1. Name of the drug product:

TALIDEXA (Dexamethasone Tablets BP 0.5 mg)

2. Qualitative and quantitative composition:
Each Uncoated Tablet Contains:
Dexamethasone BP….. 0.5 mg
Excipients……..…Q.S.

Sr. No.	Ingredients	Specifi-cation	Label Claim / Tablet (In mg)	Over-ages added (In %)	Qty. / Tablet (In mg)	Reason for Function
a)	**Dry Mixing**					
1.	Dexamethasone	BP	0.5	2.0%	0.510	Medicament
2.	Maize Starch	BP	NA	NA	12.040	Diluent
3.	Lactose Monohydrate	BP	NA	NA	98.950	Diluent
4.	Calcium Hydrogen Phosphate Dihydrate	BP	NA	NA	25.150	Diluent
b)	**Binder Preparation**					
5.	Maize Starch	BP	NA	NA	5.990	Binder
6.	Purified Water	BP	NA	NA	Q.S.	Vehicle
c)	**Lubrication**					
7.	Magnesium Stearate	BP	NA	NA	1.180	Lubricant
8.	Sodium Lauryl Sulfate	BP	NA	NA	1.180	Lubricant
	Average Weight of Uncoated Tablet (In mg)				**145.000**	

3. Pharmaceutical form: Uncoated tablet
Description: White coloured, oval shaped, biconvex, uncoated tablet breakline on one side and plain on other side.

4. Clinical Particulars

4.1 Therapeutic indications:
Neurology
Cerebral oedema caused by brain tumours, neurosurgery, bacterial meningitis, brain abscess.
Pulmonary and respiratory diseases
Severe acute asthma attack.
Dermatology
Oral initial treatment of extensive, severe, acute skin diseases that respond to glucocorticoids, such as erythroderma, pemphigus vulgaris, acute eczema.

Autoimmune disorders/rheumatology
Oral initial treatment of autoimmune diseases, such as systemic lupus erythematosus (especially visceral forms).
Severely progressive form of active rheumatoid arthritis, e.g. rapidly destructive forms and/or with extra-articular manifestations.

Infectology
Severe infections with toxic conditions (e.g. tuberculosis, typhoid) only with concomitant anti-infective therapy.
Oncology
Palliative treatment of malignant tumours.
Endocrinology
Congenital adrenogenital syndrome in adulthood.

4.2 Posology and method of administration
Posology
- Cerebral oedema due to bacterial meningitis: 0.15 mg/kg body weight every 6 hours for days, children: 0.4 mg/kg body weight every 12 hours for 2 days, starting before the first antibiotics.
- Severe acute asthma attack: Adults: 8–20 mg, then, if necessary, 8 mg every 4 hours. Children: 0.15–0.3 mg/kg body weight.
- Acute skin diseases: Depending on the nature and extent of the disease, daily doses of 8–40 mg. Followed by treatment with decreasing doses.
- Active phases of rheumatic systemic diseases: systemic lupus erythematosus 6–16 mg/day.
- Severely progressive form of active rheumatoid arthritis: in rapidly destructive forms 12–16 mg/day, in extra-articular manifestations 6–12 mg/day
- Severe infectious diseases, toxic states (e.g. tuberculosis, typhoid): 4–20 mg for a few days, only with concomitant anti-infective therapy.
- Palliative treatment of malignant tumours: initially 8–16 mg/day, in prolonged treatment 4–12 mg/day.
- Congenital adrenogenital syndrome in adulthood: 0.25–0.75 mg/day as a single dose. If necessary, addition of a mineralcorticoid (fludrocortisone). In cases of particular physical stress (e.g. trauma, surgery), intercurrent infections, etc., a 2- to 3-fold dose increase may be required and under extreme stress (e.g. birth) a 10-fold increase.

The tablets should not be split to adjust doses. If patients need a dose that cannot be provided by one or more tablets of 0.5mg, other appropriate formulations should be used.

Method of administration
The tablets should be taken during or after a meal. They should be swallowed whole, with a sufficient amount of liquid. The daily dose should be administered as a single dose in the morning, if possible (circadian therapy). In patients who require a high-dose therapy because of their disease, multiple daily dosing is often required to achieve maximum effect.

4.3 Contraindications
Contraindicated in systemic fungal infections and patients with known hypersensitivity to the product and its constituents.

4.4 Special warnings and precautions for use
Through immunosuppression, treatment with Dexamethasone can lead to an increased risk of bacterial, viral, parasitic, opportunistic and fungal infections. It can mask the symptoms of an existing or developing infection, thereby making a diagnosis more difficult. Latent infections, like tuberculosis or hepatitis B, can be reactivated.

