SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Voltaren 25 mg Suppositories

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains 25 mg of diclofenac sodium.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suppositories.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

GRT

Treatment of:

•Inflammatory and degenerative forms of rheumatism: rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and spondylarthritis, painful syndromes of the vertebral column, non-articular rheumatism.

•Acute attacks of gout.

•Post-traumatic and post-operative pain, inflammation and swelling, e.g., following dental or orthopaedic surgery.

•Painful and/or inflammatory conditions in gynecology, e.g., primary dysmenorrhea or adnexitis.

•As an adjuvant in severe painful inflammatory infections of the ear, nose or throat, e.g., pharyngotonsillitis, otitis. In keeping with general therapeutic principles, the underlying disease should be treated with basic therapy, as appropriate. Fever alone is not an indication.

PRT

Treatment of:

•Inflammatory and degenerative forms of rheumatism: rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and spondylarthritis, painful syndromes of the vertebral column, non-articular rheumatism.

•Post-traumatic and post-operative pain, inflammation, and swelling, e.g., following dental or orthopaedic surgery.

•Painful and/or inflammatory conditions in gynaecology, e.g., primary dysmenorrhoea or adnexitis.

Suppositories

Treatment of:

- Inflammatory and degenerative forms of rheumatism: rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and spondylarthritis, painful syndromes of the vertebral column, non-articular rheumatism.
- Acute attacks of gout.
- Post-traumatic and post-operative pain, inflammation and swelling, e.g., following dental or orthopaedic surgery.
- Painful and/or inflammatory conditions in gynaecology, e.g., primary dysmenorrhoea or adnexitis.
- Migraine attacks.
- As an adjuvant in severe painful inflammatory infections of the ear, nose or throat, e.g., pharyngotonsillitis, otitis. In keeping with general therapeutic principles, the underlying disease should be treated with basic therapy, as appropriate. Fever alone is not an indication.

4.2 Posology and Method of Administration

As a general recommendation, the dose should be individually adjusted. Adverse 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 initial daily dose is 100 to 150 mg. In milder cases, as well as for long-term therapy, 75 to 100 mg daily is usually sufficient. The total daily dose should generally be divided into 2 to 3 separate doses. To suppress nocturnal pain and morning stiffness, treatment with tablets during the day can be supplemented by the administration of a suppository at bedtime (up to a total maximum daily dose of 150 mg).

In primary dysmenorrhoea, the daily dose should be individually adjusted and is generally 50 to 150 mg. A dose of 50 to 100 mg should be given initially and, if necessary, increased over the course of several menstrual cycles up to a maximum of 200 mg/day. Treatment should be started on appearance of the first symptoms and, depending on the symptomatology, continued for a few days.

Treatment of migraine attacks with Voltaren suppositories should be started with a dose of 100 mg at the first signs of an impending attack. Additional suppositories up to 100 mg may be taken on the same day if required. Should the patient require further therapy on the following days, the maximum daily dose should be limited to 150 mg in divided doses.

Special Populations – Renal Impairment: Voltaren is contraindicated in patients with renal failure (GFR <15 mL/min/1.73 m^2). No specific dose adjustment recommendations can be made; caution is advised (see section 4.4).

Hepatic Impairment: Voltaren is contraindicated in patients with hepatic failure. No specific dose adjustment recommendations can be made; caution is advised when administering Voltaren to patients with mild to moderate hepatic impairment (see section 4.4).

Paediatric Patients (below 18 years): Children aged 1 year or over and adolescents should be given 0.5 to 2 mg/kg body weight daily divided into 2 to 3 separate doses, depending on the severity of the disorder. For treatment of juvenile rheumatoid arthritis, the dose can be raised up to a maximum of 3 mg/kg daily, given in divided doses. The maximum daily dose of 150 mg should not be exceeded. Voltaren 12.5 mg

or 25 mg suppositories are recommended for use in children and adolescents below 14 years of age. Because of their dosage strength, Voltaren 50 mg suppositories are not recommended for children and adolescents below 14 years of age. Voltaren 100 mg suppositories are not suitable for children and adolescents.

Geriatric Patients (≥65 years): No adjustment of the starting dose is generally required for elderly patients. However, caution is indicated on basic medical grounds, especially for frail elderly patients or those with a low body weight (see section 4.4).

Established Cardiovascular Disease or Significant Cardiovascular Risk Factors: Treatment with Voltaren is generally not recommended in patients with established cardiovascular disease or uncontrolled hypertension. If needed, such patients should be treated only after careful consideration and only at doses ≤100 mg daily if treated for more than 4 weeks (see section 4.4).

