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: Aceclofenac Injection 150 mg/ml</td></tr>
<tr><td>1.2</td><td>Strength : 150 mg/ml</td></tr>
<tr><td>1.3</td><td>Pharmaceutical Form: Injection</td></tr>
<tr><td>2</td><td>Qualitative and Quantitative Compositions:</td></tr>
<tr><td></td><td>Qualitative Declaration:
Active component
INN Name: Aceclofenac BP
Quantitative Declaration:
Each ml contains:
Aceclofenac BP …….150 mg

<table>
<tr><th>Sr. No.</th><th>Content Name</th><th>Quality Standard</th><th>Qty per ml</th></tr>
<tr><td>1</td><td>Aceclofenac</td><td>BP</td><td>150.00 mg</td></tr>
<tr><td>2</td><td>TCLS-101</td><td>IH</td><td>50.00 mg</td></tr>
<tr><td>3</td><td>Diethylene Glycol Monoethyl Ether (Transcutol-P)</td><td>BP</td><td>qs to 1.00 ml</td></tr>
</table>

IH- In-house Specification
BP- British Pharmacopoeia</td></tr>
<tr><td>3</td><td>Pharmaceutical Form: Injection
Clear colourless to yellow coloured solution.</td></tr>
<tr><td>4</td><td>Clinical Particulars:</td></tr>
<tr><td>4.1</td><td>Therapeutic Indications:

It is indicated for the short term treatment of pain due to post operative and post-traumatic cases.</td></tr>
<tr><td>4.2</td><td>Posology and Method of Administration

Adults: 1 ml deep intragluteal injection (150 mg) once or twice daily, based on medical prescription in the upper outer quadrant.
Administration of Aceclofenac injection for more than two days is not recommended. If longer-lasting analgesic or anti-inflammatory treatment is required, the use of other pharmaceutical forms of Aceclofenac is advised.
Aceclofenac injection must not be combined with any other pharmaceutical form of Aceclofenac.
Method of administration: Intramuscular</td></tr>
</table>

4.3	**Contra-indications:** • Must not be administered to patients with known hypersensitivity to any of the excipients of the medicinal product. • Must not be administered to patients with antecedents of intestinal hemorrhage, or active or suspected active peptic ulcer. • Must not be administered to patients with severe renal impairment. • Must not be prescribed during pregnancy and lactation, nor to women planning pregnancy. Must not be administered to patients in whom the administration of acetylsalicylic acid or of other NSAIDs precipitate attacks of asthma, acute rhinitis or urticaria, or to patients with known hypersensitivity to these drugs.
4.4	**Special warning and precautions for use:** **WARNINGS:** Close medical surveillance is imperative in patients with symptoms indicative of gastro-intestinal disorders, with a history suggestive of gastro-intestinal ulceration, with ulcerative colitis or with Crohn's disease, bleeding diathesis or haematological abnormalities. Gastro-intestinal bleeding or ulcerative perforation, haematemesis and melaena have in general more serious consequences in the elderly. They can occur at any time during treatment, with or without warning symptoms or a previous history. In these rare instances, the drug should be withdrawn. Patients with severe hepatic impairment must suitably monitor their analytical parameters for hepatic function and must initiate treatment with 150 mg once daily. As with other NSAIDs allergic reactions including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug. Injection should not be used in children. **PRECAUTIONS:** The importance of prostaglandins in maintaining renal blood flow should be taken into account in patients with impaired cardiac or mild renal function, elderly, those being treated with diuretics or recovering from major surgery. The lowest effective dose should be used and renal function monitored regularly. Effects on renal function are usually reversible on withdrawal of injection. If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), aceclofenac should be discontinued. Hepatitis may occur without prodromal symptoms therefore, three-monthly hepatic function controls are recommended in long term treatments. Must be co-administered with caution with the following medications: lithium, digoxin, anticoagulants, oral anti-diabetic agents or other anti-inflammatory agents, as they could increase the frequency of adverse reactions. It could be necessary to adjust the dose of injection or these medications. Use in patients with hepatic porphyria may trigger an attack. Aceclofenac may reversibly inhibit platelet aggregation.
4.5	**Interaction with other drugs, other forms of interactions:** **Interaction with other drugs, other forms of interactions:** **Lithium and digoxin:** Injection**,** like many NSAIDs, may increase plasma concentrations of lithium and digoxin.

