For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

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Dexamethasone Sodium Phosphate Injection IP 4mg/ml

JB Dexa*

GENERIC NAME
Dexamethasone Sodium Phosphate Injection IP 4mg/ml

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ml contains:
Dexamethasone Sodium Phosphate IP
Eq. to Dexamethasone Phosphate.....4 mg
Methyl Paraben IP ..... 0.15% w/v
(as preservatives)
Propyl Paraben IP ..... 0.02% w/v
(as preservatives)
Water for Injections IP ..... q.s.

DOSAGE FORM AND STRENGTH
Solution for injection

CLINICAL PARTICULARS-
THERAPEUTIC INDICATION
Dexamethasone Sodium Phosphate Injection may be given by I.V. or I.M. injection when oral therapy is not feasible in the following conditions:

Endocrine Disorders: Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogs may be used in conjunction with mineralocorticoid where applicable; in infancy, mineralocorticoid supplementation is of particular importance). Acute adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; mineralocorticoid supplementation may be necessary, particularly when synthetic analogs are used). Preoperatively and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful.

Congenital adrenal hyperplasia.
Nonsupportive thyroiditis.
Shock: The adjunctive treatment of shock where high (pharmacologic) doses of corticosteroids are needed: e.g., severe shock of hemorrhagic, traumatic, surgical, or septic origin. Treatment with Dexamethasone Sodium Phosphate Injection is an adjunct to, and not a substitute for, specific or supportive measures that the patient may require, e.g., restoration of circulating blood volume, correction of fluid and electrolyte balance, oxygen, surgical measures and antibiotics.

Rheumatic disorders: As adjunctive therapy for short-term administration (to support the patient during an acute episode of exacerbation) in post-traumatic osteoarthritis, synovitis of osteoarthritis, rheumatoid arthritis including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), acute and subacute bursitis, epicondylitis, acute nonspecific tenosynovitis, acute gouty arthritis, psoriatic arthritis, ankylosing spondylitis.

Collagen diseases: During an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus, acute rheumatic carditis.

Dermatologic diseases: Pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, severe seborrheic dermatitis, severe psoriasis, mycosis fungoides.

Allergic states: Initial control of severe allergic conditions: seasonal or perennial allergic rhinitis, bronchial asthma, contact dermatitis, atopic dermatitis, serum sickness, drug hypersensitivity reactions, urticarial transfusion reactions, acute noninfectious laryngeal edema, anaphylaxis (epinephrine is the drug of first choice).

Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa, such as: allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus (but not herpes simplex), iritis, iridocyclitis, chorioretinitis, anterior segment inflammation, diffuse posterior uveitis and choroiditis, optic neuritis, sympathetic ophthalmia.

Gastrointestinal diseases: To support the patient during a critical period of the disease (systemic therapy) in ulcerative colitis, regional enteritis.

Respiratory diseases: Loeffler's syndrome not manageable by other means, symptomatic sarcoidosis, berylliosis, fulminating or disseminated pulmonary tuberculosis when concurrently accompanied by appropriate antituberculous chemotherapy, aspiration pneumonitis.

Hematologic disorders: Idiopathic thrombocytopenic purpura in adults (I.V. only; I.M. administration is contraindicated), acquired (autoimmune) hemolytic anemia, secondary thrombocytopenia in adults, erythroblastopenia (RBC anemia), congenital (erythroid) hypoplastic anemia.

Neoplastic disorders: For palliative management of leukemias and lymphomas in adults, acute childhood leukemia, hypercalcemia associated with cancer.

Nephrotic syndrome: To induce dieresis or remission of proteinuria in the nephritic syndrome without uremia, of the idiopathic type, or that due to lupus erythematosus.

Cerebral edema: May be used to treat patients with cerebral edema from various causes: associated with primary or metastatic brain tumors; associated with cerebral vascular accident (acute stroke) involving the cerebral cortex; associated with neurosurgery; associated with head injury or pseudomotor cerebri.

