1.3.1 SUMMARY PRODUCT CHARACTERISTICS (SmPC)

<table>
<tr><td>1</td><td>Name of the Finished Medicinal Product:</td></tr>
<tr><td>1.1</td><td>Product Name: Diclofenac Gel BP 1% w/w</td></tr>
<tr><td>1.2</td><td>Strength : 1% w/w</td></tr>
<tr><td>1.3</td><td>Pharmaceutical Form: Gel</td></tr>
<tr><td>2</td><td>Qualitative and Quantitative Compositions:</td></tr>
<tr><td></td><td>Qualitative Declaration:
Active component
INN Name: Diclofenac Diethylamine BP
Quantitative Declaration:
Diclofenac Diethylamine BP…….1.16% w/w
Eq.Diclofenac Sodium BP……..1% w/w
Gel base……..q.s.

<table>
<tr><th>Sr. No.</th><th>Content Name</th><th>Quality Standard</th><th>Quantity in mg per g</th></tr>
<tr><td colspan="4">Active Ingredient:</td></tr>
<tr><td>1.</td><td>Diclofenac Diethylamine</td><td>BP</td><td>11.60</td></tr>
<tr><td colspan="4">Inactive Ingredient:</td></tr>
<tr><td>2.</td><td>Methyl Hydroxybenzoate (Methyl Paraben)</td><td>BP</td><td>2.00</td></tr>
<tr><td>3.</td><td>Propyl Hydroxybenzoate (Propyl Paraben)</td><td>BP</td><td>1.00</td></tr>
<tr><td>4.</td><td>Phenoxyethanol</td><td>BP</td><td>10.00</td></tr>
<tr><td>5.</td><td>Tocopheryl Phosphate Hydrolysate (TPM)</td><td>IH</td><td>10.00</td></tr>
<tr><td>6.</td><td>Isopropyl Alcohol</td><td>BP</td><td>100.00</td></tr>
<tr><td>7.</td><td>Butylated Hydroxy Toluene</td><td>BP</td><td>0.50</td></tr>
<tr><td>8.</td><td>Sepineo P 600</td><td>IH</td><td>65.00</td></tr>
<tr><td>9.</td><td>Sodium Hydroxide</td><td>BP</td><td>q.s.</td></tr>
<tr><td>10.</td><td>Lavender Perfume</td><td>IH</td><td>1.00</td></tr>
<tr><td>11.</td><td>Purified Water</td><td>BP</td><td>q.s. upto 1.00 g</td></tr>
</table>

IH- In-house Specification
BP- British Pharmacopoeia</td></tr>
<tr><td>3</td><td>Pharmaceutical Form: Gel
White to off white colour, semisolid homogeneous viscous gel.</td></tr>
<tr><td>4</td><td>Clinical Particulars:</td></tr>
<tr><td>4.1</td><td>Therapeutic Indications:

Diclofenac Gel is Non-Steroidal Anti-Inflammatory Gel which provides relief of pain and inflammation in a wide range of conditions including:
i) Arthritic conditions: Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute gout.</td></tr>
</table>

