NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DEXMETHSONE dexamethasone 0.5 mg tablet.

DEXMETHSONE dexamethasone 4 mg tablet.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains either dexamethasone 0.5 mg or 4 mg.

Excipients with known effect: lactose monohydrate and wheat starch (0.5 mg tablet only). For the list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

0.5 mg: Round, slightly biconvex white tablets plain on one side and 'DS/0.5' with breakline on the other side.

4 mg: Round, white tablets plain on one side and 'DS/4' with breakline on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Dexamethasone is indicated for replacement therapy in secondary adrenal insufficiency arising from insufficient corticotrophin secretion. It is not indicated for primary adrenal insufficiency states, such as Addison's disease or after adrenalectomy. In such cases hydrocortisone and fludrocortisone in combination is more appropriate.

Dexamethasone is also indicated for allergic disorders such as bronchial asthma and allergic skin reactions, blood disorders such as leukaemia, thrombocytopoenia and haemolytic anaemias, selected collagen and rheumatic disorders (only rarely in rheumatoid arthritis), gastrointestinal disorders such as inflammatory bowel disease, connective tissue disorders such as arteritis, systemic lupus erythematosus (but not scleroderma), some skin diseases such as pemphigus, oedema, some eye disorders, certain neoplastic disorders such as cerebral neoplasm, secondary hypercalcaemia, and acute leukaemia in children. It may also be used to prevent neonatal respiratory distress syndrome and in the diagnosis of Cushing's syndrome.

Dexamethasone 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.

4.2 Dose and method of administration

The dose of dexamethasone varies according to the condition being treated. The tablets are for oral administration in a dose of 4 mg-20 mg daily.

The duration of therapy is dependent on the clinical response of the patient and as soon as improvement is indicated, the dosage should be adjusted to the minimum required to

maintain the desired response. Withdrawal of dexamethasone at completion of treatment should be gradual.

For the treatment of COVID-19
Patients aged 12 years and over: 6 mg orally, once a day for up to 10 days.

Duration of treatment should be guided by clinical response and individual patient requirements. No dose adjustment is needed for elderly patients or patients with renal or hepatic impairment.

4.3 Contraindications

- Hypersensitivity to any ingredient
- Systemic infections unless specific anti-infective therapy is given
- Live virus immunisation

4.4 Special warnings and precautions for use

Caution is necessary when oral corticosteroids are used in patients with the following conditions and frequent monitoring is necessary:

- Hypertension
- Hypothyroidism
- Congestive Heart failure or recent myocardial infarction
- Liver failure
- Renal insufficiency
- Diabetes mellitus or in those with a family history of diabetes
- Osteoporosis
- Glaucoma
- Patients with a history of severe affective disorders particularly of steroid induced psychoses
- Epilepsy and/or seizure disorder
- Peptic ulceration
- Previous steroid myopathy
- Tuberculosis
- Patients with myasthenia gravis receiving anticholinesterase therapy since corticosteroid use may decrease plasma anticholinesterase activity
- Patients with thromboembolic disorders
- Patients with Duchenne's muscular dystrophy since transient rhabdomyolysis and myoblobinuria have been reported following strenuous physical activity
- Patients with Cushing's disease.

Adrenocortical insufficiency
Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration and duration of therapy.

Symptoms of adrenal insufficiency include: malaise, muscle weakness, mental changes, muscle and joint pain, desquamation of the skin, dyspnoea, anorexia, nausea and vomiting, fever, hypoglycaemia, hypotension and dehydration.

During prolonged courses of corticosteroid therapy sodium intake may need to be reduced and calcium and potassium supplements may be necessary. Monitoring of fluid intake and output and daily weight records may give an early warning of fluid retention.

Acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are

withdrawn abruptly, therefore withdrawal of corticosteroids should always be gradual. A degree of adrenal insufficiency may persist for 6 to 12 months; therefore in any situation of stress occurring during that period steroid therapy may need to be reinstituted. Since mineralocorticoid secretion may be impaired treatment with salt and/or a mineralocorticoid may also be needed. During prolonged therapy, any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage.

