Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT(S)

Prednisone Rekah 1 mg
Prednisone Rekah 5 mg
Prednisone Rekah 20 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Prednisone Rekah 1 mg: Each tablet contains 1 mg of prednisone.
Excipients with known effect: Each tablet contains 59 mg of lactose and 0.006 mg of Sunset Yellow (E 110) (see section 4.4).
Prednisone Rekah 5 mg: Each tablet contains 5 mg of prednisone.
Excipient with known effect: Each tablet contains 25 mg of lactose (see section 4.4).
Prednisone Rekah 20 mg: Each tablet contains 20 mg of prednisone.
Excipient with known effect: Each tablet contains 33.68 mg of lactose (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Uncoated tablet.
Prednisone Rekah 1 mg: An orange tablet, “REKAH” engraved on one side and plain on the other.
Prednisone Rekah 5 mg: A white tablet, “R” engraved on one side and plain on the other.
Prednisone Rekah 20 mg: A pink tablet, “R” engraved on one side and plain on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prednisone is indicated wherever corticosteroid therapy is indicated such as: pemphigus vulgaris, allergic dermatitis, eczema, exfoliative dermatitis, dermatitis herpetiformis, dermatitis medicamentosa, erythema multiforme; disseminated lupus erythematosus, dermatomyositis, polyarteritis nodosa; severe bronchial asthma and status asthmaticus, emphysema, pulmonary fibrosis; adrenal hyperplasia (adrenogenital syndrome); idiopathic thrombocytopenic purpura, acquired haemolytic anaemia, acute leukemia; nephrotic syndrome; iridochoroiditis; ulcerative colitis; rheumatoid arthritis; ankylosing spondylitis, rheumatic fever, gout, periarthritis of the shoulder.

4.2 Posology and method of administration

Posology

Adults:

The initial dosage of prednisone may vary from 5 mg to 60 mg of prednisone per day depending on the specific disease entity being treated. In situations of less severity lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, prednisone should be discontinued and the patient transferred to other appropriate therapy. **IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE**

INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.

After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that 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 of prednisone for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

ADT (Alternate Day Therapy)

ADT is a corticosteroid dosing regimen in which twice the usual daily dose of corticoid is administered every other morning. The purpose of this mode of therapy is to provide the patient requiring long-term pharmacologic dose treatment with the beneficial effects of corticoids while minimizing certain undesirable effects, including pituitary-adrenal suppression, the Cushingoid state, corticoid withdrawal symptoms, and growth suppression in children.

The rationale for this treatment schedule is based on two major premises: (a) the anti- inflammatory or therapeutic effect of corticoids persists longer than their physical presence and metabolic effects and (b) administration of the corticosteroid every other morning allows for re-establishment of more nearly normal hypothalamic-pituitary- adrenal (HPA) activity on the off-steroid day.

A brief review of the HPA physiology may be helpful in understanding this rationale. Acting primarily through the hypothalamus a fall in free cortisol stimulates the pituitary gland to produce increasing amounts of corticotropin (ACTH) while a rise in free cortisol inhibits ACTH secretion. Normally the HPA system is characterized by diurnal (circadian) rhythm. Serum levels of ACTH rise from a low point about 10 pm to a peak level about 6 am. Increasing levels of ACTH stimulate adrenocortical activity resulting in a rise in plasma cortisol with maximal levels occurring between 2 am and 8 am. This rise in cortisol dampens ACTH production and in turn adrenocortical activity. There is a gradual fall in plasma corticoids during the day with lowest levels occurring about midnight.

The diurnal rhythm of the HPA axis is lost in Cushing's disease, a syndrome of adrenocortical hyperfunction characterized by obesity with centripetal fat distribution, thinning of the skin with easy bruisability, muscle wasting with weakness, hypertension, latent diabetes, osteoporosis, electrolyte imbalance, etc. The same clinical findings of hyperadrenocorticism may be noted during long-term pharmacologic dose corticoid therapy administered in conventional daily divided doses. It would appear, then, that a disturbance in the diurnal cycle with maintenance of elevated corticoid values during the night may play a significant role in the development of undesirable corticoid effects. Escape from these constantly elevated plasma levels for even short periods of time may be instrumental in protecting against undesirable pharmacologic effects.

