1. **NAME OF MEDICINE**

   HYDROCORTISONE ERFA 20 mg tablets

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

   1 tablet contains 20 mg of hydrocortisone.

   Excipient with notable effects: lactose.
   For the full list of excipients, see section 6.1.

3. **PHARMACEUTICAL FORM**

   Tablet.

4. **CLINICAL DATA**

4.1 **Indications for use**

   - Primitive or secondary adrenal failure (Addison’s disease, panhypopituitarism, adrenalectomy, hypophysectomy).
   - Adreno-genital syndrome and rarer forms of congenital hyperplasia of the adrenal glands.

4.2 **Dose and method of administration**

   The dose mentioned is a dose for adults.

   In the case of adrenal failure, adequate compensation generally requires 30 mg of hydrocortisone per day. It is preferable for this dose to be administered in the form of 20 mg in the morning and 10 mg in the evening, in order to respect the circadian rhythm.

   In case of stress (e.g., infections, traumatisms, etc.) the dose should at least be doubled for as long as is necessary (e.g., several days). If the stress is considerable (surgery under general anaesthetic), hydrocortisone or another glucocorticoid should be used by intravenous route.

   In the case of adreno-genital syndrome, the entire dose necessary to inhibit the secretion of ACTH should be taken in the evening (10 to 40 mg depending on needs).

   Except in short treatments, never abruptly stop the cortico-therapy. Instead, decrease the dose more or less gradually, depending on the length of treatment and under strict medical control.

   In the case of prolonged treatment, the minimum efficient dose must be sought in decreasing fashion and depending on the ailment in question.

   To be administered by oral route.

4.3 **Contra-indications**

   Hypersensitivity to the active ingredient or to one of the excipients mentioned in section 6.1.
Normal contra-indications for general cortico-therapy are not applicable to the use of this form in the uses of replacement cortico-therapy.

This medicine contains lactose and is not suitable for patients who display intolerance to galactose, a deficiency in Lap lactase or a syndrome of glucose and galactose malabsorption (rare hereditary diseases).

4.4 Special warnings and precautions of use

Since this is a replacement therapy, no specific precautions are necessary in general. However, if higher doses are given over a certain period of time, it is recommended to monitor the glucidic balance, blood pressure, kalemia and occurrence of any possible infectious complications (by bacteria, Koch's bacillus or yeasts).

During the period of higher dosage, vaccinations must be avoided and it may be necessary to administer a tuberculosis prophylaxis. Restrictions on intake of salt and sugars may be necessary.

In periods of stress (infection, high fever, traumas, surgical operations, severe illness, etc.) the dose must be temporarily increased before quickly returning to the previous dose once the acute episode has passed. In case of significant heat, it may also be necessary to increase the dose and especially the mineralocorticoid intake in case of primary adrenal failure.

4.5 Interactions with other medicines and other forms of interactions

Such interactions only occur in the case of therapeutic overdosage:

Inadvisable combinations:
Erythromycin I.V., sulotrope, and vincamine, due to the risk of wave burst arrhythmia (hypokalemia is a predisposing cause as are bradycardia and a pre-existing long QT interval).

Combinations requiring precautionary measures:
- Antiarrhythmics which cause wave burst arrhythmia:
  o Bepridil, bretylium, disopyramide, sotalol and amiodarone.
  o Hypokalemia is a predisposing cause as are bradycardia and a pre-existing long QT interval. Monitoring of the ECG and in particular the QT interval: in case of wave burst arrhythmia, do not administer an antiarrhythmic (cardiac pacing).

- Digitalis:
  o Hypokalemia can enhance the toxic effect of digitalins.

- Other hypokalimecs:
  o Increased risk of hypokalemia (by additive effect).

For all these cases, the kalemia must be monitored as well as the ECG and, if necessary, hypokalemia must be corrected.

- Acetylsalicylic acid:
The decrease of the salicylemia during the treatment with corticoids and the risk of salicylic overdosage after it has been halted (an increase in the elimination of salicyl by the corticoids) requires adaptation of salicyl doses during combined intake and following the halt in treatment with the corticoids.

- Oral and heparin anti-coagulants (parenteral route):
  - Aggravation of the risk of bleeding specific to corticosteroid therapy (digestive mucosa, vascular fragility), at high doses or during prolonged treatment lasting more than 10 days. When such a combination is justified, increase monitoring.