Anti-inflammatory/ Immunosuppressive effects and Infection
Suppression of the inflammatory response and immune function increases susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognized when corticosteroids are used. The immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

Chickenpox is of particular concern since this may be fatal in immunosuppressed patients. Patients without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunization is recommended for non-immune patients who do come into contact with chickenpox. If a diagnosis of chickenpox is confirmed the illness warrants specialist care and urgent treatment.

Live vaccines are contraindicated in individuals on high doses of corticosteroids and should be postponed until at least 3 months after stopping corticosteroid therapy.

Ocular effects
Prolonged use of corticosteroids may produce subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves.

Corticosteroids should only be initiated in patients with ocular herpes simplex with appropriate viral cover by ophthalmologists because of the risk of corneal scaring, loss of vision and corneal perforation.

Psychiatric effects
Patients and/or carers should be warned that potentially severe psychiatric reactions may occur. Symptoms typically emerge within a few days or weeks of starting treatment. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients and/or carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected.

Particular care is required when considering the use of corticosteroids in patients with existing or previous history of severe affective disorders.

Psychic derangements range from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations.

Pheochromocytoma crisis
Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

For the treatment of COVID-19
Systemic corticosteroids should not be stopped for patients who are already treated with systemic (oral) corticosteroids for other reasons (e.g. patients with chronic obstructive pulmonary disease) but not requiring supplemental oxygen.

Use in children
Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible and therefore long-term administration of pharmacological doses should be avoided. If prolonged therapy is necessary, treatment should be limited to the minimum suppression of the hypothalamo-pituitary adrenal axis and growth retardation, the growth and development of infants and children should be closely monitored. Treatment should be administered where possible as a single dose on alternate days.

Children are at special risk from raised intracranial pressure.

Use in the elderly
Longterm use in the elderly should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, hypokalaemia, susceptibility to infection and thinning of the skin. Close medical supervision is required to avoid life threatening reactions.

Instructions to patients
Patients should be warned of the long term adverse effects of corticosteroids.

The necessity for increasing dosage in situations of intercurrent stress or infection should be advised. The patient should seek medical advice for any but the most minor infections. The danger of interrupting steroid therapy should be explained and the need to inform medical personnel that corticosteroid medication is being taken.

Patients on a dose reduction regime should be advised of the symptoms of acute glucocorticoid deficiency (faintness, weakness, vomiting).

Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice.

4.5 Interaction with other medicines and other forms of interaction
Hepatic microsomal enzyme inducers
Medicines that induce hepatic enzyme cytochrome P450 isozyme 3A4 such as Phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and aminogluethimide may reduce the therapeutic efficacy of corticosteroids by increasing the rate of metabolism.

Hepatic microsomal enzyme inhibitors
Medicines that inhibit hepatic enzyme cytochrome P450 isozyme 3A4 such as ketoconazole, ciclosporin or ritonavir may decrease glucocortiocoid clearance. A reduction in corticosteroid dose may be needed to reduce the risk of adverse effects.

Antidiabetic agents
Corticosteroids may increase blood glucose levels. Patients may need dosage adjustment of any concurrent antidiabetic therapy.

Nonsteroidal antiinflammatory drugs (NSAIDs)
Concomitant administration may increase the risk of GI ulceration. Aspirin should be used

cautiously in conjunction with corticosteroids in patients with hypothrombinaemia. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Patients should be observed closely for adverse effects of either medicine.

Anticoagulants
Response to anticoagulants may be reduced or less often enhanced by corticosteroids. Close monitoring of the INR or prothrombin time is recommended.

Antifungals
The risk of hypokalaemia may be increased with amphotericin.

Cardiac glycosides
There is a risk of toxicity if hypokalaemia occurs due to corticosteroid treatment.

Mifepristone
The effect of corticosteroids may be reduced for 3-4 days after mifepristone.

Vaccines
Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

Oestrogens
Oestrogens may potentiate the effects of glucocorticoids. The dose of corticosteroid may need to be adjusted if oestrogen therapy is commenced or stopped.

Somatropin
The growth promoting effect may be inhibited.

Sympathomimetics
There is an increased risk of hypokalaemia if high doses of corticosteroids are given with high doses of salbutamol, salmeterol, terbutaline or formoteral.