Method of Administration: The suppositories should be inserted well into the rectum. It is recommended to take the suppositories after passing stools. Not to be taken by mouth – for rectal use only.

4.3 Contraindications

- Active gastric or intestinal ulcer, bleeding or perforation (see sections 4.4 and 4.7).
- Last trimester of pregnancy (see section 4.5).
- Hepatic failure.
- Renal failure (GFR <15 mL/min/1.73 m^2).
- Severe cardiac failure (see section 4.4).
- Patients in whom the use of acetylsalicylic acid or other NSAIDs can precipitate asthma, angioedema, urticaria, or acute rhinitis (NSAID-induced cross-reactivity reactions) (see sections 4.4 and 4.7).
- Proctitis (suppositories only).

4.4 Special Warnings and Precautions for Use

Gastrointestinal Effects: Gastrointestinal bleeding, ulceration or perforation, which can be fatal, have been reported with all NSAIDs including diclofenac, and may occur at any time during treatment with or without warning symptoms. They generally have more serious consequences in the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving Voltaren, the treatment should be discontinued. Close medical surveillance and particular caution should be exercised when prescribing Voltaren in patients with symptoms indicative of gastrointestinal disorders or with a history of gastric or intestinal ulceration, bleeding or perforation. Combination therapy with protective agents (e.g. proton pump inhibitors or misoprostol) should be considered for high-risk patients.

Cardiovascular Effects: Treatment with NSAIDs including diclofenac, particularly at high dose and long term, may be associated with a small increased risk of serious cardiovascular thrombotic events (including myocardial infarction and stroke). As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, the lowest effective daily dose should be used for the shortest duration possible.

Haematologic Effects: During prolonged treatment with Voltaren, monitoring of the blood count is recommended. Like other NSAIDs, diclofenac may temporarily inhibit platelet aggregation. Patients with defects of haemostasis should be carefully monitored.

Respiratory Effects (Pre-existing Asthma): In patients with asthma, seasonal allergic rhinitis, nasal polyps, chronic obstructive pulmonary diseases or chronic infections of the respiratory tract, reactions on NSAIDs such as asthma exacerbations, Quincke's oedema or urticaria are more frequent than in other patients. Special caution is recommended in such patients.

Hepatobiliary Effects: Close medical surveillance is required when prescribing Voltaren to patients with impaired hepatic function, as their condition may be exacerbated. Values of one or more liver enzymes may increase. If abnormal liver function tests persist or worsen, or if clinical signs or symptoms consistent with liver

disease develop, Voltaren should be discontinued. Hepatitis may occur with use of diclofenac without prodromal symptoms.

Skin Reactions: 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 Voltaren. Voltaren should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Renal Effects: As fluid retention and oedema have been reported in association with NSAID therapy including diclofenac, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and in those patients with substantial extracellular volume depletion. Monitoring of renal function is recommended as a precautionary measure.

Geriatric Patients: Caution is indicated in the elderly on basic medical grounds, especially in frail elderly patients or those with a low body weight.

Masking Signs of Infections: Like other NSAIDs, diclofenac may mask the signs and symptoms of infection due to its pharmacodynamic properties.

Excipients: This medicine contains hard fat as the only excipient in suppositories.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

CYP2C9 Inhibitors: Caution is recommended when co-prescribing diclofenac with CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac.

Lithium: Diclofenac may raise plasma concentrations of lithium. Monitoring of the serum lithium level is recommended.

Digoxin: Diclofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.

Diuretics and Antihypertensive Agents: Concomitant use of diclofenac with diuretics or antihypertensive agents may cause a decrease in their antihypertensive effect. Patients should have their blood pressure periodically monitored and be adequately hydrated.

Ciclosporin and Tacrolimus: Diclofenac may increase the nephrotoxicity of ciclosporin and tacrolimus due to the effect on renal prostaglandins. Therefore, it should be given at lower doses than those that would be used in patients not receiving ciclosporin or tacrolimus.

Drugs Known to Cause Hyperkalaemia: Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently.

Quinolone Antibacterials: There have been isolated reports of convulsions which may have been due to concomitant use of quinolones and NSAIDs.

Other NSAIDs and Corticosteroids: Concomitant administration of diclofenac and other systemic NSAIDs or corticosteroids may increase the frequency of gastrointestinal undesirable effects.