During conventional pharmacologic dose corticosteroid therapy, ACTH production is inhibited with subsequent suppression of cortisol production by the adrenal cortex. Recovery time for normal HPA activity is variable depending upon the dose and duration of treatment. During this time the patient is vulnerable to any stressful situation. Although it has been shown that there is considerably less adrenal suppression following a single morning dose of prednisolone (10 mg) as opposed to a quarter of that dose administered every 6 hours, there is evidence that some suppressive effect on adrenal activity may be carried over into the following day when pharmacologic doses are used. Further, it has been shown that a single dose of certain corticosteroids will produce adrenocortical suppression for two or more days. Other corticoids, including methylprednisolone, hydrocortisone, prednisone, and prednisolone, are considered to be short acting (producing adrenocortical suppression for 1¼ to 1½ days following a single dose) and thus are recommended for alternate day therapy.

The following should be kept in mind when considering alternate day therapy:

1. Basic principles and indications for corticosteroid therapy should apply. The benefits of ADT should not encourage the indiscriminate use of steroids.
2. ADT is a therapeutic technique primarily designed for patients in whom long-term pharmacologic

corticoid therapy is anticipated.

3. In less severe disease processes in which corticoid therapy is indicated, it may be possible to initiate treatment with ADT. More severe disease states usually will require daily divided high dose therapy for initial control of the disease process. The initial suppressive dose level should be continued until satisfactory clinical response is obtained, usually four to ten days in the case of many allergic and collagen diseases. It is important to keep the period of initial suppressive dose as brief as possible particularly when subsequent use of alternate day therapy is intended. Once control has been established, two courses are available: (a) change to ADT and then gradually reduce the amount of corticoid given every other day or (b) following control of the disease process reduce the daily dose of corticoid to the lowest effective level as rapidly as possible and then change over to an alternate day schedule. Theoretically, course (a) may be preferable.
4. Because of the advantages of ADT, it may be desirable to try patients on this form of therapy who have been on daily corticoids for long periods of time (e.g., patients with rheumatoid arthritis). Since these patients may already have a suppressed HPA axis, establishing them on ADT may be difficult and not always successful. However, it is recommended that regular attempts be made to change them over. It may be helpful to triple or even quadruple the daily maintenance dose and administer this every other day rather than just doubling the daily dose if difficulty is encountered. Once the patient is again controlled, an attempt should be made to reduce this dose to a minimum.
5. As indicated above, certain corticosteroids, because of their prolonged suppressive effect on adrenal activity, are not recommended for alternate day therapy (e.g., dexamethasone and betamethasone).
6. The maximal activity of the adrenal cortex is between 2 am and 8 am, and it is minimal between 4 pm and midnight. Exogenous corticosteroids suppress adrenocortical activity the least, when given at the time of maximal activity (am).
7. In using ADT it is important, as in all therapeutic situations to individualize and tailor the therapy to each patient. Complete control of symptoms will not be possible in all patients. An explanation of the benefits of ADT will help the patient to understand and tolerate the possible flare-up in symptoms which may occur in the latter part of the off-steroid day. Other symptomatic therapy may be added or increased at this time if needed.
8. In the event of an acute flare-up of the disease process, it may be necessary to return to a full suppressive daily divided corticoid dose for control. Once control is again established alternate day therapy may be re-instituted.
9. Although many of the undesirable features of corticosteroid therapy can be minimized by ADT, as in any therapeutic situation, the physician must carefully weigh the benefit-risk ratio for each patient in whom corticoid therapy is being considered.

Children:

Initial dosage: 0.5 mg/kg daily in three or four divided doses. This dosage can be doubled or trebled if necessary.

Maintenance dosage: 0.125 to 0.25 mg/kg daily.

For infants and children, the recommended dosage should be governed by the same considerations as adults rather than by strict adherence to the ratio indicated by age or body weight.

Hepatic and renal impairment patients:

For hepatic and renal impairment, see section 4.4.

