



Summary of Investigation Results

Hydrocortisone preparations (oral and injectable dosage forms)

July 20, 2021

Non-proprietary name

- a, b. Hydrocortisone sodium succinate
- c. Hydrocortisone
- d. Hydrocortisone sodium phosphate

Branded name (Marketing authorization holder)

- a. Solu-Cortef Injection 100 mg (Pfizer Japan Inc.), and the others
- b. Solu-Cortef for Intravenous Use 250 mg, 500 mg, 1000 mg (Pfizer Japan Inc.), and the others
- c. Cortril Tablets 10 mg (Pfizer Japan Inc.)
- d. Hydrocortone Injection (Aqueous) 100 mg, 500 mg (Nichi-Iko Pharmaceutical Co., Ltd.), and the others

Indications

See Attachment

Summary of revisions

A cautionary statement for hypertrophic cardiomyopathy in neonates and infants should be added to the Pediatric Use section.

Investigation results and background of the revision

Cases of hypertrophic cardiomyopathy have been reported in neonates and infants treated with hydrocortisone preparations overseas. MHLW/PMDA in consultation with expert advisors concluded that revision of the package insert was necessary.

Number of cases and patient mortalities reported in Japan during the previous 3 fiscal years

No cases of hypertrophic cardiomyopathy in neonates and infants have been reported to

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

date.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Attachment

No.	Non-proprietary name	Indications
1.	Hydrocortisone sodium succinate	<p>1. Internal medicine and pediatrics field</p> <p>(1) Endocrine disease Acute adrenocortical insufficiency (adrenal crisis), thyrotoxicosis [thyroid (toxic) crisis], chronic adrenocortical insufficiency (primary, secondary, pituitary, iatrogenic), isolated ACTH deficiency</p> <p>(2) Collagen disease Rheumatic fever (including rheumatic carditis), lupus erythematosus (systemic and chronic discoid)</p> <p>(3) Allergic disease Bronchial asthma, anaphylactic shock, asthmatic bronchitis (including childhood asthmatic bronchitis), allergies/poisoning caused by drugs or other chemical substances (including drug eruption, toxicoderma), urticarial (excluding chronic cases) (limited to severe cases)</p> <p>(4) Neurological disorder Encephalomyelitis (including encephalitis, myelitis) (In the case of primary encephalitis, it should be used for a short period when symptoms of increased intracranial pressure are observed and patients do not sufficiently respond to other treatments.), myasthenia gravis, multiple sclerosis (including neuromyelitis optica), peripheral neuritis (including Guillain-Barré syndrome), Sydenham's chorea, facial palsy, spinal arachnoiditis, spinal cord oedema</p> <p>(5) Digestive disease Regional enteritis, ulcerative colitis</p> <p>(6) Respiratory disease</p>



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

No.	Non-proprietary name	Indications
		<p>Diffuse interstitial pneumonia (pulmonary fibrosis) (including radiation pneumonitis)</p> <p>(7) Severe infection Severe infection (in combination with chemotherapy)</p> <p>(8) Metabolic disease Idiopathic hypoglycaemia</p> <p>(9) Other internal medical diseases Improvement of general condition of severely debilitating illness (including end stage cancer, sprue), malignant lymphoma (lymphosarcoma, reticulosarcoma, Hodgkin's disease, cutaneous reticulosis, mycosis fungoides) and similar diseases (closely related diseases), eosinophilic granuloma, recurrent metastatic breast cancer</p> <p>2. Surgical field Adrenalectomy, organ/tissue transplantation, surgical invasion for patients with adrenal cortical insufficiency, pulmonary oedema after invasion, surgical shock and surgical shock-like state, brain oedema, side effect due to transfusion, bronchospasm (intraoperative), prevention of peritoneal adhesions after surgery, snake/insect venom (including severe insect bite)</p> <p>3. Orthopedic field Rheumatoid arthritis, juvenile rheumatoid arthritis (including Still's disease), polymyalgia rheumatica, ankylosing spondylitis (rheumatoid spondylitis), limb arthritis accompanied by ankylosing spondylitis (rheumatoid spondylitis)</p> <p>4. Urological field Prostate cancer (when other treatments are ineffective), penile induration</p>