Anticoagulants and Anti-platelet Agents: Caution is recommended since concomitant administration could increase the risk of bleeding. Close monitoring of such patients is recommended.

SSRIs: Concomitant administration of systemic NSAIDs including diclofenac and SSRIs may increase the risk of gastrointestinal bleeding.

Antidiabetics: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of both hypoglycaemic and hyperglycaemic effects necessitating changes in the dosage of the antidiabetic agents during treatment with diclofenac.

Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

Methotrexate: Caution is recommended when NSAIDs including diclofenac are administered less than 24 hours before or after treatment with methotrexate, since

blood concentrations of methotrexate may rise and the toxicity of this substance be increased.

CYP2C9 Inducers: Caution is recommended when co-prescribing diclofenac with CYP2C9 inducers (such as rifampicin), which could result in a significant decrease in plasma concentration and exposure to diclofenac.

4.6 Fertility, Pregnancy and Lactation

Pregnancy: There are insufficient data on the use of diclofenac in pregnant women. Use of NSAIDs including diclofenac can cause uterine inertia, premature closure of the foetal ductus arteriosus and foetal renal impairment leading to oligohydramnios. Because of these risks, Voltaren should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the foetus. In addition, Voltaren should not be used during the third trimester of pregnancy (see section 4.3). If an NSAID is necessary from the 20th week of gestation to the end of the 2nd trimester, limit the use to the lowest effective dose and shortest duration possible.

Lactation: Like other NSAIDs, diclofenac passes into the breast milk in small amounts. Therefore, Voltaren should not be administered during breast-feeding in order to avoid undesirable effects in the infant.

Female Fertility: As with other NSAIDs, the use of Voltaren 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 Voltaren should be considered.

Male Fertility: There is no human data on the effect of Voltaren on male fertility.

4.7 Effects on Ability to Drive and Use Machines

Patients experiencing visual disturbances, dizziness, vertigo, somnolence or other central nervous system disturbances while taking Voltaren should refrain from driving or using machines.

4.8 Undesirable Effects

Adverse drug reactions from clinical trials and/or spontaneous or literature reports are listed below. Within each system organ class, adverse drug reactions are ranked by frequency. The following convention is used: very common (>1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Blood and lymphatic system disorders: Very rare: thrombocytopenia, leukopenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis.

Immune system disorders: Rare: hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock). Very rare: angioedema (including face oedema).

Psychiatric disorders: Very rare: disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.

Nervous system disorders: Common: headache, dizziness. Rare: somnolence. Very rare: paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, dysgeusia, cerebrovascular accident.

Eye disorders: Very rare: visual impairment, blurred vision, diplopia.

Ear and labyrinth disorders: Common: vertigo. Very rare: tinnitus, impaired hearing.

Cardiac disorders: Uncommon: myocardial infarction, cardiac failure, palpitations, chest pain. Frequency not known: Kounis syndrome.

Vascular disorders: Very rare: hypertension, vasculitis.

Respiratory, thoracic and mediastinal disorders: Rare: asthma (including dyspnoea). Very rare: pneumonitis.

Gastrointestinal disorders: Common: nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, decreased appetite. Rare: gastritis, gastrointestinal haemorrhage, haematemesis, haemorrhagic diarrhoea, melaena, gastrointestinal ulcer (with or without bleeding or perforation), proctitis (suppositories only). Very rare: colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis, glossitis, pancreatitis, haemorrhoids (suppositories only).

Hepatobiliary disorders: Common: transaminases increased. Rare: hepatitis, jaundice, liver disorder. Very rare: fulminant hepatitis, hepatic necrosis, hepatic failure.

Skin and subcutaneous tissue disorders: Common: rash. Rare: urticaria. Very rare: bullous dermatitis, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), exfoliative dermatitis, alopecia, photosensitivity reaction, purpura, Henoch-Schoenlein purpura, pruritus.

Renal and urinary disorders: Very rare: acute kidney injury (acute renal failure), haematuria, proteinuria, nephrotic syndrome, tubulointerstitial nephritis, renal papillary necrosis.

Arteriothrombotic Events: Meta-analysis and pharmacoepidemiological data point towards a small increased risk of arteriothrombotic events (for example myocardial infarction) associated with the use of diclofenac, particularly at a high dose (150 mg daily) and during long-term treatment (see section 4.4).

Reporting of suspected adverse reactions

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

Health care professionals are asked to report any suspected adverse reactions via the https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms: There is no typical clinical picture resulting from diclofenac overdosage. Overdosage can cause symptoms such as vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible.

