredness, stomach ulcers or bleeding, haemorrhoids, itching, fluid retention (symptoms of which include swollen ankles)

Very rare (occurs in less than 1 in 10,000 people):
- pets and needles, tremor, blurred or double vision, hearing loss or impairment, tinnitus (ringing in the ears), difficulty sleeping, nightmares, depression, irritation, anxiety, psychotic reactions, disorientation, loss of memory, numbness, sensitivity to light, taste disturbance, constipation, inflammation of the tongue, mouth ulcers, ulcers inside the mouth, fever, sweating, 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 rashes, urticaria, Erythema Multiforme (round red patches on the skin), Stevens-Johnson Syndrome (severe skin rash with flaking, 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 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 tablets
Keep out of the reach and sight of children. This medicine has no special storage precautions. 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 tablets contain
The active substance in the ingredient that makes the tablet work is Diclofenac. Each tablet contains 25mg or 50mg Diclofenac potassium. The tablets also contain silica colloidial anhydrous, sodium starch glycolate, povidone, maize starch, calcium hydrogen phosphate anhydrous, magnesium stearate, polyvinyl alcohol partially hydrolysed, titanium dioxide E171, talc, lecithin soya E322, iron oxide red, iron oxide yellow and xanthan gum E415.

What Diclofenac potassium tablets look like and contents of the pack
The 25mg tablets are pink, round, uncoated, biconvex 6mm film-coated tablets. The 50mg tablets are reddish brown, round, uncoated, biconvex 8mm film-coated tablets.

Pack sizes
Blister packs 7, 12, 21, 28, 30, 50, 56, 60, 84 and 100 film-coated tablets.

Plastic bottles: 100 and 500 film-coated tablets (Not all pack sizes may be available)

Marketing Authorisation Holder
Rockspring Healthcare Limited, 35-40 Chamberlayne Road, London, NW10 3JE

Manufacturer
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