1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

BETANOID SYRUP 0,60 mg /5 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of BETANOID SYRUP contains 0,60 mg of betamethasone (equivalent in anti-inflammatory activity to about 5 mg prednisolone).

Preservative: Sodium benzoate 0,15 % *m/v*

Contains sugar: Glucose 1,5 g and sucrose 0,625 g

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup

BETANOID SYRUP is a clear orange syrup with a fruity flavour.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

BETANOID SYRUP is indicated for :

- Symptomatic treatment of inflammatory conditions where a steroid is indicated.

4.2. Posology and method of administration

Dosing requirements are variable and must be individualised on the basis of the specific disease, its severity and the response of the patient.

Posology

Betamethasone has a usual dose range of 0,6 mg to 4,8 mg daily in divided doses (5 ml to 40 ml BETANOID SYRUP) depending on the specific disease being treated.

In situations of less severity, low doses generally will suffice while in selected patients higher initial doses may be required.

The initial dose should be maintained or adjusted until a satisfactory response is observed.

If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.

Once a day dosage:

The total daily maintenance dose can be administered once early in the morning.

Paediatric population

Dosage for infants and children should be governed by the same considerations as adults, rather than strict adherence to ratios indicated by age or body weight.

Method of administration

For oral administration.

4.3. Contraindications

BETANOID SYRUP is contraindicated in:

- Patients with hypersensitivity to betamethasone or to any excipients in BETANOID SYRUP (see section 6.1).
- Patients sensitive to other corticosteroids.
- Patients with systemic fungal infections.
- Patients with peptic ulceration, osteoporosis, psychosis or severe psychoneuroses.
- Patients with active or doubtfully quiescent tuberculosis, except, very rarely, as adjuncts to treatment with anti-tubercular medicine.
- The presence of acute viral infections including herpes zoster or herpes simplex ulceration of the eye.
- Vaccination with live vaccines.

The safety of BETANOID SYRUP use during pregnancy and in nursing mothers has not been established.

4.4. Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the minimum period.

Frequent patient review is required to appropriately titrate the dose against disease activity.

Myocardial infarction

Caution is advised with the use of corticosteroids in patients who have suffered a recent myocardial infarction because of the risk of myocardial rupture.

Hypothyroidism and myasthenia gravis

Caution is advised on the use of corticosteroids, such as BETANOID SYRUP, in patients with hypothyroidism or myasthenia gravis.

Suppression of the inflammatory response and immune function

BETANOID SYRUP may mask some signs of infection.

Suppression of the inflammatory response and immune function increases the susceptibility to all kinds of infection, including sepsis and fungal 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.

Infectious diseases

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 non-immune 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, such as BETANOID SYRUP, should not be stopped and the dose may need to be increased.

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.

Adrenal suppression:

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment.

In patients who have received more than physiological doses of systemic corticosteroids (approximately 1 mg betamethasone or equivalent) 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 a 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 hypothalamic-pituitary-adrenal (HPA) suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose equivalent to 1 mg betamethasone, as in BETANOID SYRUP, 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 6 mg daily of betamethasone, or equivalent 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 have reasons for adrenocortical insufficiency other than exogenous corticosteroids therapy,
- Patients receiving doses of systemic corticosteroid greater than 6 mg daily of betamethasone, as on BETANOID SYRUP (or equivalent),
- 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, as in BETANOID SYRUP, have been stopped following prolonged therapy they may need to be temporarily reintroduced.

Special precautions

Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

- Post-menopausal females as they are at particular risk of osteoporosis.
- Hypertension or congestive heart failure.
- Diabetes mellitus (or a family history of diabetes).
- History of tuberculosis.
- Glaucoma (or a family history of glaucoma).
- Previous corticosteroid-induced myopathy.
- Liver failure - blood levels of corticosteroid may be increased, (as with other medicines which are metabolised in the liver).
- Renal insufficiency, uraemia, chronic renal failure.
- Epilepsy.
- Elderly persons.
- Diverticulitis.
- Thromboembolic tendencies.

Psychiatric disturbances

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 treatment. Risks may be higher with high doses/systemic exposure, 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.

Pheochromocytoma Crisis

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids, as in BETANOID SYRUP.

Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

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.

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.

Diabetic patients

The insulin requirements of diabetic patients are increased.