- Insulin, methformin, sulpha-based hypoglycemics:
  - In the case of a rise in glycaemia sometimes with ketosis (a decrease in tolerance of sugars due to the corticoids), patients should be warned and must pay extra attention to monitoring their blood and urine.
  - It is possible to adapt the dose of the anti-diabetic during the treatment with corticoids and following halt of this treatment.

- Phenobarbital, phenytoin and primidone and rifampicin (enzyme-inducing agents):
  - Decrease in the efficacy of the corticoids (increase in their dissimilation). Clinical and biological signs should be monitored, with possible adaptation of the corticoids during combined intake and after the halt in treatment of the enzyme-inducing agent.

Combinations to be monitored:
- Anti-hypertensive drugs:
  - decrease of the anti-hypertensive effect (sodium and water retention of corticoids).
- Alpha interferon:
  - risk of interferon action inhibition.
- Live attenuated vaccines: risk of generalised and possibly mortal illness. This risk is aggravated in patients who are already immuno-depressed by the underlying illness. Use an inactivated vaccine when possible (poliomyelitis).

4.6 Fertility, pregnancy and breast-feeding

The dose of hydrocortisone must be adapted to the physiological needs of the pregnant or breast-feeding woman, which may be heightened. Dosages of ACTH and cortisoluria can be used to guide such a physiological adaptation.

4.7 Effects on the ability to drive vehicles and use machines

Data not supplied.

4.8 Side effects

Side effects are most likely during prolonged treatment or when the physiological dose (30 mg per day) is exceeded.

The side effects are classified by system organ class with indication of frequency evaluation: Very frequent (≥ 1/10), frequent (≥ 1/100, < 1/10), not frequent (≥ 1/1000, < 1/100), rare (≥ 1/10000, < 1/1000), very rare (<1/10000), including isolated reports.

Endocrinal disorders & metabolic and nutritional disorders:
Iatrogenic Cushing’s syndrome, decrease in the tolerance of glucose (reversible), reversible diabetes in case of normalisation of doses, stunt ing of growth in children, irregular menstruation, fluid and electrolyte disorders, in particular potassium levels in the blood that are too low with a loss of acid in the body, water and salt retention with sometimes high blood pressure.

Cardiac disorders:
Congestive heart failure due to fluid and electrolyte disorders.

Gastro-intestinal disorders:
Peptic ulcers (possibly with bleeding or perforations).
Very rare: acute pancreatitis.

Skin and subcutaneous tissue disorders:
acne, hypertrichosis, bruising, purpura, delayed healing.

Musculoskeletal and systemic disorders:
Muscular weakness and atrophy, osteoporosis, pathological fractures, in particular vertebral collapse, aseptic necrosis of the femoral heads.

4.9 Overdoses

There are no clinical risks associated with acute overdosing.

Chronic overdosing gives rise to Cushing’s syndrome (see section 4.8, Side Effects).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmaco-dynamic properties

Pharmaco-therapeutic class: glucocorticoids, ATC code: H02AB09

Hydrocortisone or cortisol is the glucocorticoid hormone of the adrenal cortex; it also possesses mineralocorticoid hydrosaline retention action that, however, is lower than that of aldosterone or deoxycorticosterone, at rates of 1 to 3,000 and 1 to 100 respectively.

At supra-physiological doses, it possesses anti-inflammatory and immunosuppressive properties.

5.2 Pharmaco-kinetic properties

After oral absorption, the maximum blood content is reached in one hour; the biological half-life is approximately 100 minutes and the liaison with proteins is 90%.

Bio-transformation mainly takes place in the liver and to a lesser degree in the kidneys.

It is eliminated in urine, especially in the form of conjugated glucuronides.

5.3 Pre-clinical safety data

Data not supplied.
6. PHARMACEUTICAL DATA

6.1 List of excipients

Lactose, gelatin, potato starch, talc, magnesium stearate.

6.2 Incompatibilities

Data not supplied.

6.3 Shelf life

5 years.

6.4 Special storage precautions

Store at room temperature, between 15° and 25°C.

6.5 Type and content of external packaging

Box of 20 tablets in a brown type III glass bottle, sealed with a white low-density polyethylene cap.

6.6 Specific handling and waste disposal precautions

No specific requirements.

7. MARKETING AUTHORISATION HOLDER

BePharBel Manufacturing S.A.
Rue du Luxembourg 13
B-6180 Courcelles, Belgium

8. MARKETING AUTHORISATION NUMBER

BE030755

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

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Date of most recent renewal: 18/04/2008

10. DATE ON WHICH THIS TEXT WAS UPDATED

March 2014

Date approved: