SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1.3.1 Summary of product characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT:

ARTEMIS-DEXAMETHASONE TABLETS 1mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Composition:

Each uncoated tablet contains:

Dexamethasone B.P. ---------1mg

List of excipients:

Aerosil 200, Purified talc, Magnesium stearate, Methyl paraben , Propyl paraben, Dicalcium phosphate, cross carmellose sodium and sodium starch glycolate.

{For a full list of excipients, see section 6.1}

3. PHARMACEUTICAL FORM:

A white round, concave, uncoated tablet, 7.93mm diameter. Plain on both sides.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications:

Dexamis 1mg Tablet

Orally: Palliative treatment of rheumatoid arthritis, rheumatic spondylitis osteoarthritis, polyarthritis, chronic psoriatic arthritis, bursitis, tendinitis, synovitis, fibrositis, mucositis, neuritis, bronchial asthma, rheumatic fever, addition's disease, Waterhouse Friedrichsens' syndrome allergies, serum sickness, drug sensitivity.

4.2 Posology and Method of Administration:

Posology

In general, glucocorticoid dosage depends on the severity of the condition and response of the patient. Under certain circumstances, for instance in stress and changed clinical picture, extra dosage adjustments may be necessary. If no favourable response is noted within a couple of days, glucocorticoid therapy should be discontinued.

Adults

Usually, daily oral dosages of 0.5 - 10 mg are sufficient. In some patients higher dosages may be temporarily required to control the disease. Once the disease is under control the dosage should be reduced or tapered off to the lowest suitable level under continuous monitoring and observation of the patient. **(See Section 4.4)**

For a short dexamethasone suppression test, 1mg dexamethasone is given at 11 p.m. and plasma cortisol measured the next morning. Patients who do not show a decrease in cortisol can be exposed to a longer test: 500 micrograms dexamethasone is given at 6 hourly intervals for 48 hours followed by 2mg every 6 hours for a further 48 hours. 24 hour-urine collections are made before, during and at the end of the test for determination of 17-hydroxycorticosteroids.

Paediatric population
0.01-0.1mg/kg of body weight daily.
Dosage of glucocorticoids should be adjusted on the basis of the individual patient's response.

4.3 Contraindications
Systemic infection unless specific anti-infective therapy is employed.
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Avoid live vaccines in patients receiving immunosuppressive doses (serum antibody response diminished).
In general no contraindications apply in conditions where the use of glucocorticoids may be lifesaving.

4.4 Special warnings and precautions for use
A patient information leaflet should be supplied with this product.
In post-marketing experience tumour lysis syndrome (TLS) has been reported in patients with haematological malignancies following the use of dexamethasone alone or in combination with other chemotherapeutic agents. Patients at high risk of TLS such as patients with high proliferative rate, high tumour burden, and high sensitivity to cytotoxic agents, should be monitored closely and appropriate precaution taken.
Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 for pharmacokinetic interactions that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.
Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.
The results of a randomised, placebo-controlled study suggest an increase in mortality if methylprednisolone therapy starts more than two weeks after the onset of Acute Respiratory Distress Syndrome (ARDS). Therefore, treatment of ARDS with corticosteroids should be initiated within the first two weeks of onset of ARDS (see also section 4.2.).
Preterm neonates:
Available evidence suggests long-term neurodevelopmental adverse events after early treatment (<96 hours) of premature infants with chronic lung disease at starting doses of 0.25 mg/kg twice daily.
Undesirable effects may be minimised by using the lowest effective dose for the minimum period, and by administering the daily requirement as a single morning dose or whenever possible as a single morning dose on alternative days. Frequent patient review is required to appropriately titrate the dose against disease activity.
Dexamethasone withdrawal
Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must

therefore always be gradual to avoid acute adrenal insufficiency, being tapered off over weeks or months according to the dose and duration of treatment.
In patients who have received more than physiological doses of systemic corticosteroids (approximately 1mg dexamethasone) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids but there is uncertainty about HPA suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose of 1mg dexamethasone is reached, dose reduction should be slower to allow the HPA-axis to recover.
Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses of up to 6mg daily of dexamethasone for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression in the majority of patients. In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:

- Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks.
- When a short course has been prescribed within one year of cessation of long-term therapy (months or years).
- Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy.
- Patients receiving doses of systemic corticosteroid greater than 6mg daily of dexamethasone.
- Patients repeatedly taking doses in the evening.

During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.
Patients should carry 'Steroid treatment' cards which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the duration of treatment.
Anti-inflammatory/Immunosuppressive effects and Infection
Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical, and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.
Appropriate anti-microbial therapy should accompany glucocorticoid therapy when necessary e.g. in tuberculosis and viral and fungal infections of the eye.
Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunisation with varicella zoster immunoglobulin (VZIG) is needed by exposed nonimmune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.
Measles. Patients should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs; prophylaxis with intramuscular normal immunoglobulin may be needed.

Visual disturbance
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.
Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary

a. Osteoporosis (post-menopausal females are particularly at risk)
b. Hypertension or congestive heart failure
c. Existing or previous history of severe affective disorders (especially previous steroid psychosis)
d. Diabetes mellitus (or a family history of diabetes)
e. History of tuberculosis
f. Glaucoma (or a family history of glaucoma)
g. Previous corticosteroid-induced myopathy
h. Liver failure
i. Renal insufficiency
j. Hypothyroidism
k. Epilepsy
l. Peptic ulceration
m. Migraine
n. Certain parasitic infestations in particular amoebiasis
o. Incomplete natural growth since glucocorticoids on prolonged administration may accelerate epiphyseal closure.