Coronavirus disease 2019 (COVID-19): Dexamthasone is indicated in the treatment of coronavirus disease 2019 (COVID-19) in adult and adolescent patients (aged 12 years and older with body weight at least 40 kg) who require supplemental oxygen therapy.

Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block when concurrently accompanied by appropriate antituberculous chemotherapy. Trichinosis with neurologic or myocardial involvement.

POSOLOGY AND METHOD OF ADMINISTRATION
Dexamethasone Sodium Phosphate Injection can be given directly from the vial without mixing or dilution. If preferred, it can be added to Sodium Chloride Injection, or Dextrose Injection, or compatible blood for transfusion, without loss of potency, and administered by I.V. drip.

Dexamethasone Sodium Phosphate Injection may be further diluted to 0.5 mg/mL to 5.0 mg/mL in 5% dextrose injection or 0.9% Sodium Chloride injection. When diluted as directed, resulting solution is stable for 24 hours at room temperature.

When Dexamethasone Sodium Phosphate Injection is added to an infusion solution, use the mixture within 24 hours since infusion solutions do not contain preservatives.

Observe the usual aseptic technique governing injections.

As with all parenteral drug products, intravenous admixtures should be visually inspected prior to administration, whenever solution and container permit. Solutions showing haziness or cloudiness, particulate matter, precipitation, discolouration or leakage should not be used. Discard unused portion.

The usual initial dosage of Dexamethasone Sodium Phosphate Injection varies from 0.5 mg to 20 mg per day, depending on the disease being treated. In less severe conditions, lower doses will usually suffice, while in selected patients higher initial doses may be needed. The parenteral dosage range are usually 33% to 50% of the oral dose given every 12 hours. However, in certain overwhelming acute, life-threatening situations, administration of dosages exceeding the usual dosages may be justified and may be in multiples of the oral dosage. In these circumstances, the slower rate of absorption following I.M. administration should be recognized.

Treatment should be individualized. The initial dosage should be maintained or adjusted until the desired effect occurs. If after a reasonable period of time, there is a lack of clinical response, therapy should be discontinued and appropriate alternate therapy instituted.

After a favourable response is obtained, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small amounts at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. Constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment, in this latter situation it may be necessary to increase the dosage for a period of time consistent with the patient's condition. If the drug is to be stopped after it has been given for more than a few days, it is recommended that it be withdrawn gradually rather than stopped abruptly.

Whenever possible, use the I.V. route for the initial and for as many subsequent doses as are given while the patient is in shock (because of the irregular rate of absorption of any medication administered by any other route in such patients). When the blood pressure responds, use the I.M. route until oral therapy can be substituted. For the patient's comfort, not more than 8 mg should be injected I.M. at any one site.

In emergencies, the usual doses of I.V. or I.M. Dexamethasone Sodium Phosphate Injection is 4 to 20 mg depending on the severity of the condition (see also Shock). This dose may be repeated until adequate response is obtained.

After initial improvement, singles doses of 2 to 4 mg repeated as necessary, may be sufficient. Determine the proper maintenance dosage by decreasing the initial drug dosage in small amounts at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. The total daily dosage usually need not exceed 80 mg, even in severe conditions.

When constant maximal effect is desired, repeat dosage at 3 to 4 hour intervals or maintain by slow I.V. drip.

Intravenous and intramuscular injections are advised in acute illness. When the acute stage has passed, substitute oral steroid therapy as soon as feasible.

Shock: The usual dose is 2 to 6 mg/kg given in a single I.V. injection. This may be repeated in 2 to 6 hours, if shock persists. As an alternative, given 2 to 6 mg/kg as a single I.V. injection followed immediately by the same dose in an I.V. infusion. Therapy with Dexamethasone Sodium Phosphate Injection is an adjunctive and not a replacement for conventional therapy (see Precautions). These recommendations reflect the current tendency to use high (pharmacologic) doses of corticosteroids in the treatment of shock. Continue administration of high dose corticosteroid therapy only until patient's condition has stabilized and usually no longer than 48 to 72 hours. Avoid prolonged therapy at such high doses to prevent possible complications, such as adrenal suppression or gastrointestinal ulcer.