Sodium intake

Sodium intake may need to be reduced and potassium supplements may be necessary.

Paediatric population

Caution is advised in children as they are more susceptible to systemic toxicity from betamethasone, as in BETANOID SYRUP.

Corticosteroids, as in BETANOID SYRUP, cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time. In order to minimise suppression of the HPA axis and growth retardation, consideration should be given to administration of a single dose on alternate days.

Excipients

Sucrose/Glucose warning:

BETANOID SYRUP contains sucrose and glucose.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5. Interaction with other medicines and other forms of interaction

Steroids may reduce the effects of anticholinesterases in myasthenia gravis, cholecystographic X-ray media and non- steroidal anti-inflammatory medicines.

Hepatic enzyme inducers (e.g., aminoglutethemide, barbiturates, phenytoin, carbamazepine, primidone, rifabutin, rifampicin):

Concurrent administration of barbiturates(phenobarbitone), phenytoin or rifampicin, rifabutin, carbamazepine, primidone, aminoglutethimide and ephedrine may enhance the metabolism of corticosteroids and reduce the effects of BETANOID SYRUP.

Hypoglycaemic medicines, antihypertensives and diuretics

The desired effects of hypoglycaemic medicines (including insulin), antihypertensives and diuretics are antagonised by corticosteroids, and the hypokalaemic effects of acetazolamide, diuretics, thiazides or furosemide are enhanced.

Coumarin anticoagulants

The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

Salicylates

The renal clearance of salicylates is increased by corticosteroids, as in BETANOID SYRUP, and steroid withdrawal may result in salicylate intoxication.

Theophylline, carbenoxolone, amphotericin B

The risk of hypokalaemia is increased with theophylline, ulcer healing medicines such as carbenoxolone and antifungals such as amphotericin B.

Cardiac glycosides

Increased toxicity may result if hypokalaemia occurs in patients on cardiac glycosides.

Ritonavir and oral contraceptives

Ritonavir and oral contraceptives may result in increased plasma concentrations of corticosteroids, as in BETANOID SYRUP.

Mifepristone

The effect of corticosteroids, as in BETANOID SYRUP, may be reduced for 3-4 days after mifepristone.

Somatropin

The growth promoting effect of somatropin may be inhibited by corticosteroids as in BETANOID SYRUP.

Non-steroidal anti-inflammatory drugs (NSAIDs)

An increase in the incidence of gastrointestinal bleeding may occur if NSAIDs are taken concomitantly with corticosteroids, as in BETANOID SYRUP.

Vecuronium

Corticosteroids, as in BETANOID SYRUP, may antagonise the effects of neuromuscular blocking medicines such as vecuronium.

Fluoroquinolones

Concurrent use of corticosteroids, as in BETANOID SYRUP, and fluoroquinolones may result in increased risk of tendon rupture.

Quetiapine

Concomitant use of betamethasone, as in BETANOID SYRUP, with quetiapine may result in the increased metabolism of quetiapine and, depending on the clinical response, a higher dose of quetiapine may need to be considered.

CYP3A inhibitors

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

Tretinoin

Corticosteroids may enhance the metabolism of tretinoin resulting in decreased levels of tretinoin.

4.6. Fertility, pregnancy and lactation

The safety of the use of BETANOID SYRUP during pregnancy and in nursing mothers has not been established (see section 4.3).

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual medicines, however, betamethasone, as in BETANOID SYRUP, readily crosses the placenta.
Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development.
There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intrauterine growth retardation.
Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important.

Myocardial hypertrophy and gastroesophageal reflux have been reported in association with in-utero exposure to betamethasone, as in BETANOID SYRUP.

Betamethasone, as in BETANOID SYRUP, systemically administered to a woman during pregnancy may result in a transient suppression of the foetal heart rate parameters and biophysical activities that are widely used for the assessment of foetal well – being. These characteristics can include a reduction in foetal breathing movements, body movements and heart rate.

Breastfeeding

Corticosteroids may pass into breast milk, although no data are available for betamethasone, as in BETANOID SYRUP. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression**.**

Fertility

There are no data in humans to evaluate the effect of corticosteroids on fertility.

4.7. Effects on ability to drive and use machines

BETANOID SYRUP has minor influence the ability to drive or operate machinery.