Caution should be exercised when using corticosteroids in patients who have recently suffered myocardial infarction as myocardial rupture has been reported.
After administration of glucocorticoids serious anaphylactoid reactions such as glottis oedema, urticaria and bronchospasm have occasionally occurred particularly in patients with a history of allergy.
If such an anaphylactoid reaction occurs, the following measures are recommended: immediate slow intravenous injection of 0.1-0.5ml of adrenaline (solution of 1:1000: 0.1-1mgadrenaline dependent on body weight), intravenous administration of aminophylline and artificial respiration if necessary.
Paediatric population
Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible.
Use in the Elderly
The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

4.5 Drug interactions:
Dexamethasone may decrease or increase plasma concentrations of phenytoin. Like other enzyme including drugs, phenytoin also has the potential to increase the metabolism of dexamethasone Risk of GIT bleeding and ulceration associated with dexamethasone is increase when used with aspirin.
Concurrent use of barbiturates, carbamazepine, phenytoin, primidone or rifampicin may enhance the metabolism and reduce the effects of systemic corticosteroids. Conversely oral contraceptives or ritonavir may increase plasma concentrations of corticosteroids. Use of corticosteroids with potassium-depleting diuretics, such as thiazides or

furosemide, may cause excessive potassium loss. There is also an increased risk of hyperkalaemia with concurrent amphotericin 8 with xanthines or beta agonists.

4.6 Pregnancy & Lactation:
Dexamethasone is only recommended for use during pregnancy when there are no alternatives and benefit outweighs risk.

There are no data on the excretion of dexamethasone into human milk. Some corticosteroids are excreted into human milk in small amounts.
The manufacturer recommends that due to the potential for serious adverse reactions in nursing infants, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Dexamis 1mg Tablet has no influence on the ability to drive and use machines. Even No such studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects:
Undesirable effects of Dexamethasone may lead to erosion of calcium and phosphorous with osteoporosis and spontaneous fractures. Muscle wasting and nitrogen depletion may also occur. Hyperglycemia leading to accentuation or precipitation of diabetic state may arise. Impaired tissue repair can lead to delayed wound healing and increased susceptibility to infection.
Menstrual irregularities, amenorrhea, hyperhydrosis, skin thinning ocular changes including glaucoma and cataract may occur. Mental and neurological disturbances have been reported.

4.9 Over dosage:
Consult with your physician or pharmacist immediately.

Contra indications:
Hypersensitivity, active untreated infections, Tuberculosis, divertculitis chickenpox thrombophlebitis, fresh intestinal anastomoses, osteoporosis, peptic ulcer, psychotic tendencies, cushing's syndrome, vaeeina and varicella.

Warning:
To be used only as per the dosage directed by the physician.
Storage:
Store in a cool and dry place, not above 30°C. Keep out of the reach of children.

5 PHARMACOLOGICAL PROPERTIES:
5.1 Pharmacological actions:
Glucocorticoid, Corticosteroid: Ocular anti-inflammatory drug; Topical corticosteroid.
Dexamethasone has much less tendency to produce salt and water retention, potassium, depletion, edema, anorexia or psychic disturbances.

5.2 **Pharmacokinetics:**
It is readily absorbed from the GIT and it is rapidly distributed to all body tissues. It crosses the placenta to varying degrees and may be distributed in small amounts into breast milk. Most corticosteroids in the circulation are extensively bound to plasma proteins, mainly to globulin and less so to albumin. The corticosteroid - binding globulin has high affinity but low binding capacity, while albumin has low affiinity but large binding capacity.

Carticosteroids are metabolized mainly in the liver but also in other tissues, and are excreted in the urine. Its biological half-life in plasma is about 190 minutes binding of plasma proteins is about 77%, which is less than for most other corticosteroids. Up to 65% of a dose is excreted in urine within 24 hours.

5.3 Preclinical Safety Data:

Although clinical investigations have shown that Dexamethasone produces less undesirable effects than other corticosteroids, it should be borne in mind that Dexamethasone is an extremely potent product, and that therapeutic doses will, after administration over longer periods, effect some depression on the function of the adrenal cortex. The precautions for other corticosteroids should therefore be followed, and it may be necessary to institute rest periods and to stimulate adrenocortical function by use of ACTH.

If signs of infection are present, or if an infection is suspected, Dexamethasone should be administered in conjunction with adequate antibacterial therapy.

On cessation of therapy the drug should not be stopped abruptly, but should be withdrawn gradually.

Special precaution:

Patients with hypothyroidism; cirrhosis, hypertension, CHF, ulcerative colitis, thromboembolic disorders, osteoporosis, glaucoma, cataracts or TB of the eye, diabetes, peptic ulcer. Monitor blood glucose levels in diabetics and coagulation indices in patients on warfarin. Elderly, children and adolescent; pregnancy and lactation.

6.PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients

Aerosil,
Maize Starch,
Methyl Paraben,
Propyl Paraben,
Magnesium Stearate,
Purified Talc,
Di Calcium Phosphate,
Cross carmellose sodium,
Sodium starch glycolate

6.2 Incompatibilities

None known

6.3 Shelf life:

3 years.

6.4 Special precautions for storage

Store in a cool and dry place, not above 30°C.

6.5 Nature and contents of container

Dexamethasone 1mg in blister packs (Transparent PVC-aluminium)
10 tablets in blister pack
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Manufactured by:
Artemis Laboratories Ltd
Plot 4, Block 4, OGSHC &
Industrial Estate, OTA, Ogun State,
Nigeria.