Cerebral edema: Associated with acute life threatening situations;

Adults: Initially 50 mg I.V., followed by a tapering I.V. dose of 8 mg every 2 hours for 3 days, 4 mg every 2 hours the 4th day, then 4 mg every 4 hours for days 5 to 8. Reduce dose to zero over the next 7 to 10 days by a daily reduction of 4 mg.

Children (over 35 kg): Initially 25 mg I.V., followed by a tapering I.V. dose of 4 mg every 2 hours for 3 days, then 4 mg every 4 hours the 4th day, then 4 mg every 5 hours for days 5 to 8. Reduce dose to zero over the next 7 to 10 days by a daily reduction of 2 mg.

Children (under 35 kg): Initially 20 mg I.V., followed by a tapering I.V. dose of 4 mg every 3 hours for 3 days, then 4 mg every 6 hours the 4th day, then 2 mg every 5 hours for days 5 to 8. Reduce dose to zero over the next 7 to 10 days by a daily reduction of 1 mg.

Associated with acute stroke: Initially 10 mg I.V. followed by 4 mg I.M. every 6 hours for 10 days. Doses should then be tapered to zero over the ensuing 7 days.

Associated with primary or metastatic brain tumour, neurosurgery, head injury, pseudotumour cerebri or preoperative preparation of patients with increased intracranial pressure secondary to brain tumour: initially 10 mg I.V. followed by 4 mg I.M. every 6 hours until symptoms of cerebral edema subside. Response is usually noted within 12 to 24 hours; dosage may be reduced after 2 to 4 days and gradually discontinued over a period of 5 to 7 days.

For palliative management of patients with recurrent or inoperable brain tumours: Individualize maintenance therapy with oral or parenteral dexamethasone. A dosage of 2 mg, 2 or 3 times a day may be effective. Utilize the smallest dosage necessary to control cerebral edema.

Observe the usual precautions associated with corticosteroid therapy. Consider antacids, anticholinergic drugs, and dietary measures to prevent gastrointestinal ulcer or hemorrhage.

In the treatment of acute, self limited, allergic disorders or acute exacerbations of chronic allergic disorders (e.g. acute attacks of seasonal allergic bronchial asthma, urticaria medicamentosa and contact dermatoses), the following dosage schedule is suggested: first day: 4 or 8 mg intramuscularly; second and third days: 1.5 mg orally twice a day; fourth day: 0.75 mg orally twice a day; fifth and sixth days: 0.75 mg orally; seventh day: no treatment; eighth day: follow up visit.

This schedule is designed to provide adequate therapy during acute episodes, while minimizing the risk of overdosage in chronic cases. Some patients may require further treatment, such as topical corticosteroids, antihistamines, bronchodilators, or further systemic corticosteroid therapy. When acute exacerbations of asthma are accompanied by signs of infection, administer antibiotics concomitantly.

CONTRAINDICATIONS
Systemic fungal infections; hypersensitivity to dexamethasone or to any other excipients.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Warnings
In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Administration of live virus vaccines, including smallpox, is contraindicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

The use of corticosteroids in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Use corticosteroids cautiously in patients with ocular herpes simplex because of possible corneal ulceration and perforation.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Corticosteroids should not be used in the presence of systemic fungal infections unless needed to control drug reactions due to amphotericin B. Moreover, there have been cases reported in which concomitant use of the two agents was followed by cardiac enlargement and congestive failure.

Corticosteroids may mask some signs of infection and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used. Moreover, corticosteroids may affect the nitroblue tetrazolium test for bacterial infection and produce false negative results. If corticosteroids must be used in the presence of bacterial infections, institute appropriate vigorous anti-infective therapy. Corticosteroids may activate latent amebiasis. Therefore, it is recommended that latent or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or any patient with unexplained diarrhea.