Since adverse reactions such as blurred vision have been reported in patients receiving, betamethasone, as in, BETANOID SYRUP, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that BETANOID SYRUP does not adversely affect their ability to do so.

4.8. Undesirable effects

a) Tabulated list of adverse reactions

System organ class	Frequent	Less frequent	Frequency unknown
Infections and infestations			Increased susceptibility and severity of

			infections with suppression of clinical symptoms and signs (masking of infections), opportunistic infections, recurrence of dormant tuberculosis
Blood and the lymphatic system disorders			Leucocytosis
Immune system disorders			Hypersensitivity including anaphylaxis has been reported
Endocrine disorders			Cushings syndrome (moon face, buffalo hump, hirsutism, weight gain, flushing), suppression of the HPA axis, suppression of growth in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea.
Metabolism and nutrition disorders	Hypokalaemia		Hyperglycaemia with precipitation of the diabetic state, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy* sodium retention, fluid retention with oedema hypokalaemic alkalosis
Psychiatric disorders	A wide range of psychiatric reactions**		
Nervous system disorders			Intracranial hypertension, neurological disturbances
Eye disorders			Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases (see section 4.4) vision, blurred (see also section 4.4)
Cardiac disorders			Myocardial rupture following recent myocardial infarction

			cardiac failure in extreme cases
Vascular disorders			Thromboembolism hypertension, thrombo-embolic complications
Gastrointestinal disorders			Abdominal distension, oesophageal ulceration, nausea, dyspepsia, peptic ulceration with perforation and haemorrhage acute pancreatitis, candidiasis gastric discomfort, hiccups
Skin and subcutaneous tissue disorders			Impaired healing, skin atrophy, increased bruising, acne, telangiectasia, striae, Stevens-Johnson syndrome.
Musculoskeletal, connective tissue and bone disorders			Aseptic necrosis of bone, proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, spontaneous fractures.
General disorders and administrative site conditions			Hyperhidrosis, malaise
Investigations			Nitrogen depletion.

* Negative protein, nitrogen and calcium balance. Increased appetite. Hyperhidrosis. Increased high - density lipoprotein and low – density lipoprotein concentrations in the blood. Fluid and electrolyte disturbance (Sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis).

** Including affective disorder (such as irritable, euphoric, depressed and labile mood and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances and cognitive dysfunction including confusion and amnesia have been

reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to the

5-6 %. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown. Psychological dependence.

b) Description of selected adverse reactions

Acute adrenal insufficiency during prolonged treatment, or on cessation of treatment.

During long courses of corticosteroid therapy, patients should be seen regularly and checked for hypertension, glycosuria, hypokalaemia, gastric discomfort and mental changes.

Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal. Aggravation of epilepsy.

Withdrawal symptoms and signs

Too rapid reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4).

A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to: **SAHPRA** via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088 /+27 (0)11 239-6200

4.9. Overdose

Symptoms

Side effects can be precipitated and/or be of increased severity (see section 4.8)

Treatment

Treatment is symptomatic and supportive.

Treatment is unlikely to be needed in cases of acute over dosage**.**

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A 21.5.1: Corticosteroids and analogues

Pharmacotherapeutic group: Corticosteroids for systemic use, plain, Glucocorticoids,

ATC code: H02A B01

Betamethasone is a synthetic glucocorticoid analogue primarily used for its anti-inflammatory effects.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Citric acid monohydrate (for pH adjustment), colour spectoral sunset yellow (C.I. 15985), flavour passion fruit, flavour raspberry superb, glucose, propylene glycol, purified water, sodium benzoate, sodium chloride, sucrose.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 °C.

Protect from light.

Keep in original packaging until required for use.

6.5. Nature and contents of container

100 ml are packed into an amber polyvinyl chloride or glass bottle and sealed with a white screw-on polypropylene cap with or without an expanded polyethylene liner. The bottle is placed in an outer cardboard together with a leaflet.

500 ml are packed into an amber polyvinyl chloride bottle and sealed with a white screw-on cap with a polypropylene liner. The bottle is placed in an outer cardboard together with a leaflet.

Not all packs or pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

27/21.5.1/0491

9. DATE OF FIRST AUTHORISATION

30 April 1993

10. DATE OF REVISION OF TEXT

4 April 2024

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