Summary of Product Characteristics(SmPC)

1. Name of the finished pharmaceutical products

Diclofenac potassium tablets

2. Qualitative and quantitative composition

50mg

Each Tablets: Diclofenac potassium 50mg

3. Pharmaceutical form

Sugar coated tablets, inside with white powder

4. Clinical particulars

4.1 Therapeutic indications

Carefully consider the potential benefits and risks of HANBET® (diclofenac potassium film coated tablets) and other treatment options before deciding to use HANBET. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see WARNINGS).

Cataflam is indicated:

For treatment of primary dysmenorrhea

For relief of mild to moderate pain

For relief of the signs and symptoms of osteoarthritis

For relief of the signs and symptoms of rheumatoid arthritis

4.2 Posology and method of administration

Diclofenac is 100% absorbed after oral administration compared to IV administration as measured by urine recovery. However, due to first-pass metabolism, only about 50% of the absorbed dose is systemically available (see Table 1). In some fasting volunteers, measurable plasma levels are observed within 10 minutes of dosing with Diclofenac potassium film coated tablets. Peak plasma levels are achieved approximately 1 hour in fasting normal volunteers, with a range of .33 to 2 hours. Food has no significant effect on the extent of diclofenac absorption. However, there is usually a delay in the onset of absorption and a reduction in peak plasma levels of approximately 30%.

4.3 Contraindications

Diclofenac potassium film coated tablets are contraindicated in patients with known hypersensitivity to diclofenac. Diclofenac potassium film coated tablets should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients (see WARNINGS, Anaphylactoid Reactions, and PRECAUTIONS, Preexisting Asthma).

Diclofenac potassium film coated tablets are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

4.4 Interaction with other medicinal products and other forms of interaction

Aspirin:

When Diclofenac potassium film coated tablets are administered with aspirin, its protein binding is reduced. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of diclofenac and aspirin is not generally recommended because of the potential of increased adverse effects.

Methotrexate:

NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

Cyclosporine:

Diclofenac potassium film coated tablets, like other NSAIDs, may affect renal prostaglandins and increase the toxicity of certain drugs. Therefore, concomitant therapy with Diclofenac potassium film coated tablets may increase cyclosporine's nephrotoxicity. Caution should be used when Diclofenac potassium film coated tablets are administered concomitantly with cyclosporine.

ACE- inhibitors:

Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE inhibitors.

Diuretics:

Clinical studies, as well as post-marketing observations, have shown that diclofenac can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure (see PRECAUTIONS – Renal Effects), as well as to assure diuretic efficacy.

Lithium:

NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

Warfarin:

The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

4.5 Pregnancy and lactation

Teratogenic Effects: Pregnancy Category C

Reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities. However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women. Diclofenac potassium film coated tablets should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects:

Because of the known effects of nonsteroidal anti-inflammatory drugs on the fetal cardiovascular system (closure of ductus arteriosus), use during pregnancy (particularly late pregnancy) should be avoided.

Labor and Delivery

In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, and decreased pup survival occurred. The effects of diclofenac on labor and delivery in pregnant women are unknown.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Diclofenac potassium film coated tablets, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.6 Effects on ability to drive and use machines

Teratogenic Effects: Pregnancy Category C

Reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities. However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women. Diclofenac potassium film coated tablets should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

4.7 Undesirable effects

None

4.8 Overdose

Symptoms following acute NSAID overdoses are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose (5 to 10 times the usual dose). Forced diuresis, alkalinization of urine, hemodialysis, or hemoperfusion may not be useful due to high protein binding.

5. Pharmacological properties

5.1 Pharmacokinetic properties

Absorption

Diclofenac is 100% absorbed after oral administration compared to IV administration as measured by urine recovery. However, due to first-pass metabolism, only about 50% of the absorbed dose is systemically available (see Table 1). In some fasting volunteers, measurable plasma levels are observed within 10 minutes of dosing with Diclofenac potassium film coated tablets. Peak plasma levels are achieved approximately 1 hour in fasting normal volunteers, with a range of .33 to 2 hours. Food has no significant effect on the extent of diclofenac absorption. However, there is usually a delay in the onset of absorption and a reduction in peak plasma levels of approximately 30%.

Table 1. Pharmacokinetic Parameters for Diclofenac

PK Parameter	Normal Healthy Adults (20-52 yrs.)	
	Mean	**Coefficient of Variation (%)**
Absolute Bioavailability (%) [N = 7]	55	40
Tmax (hr) [N = 65]	1.0	76
Oral Clearance (CL/F; mL/min) [N = 61]	622	21
Renal Clearance (% unchanged drug in urine)	<1	—

[N = 7]		
Apparent Volume of Distribution (V/F; L/kg) [N = 61]	1.3	33
Terminal Half-life (hr) [N = 48]	1.9	29

Distribution

The apparent volume of distribution (V/F) of diclofenac potassium is 1.3 L/kg.

Diclofenac is more than 99% bound to human serum proteins, primarily to albumin. Serum protein binding is constant over the concentration range (0.15-105 µg/mL) achieved with recommended doses.

Diclofenac diffuses into and out of the synovial fluid. Diffusion into the joint occurs when plasma levels are higher than those in the synovial fluid, after which the process reverses and synovial fluid levels are higher than plasma levels. It is not known whether diffusion into the joint plays a role in the effectiveness of diclofenac.

Metabolism

Five diclofenac metabolites have been identified in human plasma and urine. The metabolites include 4'-hydroxy-, 5-hydroxy-, 3'-hydroxy-, 4',5-dihydroxy- and 3'-hydroxy-4'-methoxy diclofenac. In patients with renal dysfunction, peak concentrations of metabolites 4'-hydroxy- and 5-hydroxy-diclofenac were approximately 50% and 4% of the parent compound after single oral dosing compared to 27% and 1% in normal healthy subjects. However, diclofenac metabolites undergo further glucuronidation and sulfation followed by biliary excretion.

One diclofenac metabolite 4’-hydroxy-diclofenac has very weak pharmacologic activity.

Excretion

Diclofenac is eliminated through metabolism and subsequent urinary and biliary excretion of the glucuronide and the sulfate conjugates of the metabolites. Little or no free unchanged diclofenac is excreted in the urine. Approximately 65% of the dose is excreted in the urine and approximately 35% in the bile as conjugates of unchanged diclofenac plus metabolites. Because renal elimination is not a significant pathway of

elimination for unchanged diclofenac, dosing adjustment in patients with mild to moderate renal dysfunction is not necessary. The terminal half-life of unchanged diclofenac is approximately 2 hours.

5.2 Preclinical safety data

Safety and effectiveness in pediatric patients have not been established.

6. Phamaceutical particulars

6.1List of excipients

Sugar powder

60% Ethanol

Starch

Magnesium Stearate

6.2 Incompatibilities

No incompatibilities are known to date

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30℃. Store in the original package.

6.5 Nature and contents of container

PVC and Aluminum foil

10 Tablets/blister, 10blisters/box

6.6 Special precautions for disposal and other handling

None

7.Marketing authorization holder

Shandong Xier Kangtai Pharmaceutical Co.,Ltd.

Private economy Garden, Xinyan Town, Yanzhou District, Jining City

8.Marketing authorization number(s)

LU20160143

9.Date of first authorization of the authorization

06/06/2010

10.Date of revision of the text

06/2018