	ii) Acute musculo-skeletal disorders such as periarthritis (for example frozen shoulder), tendinitis, tenosynovitis, bursitis. iii) Other painful conditions resulting from trauma, low back pain, sprains, strains, dislocations, orthopedic.
4.2	**Posology and Method of Administration** Total dose should not exceed 32 g per day over affected area. -Lower extremities: Apply the gel (4 g) to the affected area 4 times daily. Do not apply more than 16 g daily to any one affected joint of the lower extremities. - Upper extremities: Apply the gel (2 g) to the affected area 4 times daily. Do not apply more than 8 g daily to any one affected joint of the lower extremities.
4.3	**Contra-indications:** Hypersensitivity to the active substance or any of the excipients. "Patients who have previously shown hypersensitivity reactions (e.g. Asthma, angiodema, urticaria, or acute rhinitis) to ibuprofen, aspirin or other Non-Steroidal Anti-Inflammatory Drugs. Use during the preoperative period in the setting of coronary artery bypass graft (CABG) surgery.
4.4	**Special warning and precautions for use:** Serious potentially fatal cardiovascular events, thrombotic events, myocardial infarction and stroke can occur with NSAID treatment. The lowest possible dose of Diclofenac Gel should be used in patients with known cardiovascular disease or risk factors for it. NSAID including Diclofenac can cause serious gastrointestinal adverse effect including inflammation, bleeding, ulceration and perforation, Diclofenac Gel should be prescribed with caution in those with prior history of ulcer disease or gastrointestinal bleeding. Long term administration of NSAID can result in renal papillary necrosis and other renal injury. Diclofenac Gel should be used with caution in patients at risk of this reaction including elderly and those with impaired renal function. If abnormal Liver tests persist or worsen, if clinical sign and/or symptoms consistent with liver disease develop, or if systematic manifestations occur (e.g., eosinophilla, rash, abdominal pain, diarrhea, dark urine, etc.) Diclofenac Gel should be discontinued immediately. Diclofenac Gel should be used with caution in patients with hypertension, fluid retention and edema.
4.5	**Interaction with other drugs, other forms of interactions:** ***Lithium*** Diclofenac may increase plasma concentrations of Lithium. ***Anticoagulants*** Although clinical investigations do not appear to indicate that Diclofenac has an influence on the effect of anticoagulants, there are isolated reports of an increased risk of haemorrhage with the combined use of Diclofenac and anticoagulant therapy. Therefore, to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. As with other non-steroidal anti-inflammatory agents, Diclofenac in a high dose can reversibly inhibit platelet aggregation ***Ciclosporin and Tacrolimus*** Cases of nephrotoxicity have been reported in patients receiving concomitant ciclosporin and NSAIDs, including Diclofenac. Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through combined renal anti-prostaglandin effects of both the NSAID and calcineurin inhibitor.

4.5	***Methotrexate*** Cases of serious toxicity have been reported when Methotrexate and NSAIDs are given within 24 hours of each other. This interaction is mediated through accumulation of Methotrexate resulting from impairment of renal excretion in the presence of the NSAID. ***Quinolone Antimicrobials*** Convulsions may occur due to an interaction between Quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions. Therefore, caution should be exercised when considering the use of a quinolone in patients already receiving an NSAID. ***Other NSAIDs including Cyclo-Oxygenase-2 Selective Inhibitors and Corticosteroids*** Co-administration of Diclofenac Sodium with these agents may increase the risk of gastro-intestinal bleeding or ulceration. Avoid concomitant use of two or more NSAIDs. ***Anti-platelet Agents and Selective Serotonin Reuptake Inhibitors (SSRIs)*** Increased risk of Gastrointestinal bleeding. ***Diuretics*** Like other NSAIDs, Diclofenac may inhibit the activity of Diuretics. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels, which should therefore be monitored frequently. ***Antihypertensives*** Concomitant use of NSAIDs with antihypertensive drugs (i.e. beta-blockers, angiotensin converting enzyme (ACE) inhibitors, diuretics) may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis ***Cardiac Glycosides*** Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels. ***Mifepristone*** NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the efforts of mifepristone. ***Penicillamine*** Possible increased risk of neohrotoxicity. ***Erlotinib, Iloprost, Pentoxifylline, Sibutramine. Venlafaxine*** Possible increased risk of bleeding. ***Phenytoin*** NSAID possibly enhance effects of phenytoin ***Ritonavir*** Plasma concentration of NSAIDs possibly increased by ritonavir. ***Zidovudine*** Increased risk of haematological toxicity when NSAIDs given with zidovudine.
4.6	**Usage in pregnancy& Lactation** **Pregnancy** In late pregnancy as with other NSAID, Diclofenac Gel should be avoided because it will cause permanent closure of ductus arteriosus. **Lactation** It is not known whether topical Diclofenac is excreted in human breast milk; however studies in animals detected Diclofenac In milk after oral administration. The decision should be made whether to discontinue nursing or the drug, taking in account the importance of the drug to the mother. The product should not be given during lactation.