Diuretics
Excessive potassium loss may be experienced if glucocorticoids and potassium-depleting diuretics (such as frusemide and thiazides) or carbonic anhydrase inhibitors (such as acetazolamide) are given together.

Antacids
Concurrent use of antacids may decrease absorption of corticosteroids – efficacy may be decreased sufficiently to require dosage adjustments in patients receiving small doses of corticosteroids.

4.6 Fertility, pregnancy and lactation
No data included.

4.7 Effects on ability to drive and use machines
No data included.

4.8 Undesirable effects
Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare

professionals are asked to report any suspected adverse reactions
https://pophealth.my.site.com/carmreportnz/s/

Body as a whole:
Leucocytosis, hypersensitivity including anaphylaxis, thromboembolism, fatigue, malaise

Cardiovascular:
Congestive heart failure in susceptible patients, hypertension

Gastrointestinal:
Dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, increased appetite which may result in weight gain, diarrhoea, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis

Musculoskeletal:
Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, myalgia

Metabolic/Nutritional:
Sodium and water retention, hypokalaemic alkalosis, potassium loss, negative nitrogen and calcium balance

Skin:
Impaired healing, hirsutism, skin atrophy, bruising, striae, telangiectasia, acne, increased sweating, may suppress reactions to skin tests, pruritis, rash, urticarial

Endocrine:
Suppression of the hypothalamopituitary adrenal axis particularly in times of stress as in trauma surgery or illness, growth suppression in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea. Cushingoid facies, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, manifestation of latent diabetes mellitus, increased appetite.

Nervous system:
Euphoria, psychological dependence, depression, insomnia, dizziness, headache, vertigo, raised intracranial pressure with papilloedema in children, usually after treatment withdrawal. Aggravation of schizophrenia, Aggravation of epilepsy suicidal ideation, mania, delusions, hallucinations, irritability anxiety, insomnia and cognitive dysfunction. In adults the frequency of severe psychiatric reactions has been estimated to be 5-6%.

Eye disorders:
Increased intraocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease

Anti-inflammatory and Immunosuppressive effects:
Increased susceptibility to and severity of infections with suppression of clinical symptoms and signs. Opportunistic infections, recurrence of dormant tuberculosis.

Withdrawal symptoms:
Too rapid a reduction of corticosteroids following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A steroid withdrawal syndrome seemingly unrelated to adrenocortical insufficiency may also occur and include symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, weight loss, and/or hypotension.

Post Marketing
Skin and subcutaneous tissue disorders:
Panniculitis (frequency 'not known').

4.9 Overdose

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

Adverse effects related to dexamethasone normally develop only after prolonged use. Treatment is symptomatic and where possible the dexamethasone dose should be reduced gradually.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dexamethasone is (11β,16α)-9-Fluoro-11, 17, 21-trihydroxy-16-methylpregna1, 4-diene-3, 20-dione. Its molecular formula is $C_{22}H_{29}FO_5$ and its molecular weight is 392.5.

Mechanism of action
Dexamethasone is a synthetic corticosteroid exhibiting both anti-inflammatory and immuno-suppressant properties. The anti-inflammatory potency of dexamethasone has been estimated as 25x that of hydrocortisone. It has little mineralocorticoid activity.

The RECOVERY trial (Randomised Evaluation of COVid-19 thERapY,) is an investigator-initiated, individually randomised, controlled, open-label, adaptive platform trial to evaluate the effects of potential treatments in patients hospitalised with COVID-19.

The trial was conducted at 176 hospital organizations in the United Kingdom.

There were 6425 Patients randomised to receive either dexamethasone (2104 patients) or usual care alone (4321 patients). 89% of the patients had laboratory-confirmed SARS-CoV-2 infection.

At randomization, 16% of patients were receiving invasive mechanical ventilation or extracorporeal membrane oxygenation, 60% were receiving oxygen only (with or without non invasive ventilation), and 24% were receiving neither.

The mean age of patients was 66.1+/-15.7 years. 36% of the patients were female. 24% of patients had a history of diabetes, 27% of heart disease and 21% of chronic lung disease.