Precautions
Intra-articular corticosteroid injection may produce systemic as well as local effects. Frequent intra-articular injection may result in damage to joint tissues. Avoid overdistension of the joint capsule and deposition of steroid along the needle tract in intra-articular injection, since this may lead to tissue atrophy. In intracostal neuritis and neuralgia, guard against entering the pleura.

Appropriate examination of any joint fluid present is necessary to exclude a septic process. Avoid local injection of a corticosteroid into an injected site.

The slower rate of absorption by I.M. administration must be recognized.

A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, institute appropriate antimicrobial therapy. Use the lowest possible dose of corticosteroid to control the condition under treatment, and when dosage reduction is possible, the reduction should be gradual.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt, and water retention and increased potassium excretion. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

When large doses are given to patients at risk of peptic ulcer disease, some authorities advise that H_2 receptor antagonists or sucralfate be administered between meals to help prevent peptic ulcer.

Drug induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimized by gradual dosage reduction. This type of relative insufficiency may persist for months after dis-

continuation of therapy, therefore, in any stress situation occurring during that period, reinstitute hormone therapy. If the patient is receiving steroids already, the dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Following prolonged therapy, withdrawal of corticosteroids may result in symptoms of the corticosteroid withdrawal syndrome including fever, myalgia, arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

Use acetylsalicylic acid cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Use corticosteroids with caution in: nonspecific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis and myasthenia gravis. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisonism.

There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Psychological and/or physiological dependency may develop with long-term use of corticosteroids. Discontinuance of therapy may lead to the development of withdrawal symptoms, including anorexia, vague pain, weakness and lethargy.

Corticosteroids may increase or decrease motility and number of spermatozoa in some patients.

Because rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroids therapy, take appropriate precautionary measures prior to administration especially when the patient has a history of drug allergy.

Corticosteroids may suppress reactions to skin tests

Do not inject corticosteroids into unstable joints.

Avoid injection in the deltoid muscle because of high incidence of tissue atrophy.

Patients should be impressed strongly with the importance of not overusing joints in which symptomatic benefit has been obtained as long as the inflammatory process remains active.

DRUGS INTERACTIONS
Phenytoin, phenobarbital, rifampicin and ephedrine may enhance the rate of metabolism and clearance of corticosteroids and this may require corticosteroid dosage adjustment. Interpret dexamethasone suppression test results cautiously during concurrent administration of these drugs.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalemia.

The prothrombin time should be checked frequently in patients receiving corticosteroids and coumarin anticoagulants concomitantly because of reports that corticosteroids have altered the response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

Pregnancy and Lactation: (see Warnings)

Children: Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

USE IN SPECIAL POPULATIONS
Pregnancy: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighted against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Lactation: Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacological doses of corticosteroids should be advised not to nurse.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Not relevant.

UNDESIRABLE EFFECTS
Fluid and Electrolyte Disturbances: Sodium retention; fluid retention; congestive heart failure in susceptible patients; potassium loss; hypokalemic alkalosis; hypertension; hypotension or shock-like reaction.

Musculoskeletal: Muscle weakness; steroid myopathy; loss of muscle mass; osteoporosis; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones; tendon rupture.

Gastrointestinal: Peptic ulcer with possible subsequent perforation and hemorrhage; perforation of the small and large bowel, particularly patients with inflammatory bowel disease; pancreatitis; abdominal distention; ulcerative esophagitis.

Dermatologic: Impaired wound healing; thin fragile skin; petechiae and ecchymoses; erythema; increased sweating; may suppress reactions to skin tests, burning or tingling, especially in the perineal area (after I.V. injection); other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic edema.

Neurological: Convulsions; increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment; vertigo; headache.

Endocrine: Menstrual irregularities; development of Cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; decreased carbohydrate tolerance; manifestations of latent diabetes mellitus; increased requirements for insulin or oral hypoglycaemic agents in diabetes.