Therapeutic Measures: Management of acute poisoning with NSAIDs including diclofenac essentially consists of supportive measures and symptomatic treatment. Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder, and

respiratory depression. Activated charcoal may be considered after ingestion of a potentially toxic overdose, and gastric decontamination (e.g. vomiting, gastric lavage) after ingestion of a potentially life-threatening overdose. Special measures such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs including diclofenac, due to the high protein binding and extensive metabolism.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, acetic acid derivatives and related substances.

ATC Code: M01AB05

Voltaren contains diclofenac sodium, a non-steroidal compound with pronounced antirheumatic, anti-inflammatory, analgesic, and antipyretic properties. Inhibition of prostaglandin biosynthesis, which has been demonstrated in experiments, is considered to be fundamental to its mechanism of action. Prostaglandins play an important role in causing inflammation, pain and fever.

In rheumatic diseases, the anti-inflammatory and analgesic properties of diclofenac elicit a clinical response characterised by marked relief from signs and symptoms such as pain at rest, pain on movement, morning stiffness, and swelling of the joints, as well as by an improvement in function. In post-traumatic and post-operative inflammatory conditions, diclofenac rapidly relieves both spontaneous pain and pain on movement and reduces inflammatory swelling and wound oedema.

In clinical trials Voltaren has also been found to exert a pronounced analgesic effect in moderate and severe pain of non-rheumatic origin. Clinical studies have also revealed that in primary dysmenorrhoea, Voltaren is capable of relieving the pain and reducing the extent of bleeding. Voltaren also has beneficial effects on the symptoms of migraine attacks.

5.2 Pharmacokinetic Properties

Absorption (Suppositories): Diclofenac shows a rapid onset of absorption from suppositories, although the rate of absorption is slower than from gastro-resistant tablets administered orally. After the administration of 50 mg suppositories, peak plasma concentrations are attained on average within 1 hour, but maximum concentrations per dose unit are about two thirds of those reached after administration of gastro-resistant tablets. Since about half of diclofenac is metabolised during its first passage through the liver ("first pass" effect), the area under the concentration curve (AUC) following oral or rectal administration is about half that following an equivalent parenteral dose.

Distribution: 99.7% of diclofenac binds to serum proteins, mainly to albumin (99.4%). The apparent volume of distribution calculated is 0.12 to 0.17 L/kg. Diclofenac enters the synovial fluid, where maximum concentrations are measured 2 to 4 hours after peak plasma values have been reached. Concentrations of the active substance are already higher in the synovial fluid than in the plasma within 2 hours of peak plasma levels and remain higher for up to 12 hours.

Biotransformation/Metabolism: Biotransformation of diclofenac takes place partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates.

Elimination: Total systemic clearance of diclofenac from plasma is 263 ± 56 mL/min. The terminal half-life in plasma is 1 to 2 hours. About 60% of the administered dose is excreted in the urine as the glucuronide conjugate of the intact molecule and as metabolites. Less than 1% is excreted as unchanged substance. The rest of the dose is eliminated as metabolites through the bile in the faeces.

Special Populations: No relevant age-dependent differences in the drug's absorption, metabolism, or excretion have been observed in geriatric patients. In patients with renal impairment, no accumulation of the unchanged active substance is inferred

when applying the usual dosage schedule. In patients with chronic hepatitis or non-decompensated cirrhosis, the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

5.3 Preclinical Safety Data

Preclinical data from acute and repeated dose toxicity studies, as well as from genotoxicity, mutagenicity, and carcinogenicity studies with diclofenac revealed no specific hazard for humans at the intended therapeutic doses (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Hard fat.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special Precautions for Storage

Do not store above 30°C. Store in the original package. Keep out of the reach and sight of children.

6.5 Nature and Contents of Container

PVC/LD-PE foil. Not all pack sizes may be marketed.

6.6 Special Precautions for Disposal and Other Handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Pharma AG, Lichtstrasse 35, 4056 Basel, Switzerland.

Manufacturer (Suppositories): Delpharm Huningue S.A.S., 26 rue de la Chapelle, 68330 Huningue, France.

8. MARKETING AUTHORISATION NUMBER(S)

Voltaren 25 mg suppositories Kenya: 16798

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Voltaren 25 mg suppositories Kenya: 25 November 2005.

10. DATE OF REVISION OF THE TEXT

September 2024 (CDS).