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

No.	Non-proprietary name	Indications
		<p>5. Ophthalmologic field Post-operative inflammation of ophthalmologic field</p> <p>6. Dermatological field Eczema/dermatitis group (acute eczema, subacute eczema, chronic eczema, contact dermatitis, nummular eczema, autosensitization dermatitis, atopic dermatitis, infancy and childhood dermatitis, lichen simplex chronicus Vidal, other neurodermatitises, seborrhoeic dermatitis, keratoderma tylodes palmaris progressiva, other hand dermatitides, genital or anal eczema, eczema/dermatitis of auricle and ear canal, eczema/dermatitis around the nasal vestibule and alar, etc.) (not recommended in non-severe cases unless absolutely necessary), psoriasis and similar symptoms [psoriasis vulgaris (severe cases), psoriatic arthritis, erythrodermic psoriasis, pustular psoriasis, acrodermatitis continua, impetigo herpetiformis, Reiter's syndrome], erythema (erythema exudativum multiforme, erythema nodosum) (limited to severe cases in case of erythema exudativum multiforme), Weber-Christian disease, oculomucocutaneous syndrome [ectodermosis erosiva pluriorificialis, Stevens-Johnson syndrome, cutaneous stomatitis, Fuchs' syndrome, Behcet's disease (in the absence of ocular symptoms), Lipschutz' acute vulva ulcer], pemphigus group (pemphigus vulgaris, pemphigus foliaceus, Senear-Usher syndrome, pemphigus vegetans), Duhring dermatitis herpetiformis (including pemphigoid, herpes gestationis), herpes zoster (limited to severe cases), ulcerative chronic pyoderma, erythroderma (including Hebra pityriasis rubra)</p> <p>7. Otorhinolaryngological field Meniere's disease and Meniere's syndrome, acute sensorineural hearing loss, laryngitis/laryngeal oedema, oesophageal inflammation (corrosive oesophagitis, after directoscope use) and after oesophageal dilation procedure, allergic rhinitis, pollinosis (hay fever), dysosmia, refractory stomatitis and glossitis (those that cannot be treated with local therapy)</p>



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

No.	Non-proprietary name	Indications
		8. Oral surgery field Post-therapy after oral surgery field surgery
2.		[Solu-Cortef for Intravenous Use 250 mg, 500 mg, 1000 mg] Emergency relief in acute circulatory failure (haemorrhagic shock, traumatic shock) and shock-like state [Solu-Cortef for Intravenous Use 250 mg, 500 mg] Bronchial asthma
3.	Hydrocortisone	<ul style="list-style-type: none">• Chronic adrenocortical insufficiency (primary, secondary, pituitary, iatrogenic), acute adrenocortical insufficiency (adrenal crisis), adrenogenital syndrome, subacute thyroiditis, malignant exophthalmos accompanied by thyroid disease, isolated ACTH deficiency• Rheumatoid arthritis, juvenile rheumatoid arthritis (including Still's disease), rheumatic fever (including rheumatic carditis)• Lupus erythematosus (systemic and chronic discoid), systemic vasculitis (including Takayasu's arteritis, polyarteritis nodosa, microscopic polyangiitis, granulomatosis with polyangiitis), polymyositis (dermatomyositis), scleroderma• Nephrosis and nephrotic syndrome• Bronchial asthma, allergy/poisoning caused by drugs and other chemical substances (including drug eruption, toxicoderma), serum sickness



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

No.	Non-proprietary name	Indications
		<ul style="list-style-type: none">• Severe infection (in combination with chemotherapy)• Haemolytic anaemia (immunological or suspected immunological mechanism), leukaemia (acute leukaemia, chronic myeloid leukaemia transformation, chronic lymphocytic leukaemia) (including leukaemia cutis), granulocytopenia (essential, secondary), peliosis (thrombocytopenic and non-thrombocytopenic), aplastic anaemia• Regional enteritis, ulcerative colitis• Improvement of the general condition of severely debilitating illness (including end stage cancer, sprue)• Chronic hepatitis (active type, acute flare type, cholestasis type) (limited to refractory chronic hepatitis with persistent and markedly abnormal liver function that do not respond to general treatment), hepatic cirrhosis (active type, accompanied by refractory ascites, accompanied by cholestasis)• Sarcoidosis (excluding bilateral hilar lymphadenopathy only)• Pulmonary tuberculosis (limited to miliary tuberculosis, severe tuberculosis) (in combination with anti-tuberculosis drugs), tuberculous pleurisy (in combination with anti-tuberculosis drugs), tuberculous pericarditis (in combination with anti-tuberculosis drugs)• Encephalomyelitis (including encephalitis, myelitis) (In the case of primary encephalitis, it should be used for a short period when symptoms of increased intracranial pressure are observed and patients do not sufficiently respond to other treatments.), peripheral neuritis (including Guillain-Barré syndrome), myotonia, multiple sclerosis (including neuromyelitis optica), Sydenham's chorea, facial palsy, spinal arachnoiditis• Malignant lymphoma (lymphosarcoma, reticulosarcoma, Hodgkin's disease, cutaneous reticulosis, mycosis fungoides) and similar diseases (closely related diseases), eosinophilic granuloma, recurrent metastatic breast cancer