	Diuretics Studies in animals indicate the possibility that Injection**,** like other NSAIDs, could interfere with the natriuretic action of diuretics. This property could be of clinical significance in hypertensive patients or those with impaired heart function. Although Injection was found not to have any effects on blood pressure control when administered with bendrofluazide, interaction with other antihypertensive agents cannot be ruled out. **Anticoagulants:** Like other non-steroid anti-inflammatory drugs, Injection could increase the activity of anticoagulants due to a possible inhibitory action on platelet aggregation. Patients treated simultaneously with anticoagulants and Injection must be suitably monitored. **Oral anti-diabetic agents:** The possibility of adjusting the dose of hypoglycaemic agents should be taken into account when administering Injection **Methotrexate:** Caution should be exercised if NSAIDs and methotrexate are administered within 24 hours of each other, since NSAIDs may increase methotrexate plasma levels, resulting in increased toxicity. **Other NSAIDs:** Concomitant therapy with acetylsalicylic acid and other NSAIDs may increase the frequency of side effects (See section warnings and precautions for use). **Cyclosporin:** Cyclosporin nephrotoxicity may be increased by the effect of NSAIDs on renal prostaglandins.
4.6	**Usage in pregnancy& Lactation** The use of Injection during pregnancy or lactation is contraindicated **Pregnancy** There is no information on the use of Injection during pregnancy. The regular use of NSAIDs during the last trimester of pregnancy may decrease uterine tone and contraction. NSAIDs use may result in premature closure of the foetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the new born, delay onset and increase duration of labour. Epidemiological studies in humans have not evidenced embryotoxic effects of NSAIDs. However, in a study using rabbits, treatment with aceclofenac (10 mg/kg/day) caused a series of morphological alterations in some foetes. There was no evidence of teratogenesis in rats. **Lactation** Injection should not be given during lactation. There is no information on the secretion of Injection to breast milk; there was however no notable transfer of radio-labelled (^{14}C) aceclofenac to the milk of lactating rat.
4.7	**Effects on ability to drive and operate machine:** Patients suffering from dizziness, vertigo, or other central nervous system disorders should refrain from driving or handling dangerous machinery while taking non-steroidal anti-inflammatory drugs.
4.8	**Undesirable effects:** The majority of Undesirable effects observed have been reversible and of a minor nature and include gastro-intestinal disorders (dyspepsia, abdominal pain, nausea and diarrhoea) and occasional occurrence of dizziness. Dermatological complaints including pruritus, rash, abnormal hepatic enzyme levels and raised serum creatinine have occasionally been reported.