<u>Primary endpoint</u>
Mortality at 28 days was significantly lower in the dexamethasone group than in the usual care group, with deaths reported in 482 of 2104 patients (22.9%) and in 1110 of 4321 patients (25.7%), respectively (rate ratio, 0.83; 95% confidence interval [CI], 0.75 to 0.93; P<0.001).

In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and in those receiving supplementary oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94).

There was no clear effect of dexamethasone among patients who were not receiving any respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91 to 1.55).

Secondary endpoints

Patients in the dexamethasone group had a shorter duration of hospitalization than those in the usual care group (median, 12 days vs. 13 days) and a greater probability of discharge alive within 28 days (rate ratio, 1.10; 95% CI, 1.03 to 1.17).

In line with the primary endpoint the greatest effect regarding discharge within 28 days was seen among patients who were receiving invasive mechanical ventilation at randomization (rate ratio 1.48; 95% CI 1.16, 1.90), followed by oxygen only (rate ratio, 1.15 ;95% CI 1.06-1.24) with no beneficial effect in patients not receiving oxygen (rate ratio, 0.96 ; 95% CI 0.85-1.08).

Outcome	Dexamethasone (N=2104)	Usual Care (N=4321)	Rate or Risk Ratio (95% CI)*
		no./total no. of patients (%)	
Primary outcome			
Mortality at 28 days	482/2104 (22.9)	1110/4321 (25.7)	0.83 (0.75–0.93)
Secondary outcomes			
Discharged from hospital within 28 days	1413/2104 (67.2)	2745/4321 (63.5)	1.10 (1.03–1.17)
Invasive mechanical ventilation or death†	456/1780 (25.6)	994/3638 (27.3)	0.92 (0.84–1.01)
Invasive mechanical ventilation	102/1780 (5.7)	285/3638 (7.8)	0.77 (0.62–0.95)
Death	387/1780 (21.7)	827/3638 (22.7)	0.93 (0.84–1.03)

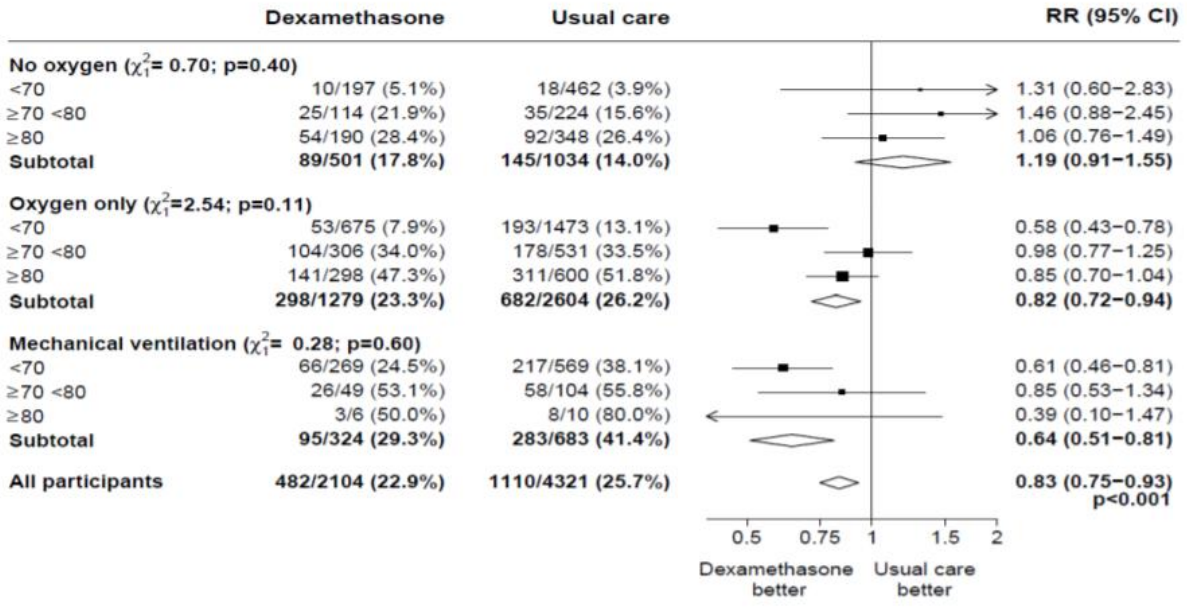
* Rate ratios have been adjusted for age with respect to the outcomes of 28-day mortality and hospital discharge. Risk ratios have been adjusted for age with respect to the outcome of receipt of invasive mechanical ventilation or death and its subcomponents.
† Excluded from this category are patients who were receiving invasive mechanical ventilation at randomization.