Treatment with Dexamethasone should only be implemented in the event of the strongest indications and, if necessary, additional targeted anti-infective treatment administered for the following illnesses:
- Acute viral infections (Herpes zoster, Herpes simplex, Varicella, herpetic keratitis)
- HBsAG-positive chronic active hepatitis
- Approximately 8 weeks prior to 2 weeks after vaccinations with live vaccines

- Systemic mycoses and parasitoses (e.g. nematodes)
- In patients with suspected or confirmed strongyloidiasis (infection with threadworms), glucocorticoids can lead to activation and mass proliferation of these parasites
- Poliomyelitis
- Lymphadenitis after BCG vaccination
- Acute and chronic bacterial infections
- In a history of tuberculosis (reactivation risk), use only under tuberculostatic protection

In addition, treatment with Dexamethasone should only be implemented under strong indications and, if necessary, additional specific treatment must be implemented for:

- Gastrointestinal ulcers
- Osteoporosis
- Severe cardiac insufficiency
- High blood pressure that is difficult to regulate
- Diabetes mellitus that is difficult to regulate
- Psychiatric disorders (also in the past), including suicidality: neurological or psychiatric monitoring is recommended
- Narrow- and wide-angle glaucoma, ophthalmic monitoring and adjunctive therapy are recommended
- Corneal ulcerations and corneal injuries, ophthalmic monitoring and adjunctive therapy are recommended. Because of the risk of an intestinal perforation, Dexamethasone may only be used under urgent indication and under appropriate monitoring for:
- Severe ulcerative colitis with threatened perforation, possibly without peritoneal irritation
- Diverticulitis
- Enteroenterostomy (immediately postoperatively)

Signs of peritoneal irritation after gastrointestinal perforation may be absent in patients receiving high doses of glucocorticoids.

The possibility of a higher need for insulin or oral antidiabetics must be taken into consideration when administering Dexamethasone to diabetics.

Regular blood pressure monitoring is necessary during treatment with Dexamethasone, particularly during administration of higher doses and in patients with high blood pressure that is difficult to regulate.

Because of the risk of deterioration, patients with severe cardiac insufficiency should be carefully monitored.

With high doses of dexamethasone bradycardia may occur.

Severe anaphylactic reactions may occur.

The risk of tendon disorders, tendinitis and tendon rupture is increased when fluoroquinolones and glucocorticoids are administered together.

A concurrent myasthenia gravis may initially worsen during treatment with Dexamethasone.

Vaccinations with inactivated vaccines are generally possible. However, it should be noted that the immune response and thus the vaccine may be compromised at higher doses of corticosteroids.

During long-term therapy with Dexamethasone, regular medical checkups (including ophthalmologic every three months) are indicated.

At high doses, sufficient calcium intake and sodium restriction should be ensured and serum potassium levels should be monitored.

4.5 Interaction with other medicinal products and other forms of interaction

Rifampicin, rifabutin, carbamazepine, phenobartital, phenytoin, primidone, and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced.

Dexamethasone is a moderate inducer of CYP 3A4. Co-administration of dexamethasone with other drugs that are metabolized by CYP 3A4 (e.g., indinavir, erythromycin) may increase their clearance, resulting in decreased plasma concentrations.
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.
Ephedrine also accelerates the metabolism of dexamethasone.
Oral contraceptives (oestrogens and progestogens) increase plasma concentration of corticosteroids. The antiviral drug ritonavir also increases the plasma concentration of dexamethasone.
Dexamethasone reduces the plasma concentration of the antiviral drugs indinavir and saquinavir.
Patients taking methotrexate and dexamethasone have an increased risk of haematological toxicity.

4.6 Pregnancy and Lactation

Pregnancy

Dexamethasone crosses the placenta. During pregnancy, especially in the first trimester, the drug should only be administered after careful benefit-risk assessment.

Lactation

Dexamethasone is excreted in breast milk. There are no known cases of harm to the infant. Nevertheless, the drug should be strongly indicated during lactation. If the disease requires higher doses, breast-feeding should be discontinued.

4.7 Effects on the ability to drive and use machines

There have been no studies on the effects on the ability to drive and use machines.