	If serious adverse reactions occur, **Injection** should be withdrawn. The following adverse reactions were notified, and are representative of all clinical trials and post-marketing experience. They appear listed under organic systems and frequency: very frequent >10%, frequent 1-10%, occasional 0.1-1%, rare or very rare cases <0.1%. **Gastro-intestinal system disorders:** Frequent: Dyspepsia (7.5%), abdominal pain (6.2%), nausea (1.5%), diarrhoea (1.5%). Occasional: Flatulence (0.8%), gastritis (0.6%), constipation (0.5%), vomiting (0.5%), ulcerative stomatitis (0.1%). Rare cases: pancreatitis, melaena, stomatitis. **Central and peripheral nervous system:** Occasional: Dizziness (1%), vertigo (0.3%). Rare cases: paraesthesia, tremor. **Psychiatric:** **Rare cases:** Depression, abnormal dreaming, somnolence, insomnia. **Skin and appendages:** **Occasional:** Pruritus (0.9%), rash (0.5%), dermatitis (0.2%). Rare cases: eczema. **Liver and biliary:** **Frequent:** Hepatic enzymes increased (2.5%). **Metabolic: Occasional:** BUN increased (0.4%), blood creatinine increased (0.3%). Rare cases: alkaline phosphatase increased, hyperkalaemia. **Cardiovascular:** **Rare cases:** Odema (dependent), palpitation, cramps legs, flushing, purpura. **Respiratory:** **Rare cases:** Dyspnoea, stridor. **Blood:** **Rare cases:** Anaemia, granulocytopenia, thrombocytopenia. **Urinary system:** **Rare cases:** Nephrotic syndrome. **Body as a whole, general:** **Rare cases:** Headache, fatigue, face oedema, hot flushes, allergic reactions, weight increase, anaphylactic shock. **Others:** **Rare cases:** Abnormal vision, abnormal taste.
4.9	**Overdose and special antidotes :** Management of acute poisoning with NSAIDs essentially consists of supportive and symptomatic measures. Given this pharmaceutical form of administration, it is very difficult an over dosage by this route.
5	**Pharmacological Properties:**
5.1	**Pharmacodynamic Properties:** Aceclofenac injection is a non-steroidal agent with marked anti-inflammatory and analgesic properties. The mode of action of Aceclofenac injection is based on the decrease in production of prostaglandins, which are the main substances involved in the process of inflammation by inhibition of the enzyme cyclo-oxygenase.
5.2	**Pharmacokinetic Properties:** After parenteral administration, Injection is rapidly and completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 15 to 30 minutes after administration. The maximum concentration that reaches after administration of 150 mg

	Injection is 5.3mcg/ml. Protein binding of Injection is 99%, the volume of distribution is approximately 25L and the mean plasma elimination half-life is around 5 hours. Injection undergoes hepatic metabolism, being 4'- hydroxyaceclofenac the main metabolite. Approximately two-thirds of the administered dose is excreted via urine, mainly as hydroxymetabolites. No changes in the pharmacokinetics of Injection have been detected in elderly. Pharmacokinetic studies showed that Tmax value for Aceclofenac Injection 150 mg by intramuscular route was lower than Aceclofenac tablets 100 mg and Cmax value was similar to the reference oral route. However, AUC value for Aceclofenac injection 150 mg by intramuscular route was higher than Aceclofenac tablets 100 mg. That profile gave special properties to intramuscular route, which means an analgesic activity was faster than the oral route with long-lasting therapeutic effect.
5.3	**Preclinical Safety Data :** In sub acute toxicity of Aceclofenac conducted in Albino Rats shows no mortality and signs of toxicity at different dose levels in any of the treatment groups. Hematological as well as biochemical parameters were unaffected at three different dose levels of aceclofenac sustain release injection. Aceclofenac was not considered to have any mutagenic activity in three *in vitro* studies and an *in vivo* study in the mouse. Aceclofenac was not found to be carcinogenic in either the mouse or rat. Animal studies indicate that there was no evidence of teratogenesis in rats although the systemic exposure was low and in rabbits, treatment with aceclofenac (10 mg/kg/day) resulted in a series of morphological changes in some fetuses.
6.	**Pharmaceuticals Particulars:**
6.1	**List of Excipients:** TCLS-101 IH Diethylene Glycol Monoethyl Ether BP (Transcutol P)
6.2	**Incompatibilities:** Not Applicable
6.3	**Shelf life:** 24 Months
6.4	**Special precautions for storage:** Store below 30°C. Protect from light.
6.5	**Nature and contents of container:** Aceclofenac Injection 150 mg/ml is packed in 1ml amber colour glass ampoule with white ring. 5 such ampoules available in tray packed in a carton 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 : ---

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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