Ophthalmic: Posterior subcapsular cataracts; increased intraocular pressure; glaucoma; exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Anaphylactoid or hypersensitivity reactions, thromboembolism, nausea, malaise, weight gain, increased appetite, psychological or physiological dependence.

OVERDOSE
Symptoms: There are two categories of toxic effects from therapeutic use of glucocorticoids: Acute adrenal insufficiency due to too rapid withdrawal of corticosteroids after long-term use and induction of Cushingoid changes from continued use of large doses. Abrupt corticosteroid withdrawal results in fever, myalgia, arthralgia, malaise, anorexia, nausea, desquamation of skin, orthostatic hypotension, dizziness, fainting, dyspnea and hypoglycemia. Cushing-like changes include moonface, central obesity, striae, hirsutism, acne ecchymoses, hypertension, osteoporosis, myopathy, sexual dysfunction, diabetes, hyperlipidemia, peptic ulcer, increased susceptibility to infection and electrolyte and fluid imbalance.

Treatment: Recovery of normal adrenal and pituitary function may require up to 9 months. Tapering of the steroid should be gradual under the supervision of a physician. Frequent lab tests are necessary. Supplementation is required during periods of stress (i.e. illness, surgery or injury). Eventually reduce to the lowest dose that will control the symptoms or discontinue the corticosteroid completely. For large, acute overdose, treatment includes usual supportive measures. Anaphylactic and hypersensitivity reactions may be treated with epinephrine, positive artificial respiration, and aminophylline. Keep the patient warm and quiet.

PHARMACOLOGICAL PROPERTIES-
PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: Corticosteroids for systemic use, Glucocorticoids, ATC code: H02AB02
Dexamethasone is a synthetic adrenocorticoid with approximately a 7 times higher anti-inflammatory potency than prednisolone and 30 times that of hydrocortisone. Adrenocorticoids act on the HPA at specific receptors on the plasma membrane. On other tissues the adrenocorticoids diffuse across cell membranes and complex with specific cytoplasmic receptors which enter the cell nucleus and stimulate protein synthesis. Adrenocorticoids have anti-allergic, antitoxic, antishock, antipyretic and immunosuppressive properties. Dexamethasone has only minor mineralocorticoid activities and does therefore, not induce water and sodium retention.

PHARMACOKINETIC PROPERTIES
Absorption
After administration of Dexamethasone solution for injection, dexamethasone sodium phosphate is rapidly hydrolysed to dexamethasone. After an IV dose of 20 mg dexamethasone plasma levels peak within 5 minutes.

Distribution
Dexamethasone is bound (up to 77%) by plasma proteins, mainly albumin. There is a high uptake of dexamethasone by the liver, kidney and adrenal glands.
Biotransformation and Elimination
Metabolism in the liver is slow and excretion is mainly in the urine, largely as unconjugated steroids. The plasma half-life is 3.5 - 4.5 hours but as the effects outlast the significant plasma concentrations of steroids the plasma half-life is of little relevance and the use of biological half-life is more applicable. The biological half-life of dexamethasone is 36 - 54 hours; therefore, dexamethasone is especially suitable in conditions where continuous glucocorticoid action is desirable.

NONCLINICAL PROPERTIES
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, intra-uterine growth can be delayed. All these effects were seen at high dosages.

INCOMPATIBILITIES
No incompatibilities have been identified.

SHELF-LIFE
Refer the pack

PACKAGING INFORMATION
Vial of 2ml and 20ml

STORAGE AND HANDING INSTRUCTIONS
Store protected from light at temperature not exceeding 30°C. Do not freeze.

Marketed by:
J. B. CHEMICALS & PHARMACEUTICALS LTD.
Neelam Centre, 'B' Wing, Hind Cycle Road, Worli, Mumbai - 400 030, India.

Note: This prescribing information is applicable for India Market only

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