

VI.2 Elements for a Public Summary

VI.2.1 *Overview of disease epidemiology*

Hydrocortisone (i.e. cortisol) is a natural hormone that belongs to a class of medicines called corticosteroids. Corticosteroids mimic the effects of hormones body produces naturally in adrenal glands that are located on top of each kidney. These hormones are essential for life. When prescribed in doses that exceed body's usual levels, corticosteroids suppress inflammation. This can reduce the signs and symptoms of inflammatory conditions. Corticosteroids also suppress immune system, which can e.g. help control conditions in which immune system mistakenly attacks its own tissues.

Adrenal insufficiency is a hormonal-disorder that occurs when the adrenal glands do not produce enough of certain hormones. Adrenal insufficiency can be primary or secondary.

Primary adrenal insufficiency, also called Addison's disease, occurs when the adrenal glands are damaged and cannot produce enough of the hormone cortisol and often the hormone aldosterone. Addison's disease affects one to four of every 100,000 people, in all age groups and both sexes. Addison's disease can be life-threatening. Secondary adrenal insufficiency occurs when the pituitary gland-a bean-sized organ in the brain-fails to produce enough adrenocorticotropin (ACTH), a hormone that stimulates the adrenal glands to produce cortisol. If ACTH output is too low, cortisol production drops. Eventually, the adrenal glands can shrink due to lack of ACTH stimulation. Secondary adrenal insufficiency is much more common than Addison's disease.

VI.2.2 *Summary of treatment benefits*

Hydrocortisone tablets contain a medicine called hydrocortisone. This belongs to a group of medicines called 'steroids'. These corticosteroids occur naturally in the body, and help to maintain health and well-being. Boosting your body with extra corticosteroid (such as Hydrocortisone Tablets) is an effective way to treat various illnesses involving inflammation in the body. Hydrocortisone Tablets reduce this inflammation, which could otherwise go on making the condition worse.

The role of hydrocortisone in treatment of especially chronic adrenal insufficiency has been firmly established by long-term clinical experience. Treatment of adrenal insufficiency involves substituting the hormones that the adrenal glands are not producing. Cortisol is replaced with a synthetic glucocorticoid such as hydrocortisone. Corticosteroids, such as hydrocortisone, are also frequently used drugs that mediate immunosuppressive and anti-inflammatory effects. They relieve the inflammation, pain and discomfort of many different diseases and conditions. They lessen swelling, redness, itching, and allergic reactions. Therefore they are often used as part of the treatment for a number of different diseases, such as severe allergies or asthma. High doses of corticosteroids are usually required in patients with severe diseases involving major organs. In intensive or emergency therapy, parenteral (given e.g. intravenously or injected in muscle) administration may be required.

VI.2.3 *Unknowns relating to treatment benefits*

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
<p>Increased likelihood to get infections and masking of symptoms of infection</p>	<p>People who receive corticosteroids, such as hydrocortisone, for a long period of time are prone to infections as their immune system can become weak. This is the case especially if high doses are administered.</p> <p>Infections may become more severe than they usually would be and the symptoms that would usually be used to identify such infections can be hidden.</p>	<p>Any current infections and medical history of infections should be taken into account before therapy is initiated.</p> <p>Hydrocortisone should not be given to patients who have microbial infection in their body system without appropriate antimicrobial drug therapy.</p> <p>Live vaccines should not be given during high-dose hydrocortisone therapy.</p> <p>Special attention should be paid for signs and symptoms of infection during hydrocortisone therapy and doctor should be contacted if symptoms appear.</p> <p>Close contact with people who have acute infections should be avoided.</p>
<p>Psychiatric adverse reactions (depression, mania, psychosis)</p>	<p>Psychiatric disorders, such as euphoria, insomnia, mood alterations, personality changes, deep depression, or definite psychotic symptoms, may occur in connection with the use of corticosteroids. During the corticosteroid medication, the condition may become exacerbated in emotionally unstable patients or those with a psychotic tendency.</p> <p>Potentially serious psychiatric adverse effects may occur during therapy. Typically, symptoms appear after a couple of days or weeks from starting the treatment.</p>	<p>Medical history of mental problems should be taken into account and discussed with doctor.</p> <p>Most psychiatric reactions recover after either dose reduction or treatment withdrawal, although specific treatment may be needed.</p> <p>Patients and/or their carers should contact doctor, if psychiatric symptoms develop, especially if depressed mood or suicidal thoughts are suspected.</p> <p>Patients and/or their carers should be aware of the potential psychiatric effects which may occur at reduction of the corticosteroid dose or immediately after cessation of their use.</p>