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

No.	Non-proprietary name	Indications
		<ul style="list-style-type: none">• Idiopathic hypoglycaemia• Fever of unknown origin• Adrenalectomy, surgical invasion for patients with adrenal cortical insufficiency• Snake/insect venom (including severe insect bite)• Prevention of adhesion after salpingoplasty• Eczema/dermatitis group* (acute eczema, subacute eczema, chronic eczema, contact dermatitis, nummular eczema, autosensitization dermatitis, atopic dermatitis, infancy and childhood dermatitis, lichen simplex chronicus Vidal, other neurodermatitises, seborrhoeic dermatitis, keratoderma tylodes palmaris progressiva, other hand dermatitises, genital or anal eczema, eczema/dermatitis of auricle and ear canal, eczema/dermatitis around the nasal vestibule and alar, etc.) (not recommended in non-severe cases unless absolutely necessary), prurigo group* (including strophulus infantum, urticaria-like lichen, urticaria perstans (limited to severe cases), urticarial (excluding chronic case) (limited to severe case), psoriasis and similar symptoms* [psoriasis vulgaris (severe cases), psoriatic arthritis, erythrodermic psoriasis, pustular psoriasis, acrodermatitis continua, impetigo herpetiformis, Reiter's syndrome], palmoplantar pustulosis* (limited to severe case), scleredema adutorum, erythema (erythema exudativum multiforme, erythema nodosum) (limited to severe cases in case of erythema exudativum multiforme), Weber-Christian disease, oculomucocutaneous syndrome [ectodermosis erosiva pluriorificialis, Stevens-Johnson syndrome, cutaneous stomatitis, Fuchs' syndrome, Behcet's disease (in the absence of ocular symptoms), Lipschutz' acute vulva ulcer], alopecia areata* (limited to malignant type), pemphigus group (pemphigus vulgaris, pemphigus foliaceus, Senejar-Usher syndrome, pemphigus vegetans), Duhring dermatitis herpetiformis (including pemphigoid, herpes gestationis), erythroderma* (including Hebra pityriasis rubra), lupus miliaris disseminatus faciei (limited



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

No.	Non-proprietary name	Indications
		<p>to severe cases), allergic vasculitis and similar symptoms (including pityriasis lichenoides et varioriformis acuta)</p> <ul style="list-style-type: none">• Symptomatic treatment of inflammatory diseases of the inner eye/optic nerve/orbit/ocular muscles (uveitis, chorioretinitis, retinal vasculitis, optic neuritis, orbital pseudotumour, orbital apex syndrome, ophthalmoplegia), cases where eye drops are inappropriate or ineffective for symptomatic treatment of inflammatory diseases of the external and anterior segment of the eye (blepharitis, conjunctivitis, keratitis, scleritis, iridocyclitis)• Acute/chronic otitis media, serous otitis media/eustachian tube stenosis, Meniere's disease and Meniere's syndrome, acute sensorineural hearing loss, allergic rhinitis, pollinosis (hay fever), progressive gangrenous rhinitis, oesophageal inflammation (corrosive oesophagitis, after directoscope use) and after oesophageal dilation procedure, post-therapy of otorhinolaryngological field surgery• Refractory stomatitis and glossitis (those that cannot be treated with local therapy) <p>* It should be used only when the effects of topical agents are ineffective or when it is assumed that effectiveness cannot be expected.</p>
4.	Hydrocortisone sodium phosphate	Emergency relief in surgical shock or shock-like state or intra- and postoperative shock