4.7	**Effects on ability to drive and operate machine:** Not known
4.8	**Undesirable effects:** Most common adverse reactions are the site reactions including rash, skin eruptions, urticaria or other hypersensitivity reactions.
4.9	**Overdose and special antidotes :** The low systemic absorption of topical Diclofenac makes an overdose very unlikely. • However, undesirable effects, similar to those observed following an overdose of Voveran tablets, can be expected if Diclofenac Gel is inadvertently ingested (1 tube of 100 g contains the equivalent of 1,000 mg Diclofenac Sodium). In such cases, gastric lavage is recommended as first line of action. In addition to supportive measures, the use of oral activated charcoal may help to reduce the absorption of Diclofenac.
5	**Pharmacological Properties:**
5.1	Pharmacodynamic Properties: **Pharmacotherapeutic Group (ATC Code) :** D07817 The mechanism of action of Diclofenac is similar to that of other Non-Steroidal Anti-Inflamatory Drugs. Diclofenac inhibits the enzyme, cyclooxygenase (COX), an early component of the arachidonic acid cascade, resulting in the reduced formation of prostaglandins, thromboxanes and prostacylin. It is not completely understood hoe reduced synthesis of these compounds results in therapeutic efficacy.
5.2	**Pharmacokinetic Properties:** Systemic exposure (area under the concentration-time curve) and maximum plasma concentrations of Diclofenac are significantly lower with Diclofenac Gel than with comparable oral treatment of Diclofenac sodium. Systemic exposure with recommended use of Diclofenac Gel (4 x 4 g per day applied to 1 knee) is on average 17 times lower than with oral treatment. The amount of Diclofenac diethylamine that is systemically absorbed from Diclofenac Gel is on average 6% of the systemic exposure from an oral form of diclofenac sodium. The average peak plasma concentration with recommended use of Diclofenac Gel (4 x 4 g per day applied to 1 knee) is 158 times lower than with the oral treatment. The pharmacokinetics of Diclofenac Gel has been tested under conditions of moderate heat (application of a heat patch for 15 minutes prior to gel application) and of moderate exercise (first gel application followed by a 20-minute treadmill exercise). No clinically relevant differences of systemic absorption and of tolerability were found between applications of Diclofenac Gel (4 x 4 g per day on 1 knee) with and under the conditions of moderate heat or exercise.
5.3	**Preclinical Safety Data :** Diclofenac is a well established product. 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. There was no evidence that diclofenac had a teratogenic potential in mice, rats or rabbits. Diclofenac had no influence on the fertility of parent animals in rats. The prenatal, perinatal and postnatal development of the offspring was not affected. Topical Diclofenac Gel was found to be well tolerated and safe. There was no potential risk of phototoxicity and skin sensitization

6.	**Pharmaceuticals Particulars:**
6.1	**List of Excipients:** Methyl Paraben BP Propyl Paraben BP Phenoxyethanol BP Tocopheryl Phosphate Hydrolysate (TPM) IH Isopropyl Alcohol BP Butylated Hydroxy Toluene BP Sepineo P 600 IH Sodium Hydroxide BP Lavender Perfume IH Purified Water BP
6.2	**Incompatibilities:** Not Applicable
6.3	**Shelf life:** 24 Months
6.4	**Special precautions for storage:** Store below 30°C. Protect from light. Do not allow to freeze.
6.5	**Nature and contents of container:** 30 g of Diclofenac Gel BP 1% w/w is packed in a laminated tube in a carton along with pack insert..
6.6	**Special precaution for disposal :** Not Applicable
7	**Registrant:** **Marketing Authorisation Holder:** **M/s PHILLIPS PHARMACEUTICALS (NIGERIA) LTD.** Address : Afprint Industrial Estate, Plot 122-132, Apapa Oshodi Expressway Lagos. Country : Nigeria. Telephone : +234 806761764 Fax : --- E-mail : --- **Manufacturing Site Address:** **M/s THEMIS MEDICARE LIMITED** Address : Sector 6 A, Plot No. 16,17& 18, IIE SIDCUL,HARIDWAR-249 403, Uttarakhand Country : India Telephone : 91-1334-239322/21 Telefax : 91-1334-239217 E-Mail : hwdgmtech@themismedicare.com
8	**Date of Revision of the Text:** Not Applicable
9	**Dosimetry (if applicable):** Not Applicable
10	**Instruction for preparations of Radiopharmaceutical (if applicable):** Not Applicable