Risk	What is known	Preventability
<p>Endocrine disorders (Symptoms of too little or too much cortisol in body, diabetes)</p>	<p>Long-term use of corticosteroids may cause suppression of body's own corticosteroid production.</p> <p>Too much corticosteroids in body, especially for long-time, can cause symptoms of Cushing syndrome — a fatty hump between shoulders, a rounded face, and pink or purple stretch marks on skin. Cushing syndrome can also result in high blood pressure, bone loss and, on occasion, diabetes.</p> <p>The severity and duration of these conditions (too little or too much cortisol in body) vary by the patient and depend on the dose, dosing interval, time of day of administration, and length of therapy.</p> <p>If the dose of hydrocortisone is reduced too rapidly serious problems may occur.</p> <p>Hydrocortisone, may increase blood glucose concentration, exacerbate diabetes and predispose patients receiving long-term corticosteroid treatment to diabetes.</p>	<p>Dose should be adjusted individually using the smallest effective dose.</p> <p>Long-term corticosteroid therapy should not be stopped abruptly. The dose should be decreased gradually. If the patient's own corticosteroid production is suppressed, she/he should receive additional corticosteroids in case of stressful situations, such as illness or injury.</p> <p>Medical history of diabetes, glucose intolerance or increased blood sugar should be taken into account and discussed with doctor.</p> <p>The dose of insulin or other antidiabetic drugs may need to be adjusted.</p>
<p>Metabolism & Nutrition Disorders;</p>	<p>Use of hydrocortisone may cause few metabolism and nutrition related disorders including such as increased sodium and fluid retention in the body; weight gain and increased appetite.</p>	<p>Medical history of patient should be taken into account and discussed with doctor.</p>
<p>Nervous System Disorders</p>	<p>Use of hydrocortisone has been reported to cause convulsions, increased intracranial pressure with papilloedema usually after treatment, vertigo, headache, malaise.</p>	<p>None</p>
<p>Eye Disorders</p>	<p>The occurrence of secondary fungal and viral eye infections may increase in patients receiving corticosteroids and there is a risk of corneal perforation, in patients with ocular herpes simplex infection.</p> <p>Long term corticosteroid use may cause cataract, bulging of the eyes, or increased eye pressure, which may lead to glaucoma and a potential subsequent injury to the optic nerve.</p>	<p>Special caution should be administered when treating patients with ocular infections.</p> <p>Medical history of increased eye pressure, cataract or glaucoma should be taken into account and discussed with doctor.</p>

Risk	What is known	Preventability
Gastro-intestinal Disorders (Peptic ulcers and bleeding from stomach or intestine)	<p>Peptic ulcers are sores that develop on the inside lining of esophagus, stomach and the upper portion of small intestine. The most common symptom of a peptic ulcer is abdominal pain.</p> <p>Bleeding can occur as slow blood loss that leads to anemia or as severe blood loss that may require acute hospitalisation.</p> <p>There is no consensus on whether peptic ulcers developing during the treatment are caused by corticosteroids. However corticosteroid therapy may mask the symptoms of peptic ulcers, allowing perforation or bleeding to develop without any notable pain.</p>	<p>Medical history of diseases/conditions affecting alimentary canal and concomitant medications should be taken into account and discussed with doctor.</p> <p>Doctor should be contacted immediately in case of symptoms of stomach pain and bleeding from the anus, black or bloodstained stools and/or vomiting blood.</p>
Skin and Subcutaneous Tissue Disorders	<p>Use of hydrocortisone has been reported to cause Impaired wound healing, thin fragile skin. Patients may experience common skin reaction such as acne, erythema, skin inflammation and increased sweating.</p> <p>Hydrocortisone may suppress reactions to skin tests.</p>	None
Musculoskeletal, Connective Tissue & Bone Disorders; Bones become weak and brittle (osteoporosis)	Bones becoming weak has also been reported commonly because of prolonged high-dose corticosteroid treatment.	Vitamin D and calcium supplements, healthy diet, weight-bearing exercise and certain medications may help to prevent bone loss or strengthen already weak bones.
Cardiac disorder (Heart related disorders)	<p>Use of hydrocortisone has been reported to cause myocardial rupture following recent myocardial infarction, congestive heart failure in susceptible patients.</p> <p>Average and large dosages of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention.</p>	Blood pressure of patients should be monitored regularly.
Drug interaction with pain medicines	Concomitant use of corticosteroids with antiinflammatory pain medicines may increase the risk of bleedings and ulcers in stomach and bowel.	Anti-inflammatory pain medicines should be administered with special caution.

Risk	What is known	Preventability
Administration in children	Pharmacological corticosteroid therapy may cause growth retardation in infancy, childhood and adolescence.	Treatment should be limited to the minimum effective dosage in order to minimise suppression of the hypothalamo-pituitary-adrenal axis and growth retardation. Growth and development of infants and children on prolonged corticosteroid therapy should be carefully monitored.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Hypersensitivity and overdose	Reports of acute toxicity and/or deaths following overdosage with glucocorticoids are rare. No antidote is available. Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually susceptible to ill effects from corticosteroids. In this case, symptomatic treatment should be instituted as necessary. Anaphylactic and hypersensitivity reactions may be treated with adrenaline, positive pressure artificial respiration and aminophylline. The patient should be kept warm and quiet.
Use of hydrocortisone in pregnancy and breast feeding	Hydrocortisone crosses the placenta. Besides replacement therapy, other systemic corticosteroid therapy during pregnancy should be regarded with caution. However, treatment should not be avoided if clearly indicated. If the mother has received hydrocortisone in pharmacological doses during pregnancy, the neonate should be monitored for adrenal insufficiency. Corticosteroid therapy during pregnancy has been associated with foetal growth reduction, particularly in long-term use, and with insignificant contraction of the ductus arteriosus (a blood vessel that connects two major arteries in foetus' heart). During late pregnancy, hydrocortisone may cause adverse effects to the foetus that are similar to those of long-term therapy in general.

Missing information

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for hydrocortisone can be found in the hydrocortisone's EPAR page.

This medicine has no additional risk minimisation measures.

VI.2.6 *Planned post authorisation development plan*

None

VI.2.7 *Summary of changes to the Risk Management Plan over time*

Not applicable – first Risk Management Plan for hydrocortisone.