Method of administration

For oral administration.
The tablets should be swallowed whole after food.
There is no information available regarding the crushing, splitting, or chewing of the tablets.

4.3 Contraindications

- Hypersensitivity to the active substance prednisone or to any of the excipients listed in section 6.1.
- Systemic fungal infections.
- Vaccination against smallpox.

4.4 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.

Immunosuppression and Increased Risk of Infection

Corticosteroids, including prednisone, suppress the immune system and increase the risk of infection with any pathogen, including viral, bacterial, fungal, protozoan, or helminthic pathogens. Corticosteroids can:

- Reduce resistance to new infections
- Exacerbate existing infections
- Increase the risk of disseminated infections
- Increase the risk of reactivation or exacerbation of latent infections
- Mask some signs of infection

Corticosteroid-associated infections can be mild but can be severe and at times fatal. The rate of infectious complications increases with increasing corticosteroid dosages.
Monitor for the development of infection and consider prednisone withdrawal or dosage reduction as needed.

Tuberculosis

If prednisone is used to treat a condition in patients with latent tuberculosis or tuberculin reactivity, reactivation of tuberculosis may occur. Closely monitor such patients for reactivation. During prolonged prednisone therapy, patients with latent tuberculosis or tuberculin reactivity should receive chemoprophylaxis.

Varicella Zoster and Measles Viral Infections

Varicella and measles can have a serious or even fatal course in non-immune patients taking corticosteroids, including prednisone. In corticosteroid-treated patients who have not had these diseases or are non-immune, particular care should be taken to avoid exposure to varicella and measles:

- If a prednisone-treated patient is exposed to varicella, prophylaxis with varicella zoster immune globulin may be indicated. If varicella develops, treatment with antiviral agents may be considered.
- If a prednisone-treated patient is exposed to measles, prophylaxis with immunoglobulin may be indicated.

Hepatitis B Virus Reactivation

Hepatitis B virus reactivation can occur in patients who are hepatitis B carriers treated with immunosuppressive dosages of corticosteroids, including prednisone. Reactivation can also occur infrequently in corticosteroid-treated patients who appear to have resolved hepatitis B infection.
Screen patients for hepatitis B infection before initiating immunosuppressive (e.g., prolonged) treatment with prednisone. For patients who show evidence of hepatitis B infection, recommend consultation with physicians with expertise in managing hepatitis B regarding monitoring and consideration for hepatitis B antiviral therapy.

Fungal Infections

Corticosteroids, including prednisone, may exacerbate systemic fungal infections; therefore, avoid prednisone use in the presence of such infections unless prednisone is needed to control drug reactions. For patients on chronic prednisone therapy who develop systemic fungal infections, prednisone withdrawal or dosage reduction is recommended.

Amebiasis
Corticosteroids, including prednisone, may activate latent amebiasis. Therefore, it is recommended that latent amebiasis or active amebiasis be ruled out before initiating prednisone in patients who have spent time in the tropics or patients with unexplained diarrhea.

Strongyloides Infestation
Corticosteroids, including prednisone, should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation. In such patients, corticosteroid-induced immunosuppression may lead to Strongyloides hyper-infection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Cerebral Malaria
Avoid corticosteroids, including prednisone, in patients with cerebral malaria.

Kaposi's Sarcoma
Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement of Kaposi's sarcoma.

Fluid and Electrolyte Disturbances
Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. 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.

Immunization Procedures
Immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

Ophthalmic
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.

PRECAUTIONS

General Precautions
- Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/ or a mineralocorticoid should be administered concurrently.
- There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.
- Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.
- The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.
- 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.
- Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.
- Steroids should be used 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.
- Growth and development of infants and children on prolonged corticosteroid therapy should be carefully

observed.
- Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/ benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.
- Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin. Since concurrent use of these agents results in a mutual inhibition of metabolism, it is possible that adverse events associated with the individual use of either drug may be more apt to occur.
- Caution is necessary when oral corticosteroids are used in patients with the following conditions and frequent monitoring is necessary:
  - Renal insufficiency
  - Liver failure
- This medicine contains lactose. Patients with the rare hereditary of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- This medicine contains less than 1 mmol (23 mg) of sodium per tablet, that is to say essentially "sodium- free".
- **Prednisone Rekah 1 mg** contains Sunset Yellow (E 110), which may cause allergic reactions.