Safety

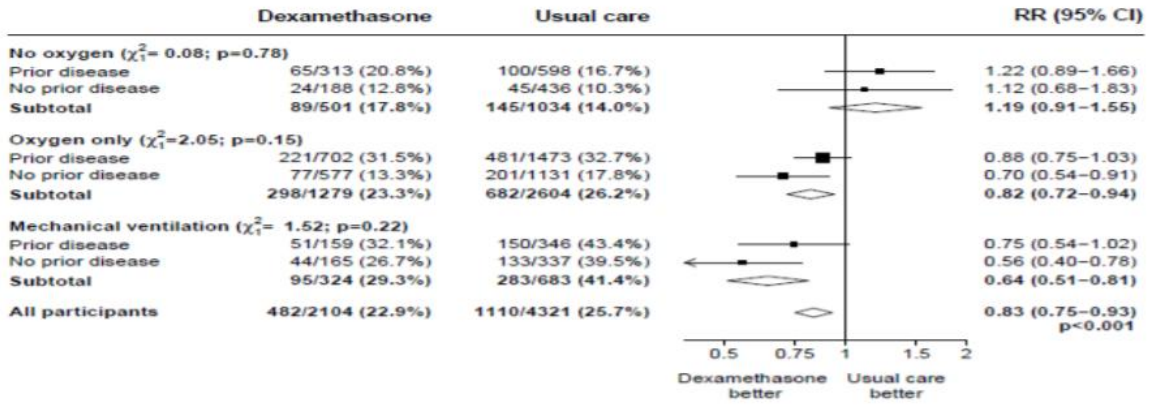
There were four serious adverse events (SAEs) related to study treatment: two SAEs of hyperglycaemia, one SAE of steroid-induced psychosis and one SAE of an upper gastrointestinal bleed. All events resolved.

Subgroup analyses

Effects of allocation to DEXAMETHASONE on 28−day mortality, by age and respiratory support received at randomisation[2]



Effects of allocation to DEXAMETHASONE on 28−day mortality, by respiratory support received at randomisation and history of any chronic disease.[3]



[2, 3] (source: Horby P. et al., 2020; https://www.medrxiv.org/content/10.1101/2020.06.22.20137273v1 ; doi: https://doi.org/10.1101/2020.06.22.20137273)

5.2 Pharmacokinetic properties

Dexamethasone is readily absorbed after oral administration achieving peak plasma concentrations after one hour. Binding to plasma proteins is less than for most other corticosteroids.

The biological half-life is approximately 190 minutes. Dexamethasone penetrates tissue and cerebrospinal fluid.

Elimination occurs via metabolism and renal excretion.

5.3 Preclinical safety data

No data included.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients include lactose monohydrate, magnesium stearate, povidone and wheat starch (0.5 mg tablet) or maize starch (4 mg tablet).

6.2 Incompatibilities

No data included.

6.3 Shelf life

0.5 mg: 36 months
4 mg: 36 months.

6.4 Special precautions for storage

Store at or below 30^{0}C, protected from light and moisture and kept out of reach of children.

6.5 Nature and contents of container

Plastic HDPE bottle of 30 tablets.

6.6 Special precautions for disposal and other handling

No data included.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Pharmacy Retailing (NZ) Limited trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand

Telephone: (09) 9185 100
aspen@aspenpharma.co.nz

9. DATE OF FIRST APPROVAL

Dexmethsone 0.5 mg tablets: 27/09/2012
Dexmethsone 4 mg tablets: 16/12/2010

10. DATE OF REVISION OF THE TEXT

8 April 2026

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.8	Addition of panniculitis AE with frequency 'not known'. Reporting URL changed to https://pophealth.my.site.com/carmreportnz/s/
4.9	'Risk assessment' added to the text.