4.8 Undesirable effects

- Severe allergic reaction
- Swelling of face, lips, eyelids, tongue, hands and feet
- Loss of vision or blurred vision
- Infections that persist for long
- Black or tarry stools
- Unusual tiredness and weakness
- Headache
- Dizziness
- Sleeplessness
- Agitation and anxiety
- steroid acne, changes in skin pigmentation
- Increased hair growth
- Irregular menstrual periods
- Easy bruising and bleeding

4.9 Overdoses

Symptoms

Acute intoxications with dexamethasone are not known. In case of chronic overdosing, an increase in undesirable effects, especially endocrine, metabolic and electrolyte-related effects, can be expected.

Management

There is no known antidote to dexamethasone.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Dexamethasone is a mono-fluorinated glucocorticoid with pronounced anti-allergic, anti-inflammatory and membrane-stabilizing properties and effects on carbohydrate, protein and fat metabolism.

Dexamethasone has an approximately 7.5 times greater glucocorticoid effect than prednisolone, and compared to hydrocortisone it is 30 times more effective, lacking mineralocorticoid effects.

Glucocorticoids, such as dexamethasone, exert their biological effects by activating the transcription of corticosteroid-sensitive genes. The anti-inflammatory, immunosuppressive and anti-proliferative effects are caused by decreased formation, release and activity of inflammatory mediators, by the inhibition of specific functions and the migration of inflammatory cells. In addition, the effect of sensitized T lymphocytes and macrophages on target cells may be prevented by corticosteroids.

5.2 Pharmacokinetic properties

Absorption and distribution

After oral administration, dexamethasone is rapidly and almost completely absorbed in the stomach and small intestine. Its bioavailability is 80–90%. Maximum blood levels are reached between 60 and 120 minutes. The binding of dexamethasone to plasma albumins is dose-dependent. At very high doses, the largest portion circulates freely in the blood. In hypoalbuminaemia the proportion of the unbound (active) corticoid rises.

Biotransformation

The average (serum) elimination half-life of dexamethasone in adults is 250 minutes (+ 80 minutes). Due to its long biological half-life of more than 36 hours, daily continuous administration of dexamethasone can lead to accumulation and overdosing.

Elimination

The elimination is largely renal in the form of free dexamethasone alcohol. Dexamethasone is partly metabolised, the metabolites are excreted as glucuronates or sulfates, also mainly by the kidneys.

5.3 Preclinical safety Data:

Acute toxicity:

In mice and rats, the LD_{50} for dexamethasone after a single oral dose is 16 g/kg body and over 3 g/kg body weight, respectively, within the first 7 days. Following a single subcutaneous dose, the LD_{50} in mice is more than 700 mg/kg body weight and in rats about 120 mg/kg body weight, within the first 7 days.

Over a period of 21 days, these values become lower, which is interpreted as a consequence of serious infectious diseases caused by the hormone-induced immunosuppression.

Chronic toxicity:

There are no data on chronic toxicity in humans and animals. Corticoid-induced intoxications are not known. In longer-term treatment with doses above 1.5 mg/day, pronounced undesirable effects can be expected.

Mutagenic and tumorigenic potential:

The available study findings for glucocorticoids show no evidence of clinically relevant genotoxic properties.

Reproductive toxicity:

In animal studies, cleft palate was observed in rats, mice, hamsters, rabbits, dogs and primates; not in horses and sheep. In some cases these divergences were combined with defects of the central nervous system and of the heart. In primates, effects in the brain were seen after exposure. Moreover, intrauterine growth can be delayed. All these effects were seen at high dosages.

6. Pharmaceutical particulars

6.1 List of excipients

- Maize starch
- Lactose Monohydrate
- Calcium Hydrogen Phosphate Dihydrate
- Magnesium Stearate
- Sodium Lauryl Sulfate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C in a dry & dark place.
Keep all medicines out of reach of children.

6.5 Nature and contents of container

Packing:
Primary packing: 10 Tablets in an ALU-PVC blister.
Secondary packing: 10 Blisters are packed in a carton along with leaflet.
Tertiary packing: 10 Cartons are packed in shrink. Such 30 Shrinks are packed in a 5 Ply corrugated box sealed with BOPP tape & strap with strapping roll.

6.5 Special precautions for disposal and other handling

None.

7. Applicant / Manufacturer

Applicant

Applicant name and address	**M/s. T.P. DRUGS LIMITED** No. A1 & A2 13, Murtala Muhammad Way, Kano.
Contact person's phone number	
Contact person's email	

Manufacturer

Manufacturer name and address	**M/s. IMPULSE PHARMA PVT. LTD.** J-201, J-202/1 , MIDC Tarapur, Boisar, Dist. Palghar - 401506, Maharashtra State, India.
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