4.5 Fertility, pregnancy and lactation

Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers or women of child-bearing potential requires that the possible benefits of the drug be weighed 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.

4.6 Undesirable effects

Fluid and Electrolyte Disturbances
- Sodium retention
- Fluid retention
- Congestive heart failure in susceptible patients
- Potassium loss
- Hypokalemic alkalosis
- Hypertension

Musculoskeletal
- Muscle weakness
- Steroid myopathy
- Loss of muscle mass
- Osteoporosis
- Tendon rupture, particularly of the Achilles tendon
- Vertebral compression fractures
- Aseptic necrosis of femoral and humeral heads
- Pathologic fracture of long bones

Gastrointestinal
- Peptic ulcer with possible perforation and hemorrhage
- Pancreatitis
- Abdominal distention
- Ulcerative esophagitis

Dermatologic
- Impaired wound healing

- Thin fragile skin
- Petechiae and ecchymoses
- Facial erythema
- Increased sweating
- May suppress reactions to skin tests

Metabolic
- Negative nitrogen balance due to protein catabolism

Neurological
- Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment
- Convulsions
- Vertigo
- Headache

Endocrine
- Menstrual irregularities
- Development of Cushingoid state
- Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness
- Suppression of growth in children
- Decreased carbohydrate tolerance
- Manifestations of latent diabetes mellitus
- Increased requirements for insulin or oral hypoglycemic agents in diabetics

Ophthalmic
- Posterior subcapsular cataracts
- Increased intraocular pressure
- Glaucoma
- Exophthalmos

Additional Reactions
- Urticaria and other allergic, anaphylactic or hypersensitivity reactions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/ risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Glucocorticoids.
ATC code: H02AB07.
Glucocorticoids are readily absorbed from the gastrointestinal tract and cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli. Glucocorticoids, both naturally occurring (hydrocortisone and cortisone) and synthetic, are classified as adrenocortical steroids.
Prednisone is a glucocorticoid, a synthetic analog that is primarily used for its potent anti-inflammatory effects in disorders of many organ systems.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Prednisone Rekah 1 mg: Lactose, Starch, Talc, Gelatine, Powdered Cellulose (Elcema), Stearic Acid, Sunset Yellow (E 110).
Prednisone Rekah 5 mg: Starch, Lactose, Microcrystalline Cellulose (Avicel PH 102), Microcrystalline Cellulose (Avicel PH 101), Talc, Croscarmellose Sodium (Ac-di-sol), Magnesium Stearate, Colloidal Silicon dioxide (Aerosil 200).
Prednisone Rekah 20 mg: Starch, Lactose, Microcrystalline Cellulose (Avicel PH 102), Talc, Croscarmellose Sodium (Ac-di-sol), Magnesium Stearate, Color Red FDC No. 3 Lake 30%, Colloidal Silicon dioxide (Aerosil 200).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
Prednisone Rekah 1 mg can be used for up to 2 months after initial opening and not later than the expiry date, that appears on the package.

6.4 Special precautions for storage

Store in a dark and dry place, below 25°C.

6.5 Nature and contents of container

Prednisone Rekah 1 mg: Polypropylene securitainer with a polyethylene cap.
Prednisone Rekah 5 mg: PVC-Aluminium blisters in a carton box. Each pack contains: 30, 250 and 1,000 tablets.
Prednisone Rekah 20 mg: PVC-Aluminium blisters in a carton box. Each pack contains: 30 and 250 tablets.

Not all package sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER AND MANUFACTURER

Rekah Pharmaceutical Industry Ltd., 30 Hamelacha St., Holon, 5881904, Israel.

8 MARKETING AUTHORISATION NUMBER(S)

Prednisone Rekah 1 mg: 118-06-26041-00
Prednisone Rekah 5 mg: 038-70-22458-01
Prednisone Rekah 20 mg: 113-33-22170-00

9 DATE OF REVISION OF THE TEXT

Revised in August 2025 according to the MOH guidelines.