Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dexamethasone 2mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2mg of Dexamethasone.

Excipient with known effect:
Each tablet contains approximately 116mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

Round, 6 mm, flat, white tablet with the code 'XC/8' engraved on one surface and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dexamethasone tablets are used for the treatment of various inflammatory and autoimmune diseases e.g.:

Rheumatism, as pain, stiffness or limitation of motion, especially in the joints and related structures, including muscles, bursae, tendons, fibrous tissue;

Collagen disease, as lupus erythematosus, dermatomyositis, polyarteritis nodosa, thrombotic purpura and rheumatoid arthritis;

Allergies, as status asthmaticus, bronchial asthma, contact dermatitis, inflammatory processes of the eye and its adnexa, severe hypersensitivity reactions to drugs or insect stings, anaphylactic shock, impending allograft rejection;

Primary or secondary adrenocortical insufficiency, and **adrenogenital syndromes**.
Besides Dexamethasone is used as an adjunct in the control of **cerebral oedema** (not in those cases where the oedema is caused by head injury), for treatment of **lymphocytic leukaemia**, as **anti-emetic** in antineoplastic regimens and for palliative treatment in terminal stages of **neoplastic disease.**

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 Posology and method of administration

Method of administration
Glucocorticoids may be administered by a number of routes, depending on the nature of the disease and the condition of the patient. Localised therapy is generally preferred because it minimises adverse effects. When systemic administration is required, the oral route is preferred for ease in regulation of dose and the variety in regimens.
Dexamethasone tablets should be taken **orally**, preferably with some fluid.

Posology
The **dosage of Dexamethasone tablets** depends on the severity of the condition and the response of the patient. Undesirable effects, such as suppression of the hypothalamus-pituitary-adrenal (HPA) axis may be minimised by using the lowest effective dose for the minimum period, preferably by taking the tablet(s) in the morning and if disease control will allow alternate day therapy. Systemic dexamethasone administered in the evening is more likely to cause clinically significant HPA suppression.

Alternate day dosing is not appropriate for patients with established adrenal insufficiency. Frequent patient review is required to appropriately titrate the dose against disease activity. If no favourable response is noted within a couple of days, continuation of glucocorticoid therapy is undesirable.

Adults
The usual **dose** in adults is 0.5-10 mg per day. As soon as symptoms diminish, the dose should be reduced under continuous observation of the clinical picture to the lowest possible level, or tapered off completely by following the withdrawal schedule below.

Paediatric population
Dexamethasone should only be administered to children with caution, since glucocorticoids can induce growth retardation. The daily dose should be determined by the physician for each child individually.

Prolonged therapy
During **prolonged therapy** any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage.

Withdrawal of prolonged therapy
In patients who have received dexamethasone for more than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out (tapered off over weeks or months) depends largely on whether the disease is likely to relapse as the dose of systemic glucocorticoids is reduced. Clinical assessment of disease activity may therefore be needed during withdrawal. If the disease is unlikely to relapse on withdrawal but there is uncertainty about hypothalamus-pituitary-adrenal (HPA) suppression, the dose of systemic dexamethasone may be reduced rapidly to physiological doses. Once a daily dose of approx. 1 mg dexamethasone is reached, dose reduction should be slower to allow the HPA-axis to recover.
Abrupt withdrawal of systemic dexamethasone treatment, which has continued for up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses up to approx. 6 mg dexamethasone for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression, in the majority of patients.

In the following patient groups, gradual withdrawal of systemic dexamethasone therapy should be considered even after courses lasting 3 weeks or less:

- Patients who have had repeated courses of systemic dexamethasone (or other corticosteroids), particularly if taken for more than 3 weeks.
- When a short course has been prescribed within one year of cessation of long-term therapy (months or years).
- Patients who may have reasons for adrenocortical insufficiency other than exogenous dexamethasone (or other corticosteroid) therapy.
- Patients receiving doses of systemic dexamethasone higher than approx. 6 mg.
- Patients repeatedly taking doses in the evening.

Patients who, during systemic treatment, encounter stresses such as trauma, surgery or infection and who are at risk of adrenal insufficiency, should receive additional systemic dexamethasone cover during these periods. This includes patients who have finished a course of systemic dexamethasone of less than three weeks duration in the week prior to the stress. Patients on systemic dexamethasone therapy who are at risk of adrenal suppression and are unable to take tablets by mouth should receive parenteral dexamethasone cover during these periods.

Too rapid a reduction of dexamethasone dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. Characteristic symptoms of a "withdrawal syndrome" that may occur are fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

<u>For the treatment of Covid-19</u>
Adult patients 6 mg PO once a day for up to 10 days.
Paediatric population
Paediatric patients (adolescents aged 12 years and older) are recommended to take 6mg/dose PO once a day for up to 10 days. Duration of treatment should be guided by clinical response and individual patient requirements.
Elderly, renal impairment, hepatic impairment
No dose adjustment is needed.

4.3 Contraindications

- gastric and duodenal ulcer;
- acute infections: viral infections and systemic fungal infections (bacterial infections: see section 4.4. Special warnings and precautions for use);
- hypersensitivity to the active substance or to any of the excipients listed in section 6.1;
- parasitic infections;
- vaccination with live vaccines (see section 4.4. Special warnings and precautions for use)

4.4 Special warnings and precautions for use

In post-marketing experience tumour lysis syndrome (TLS) has been reported in patients with haematological malignancies following the use of dexamethasone alone or in combination with other chemotherapeutic agents. Patients at high risk of TLS such as patients with high proliferative rate, high tumour burden, and high sensitivity to cytotoxic agents, should be monitored closely and appropriate precaution taken.

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must therefore always be gradual to avoid acute adrenal insufficiency, being tapered off over weeks or months according to the dose and duration of treatment (see "Withdrawal of prolonged therapy" above). During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

Anti-inflammatory/Immunosuppressive effects. Glucocorticoid therapy is non-specific, suppresses the symptoms and signs of disease and decreases the resistance to infections. 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 recognised. Strong antimicrobial therapy should accompany glucocorticoid therapy when necessary.

Vaccines should not be given to individuals with glucocorticoid therapy-induced immunosuppression. Vaccination with live vaccines, e.g. **Chickenpox** is of particular concern. Chickenpox is a normally minor illness but may be fatal in immunosuppressed patients. Patients (or parents of children) 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 with varicella/zoster immunoglobin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and even the dose may need to be increased.

Measles can have a more serious or even fatal course in immunosuppressed patients. In such children or adults, particular care should be taken to avoid exposure to measles. If exposed, prophylaxis with intramuscular pooled immunoglobulin (IVIG) may be indicated. Exposed patients should be advised to seek medical advice without delay.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerve and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Visual disturbance. Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

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

Glucocorticoids can cause dose-related **growth retardation** in infancy, childhood and adolescence, which may be irreversible. Therefore, Dexamethasone should only be used in children with caution.

The common adverse effects of systemic glucocorticoids may be associated with more serious consequences in **old age**, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

Particular care is required when considering the use of systemic glucocorticoids in patients with the following conditions and frequent patient monitoring is necessary:

- Osteoporosis (post-menopausal women are particularly at risk);
- Hypertension or congestive heart failure;
- Diabetes mellitus (or a family history of diabetes);
- History of tuberculosis;
- Glaucoma (or a family history of glaucoma);
- Previous glucocorticoid-induced myopathy;
- Liver failure;
- Renal insufficiency;
- Epilepsy;
- Peptic ulceration.

Patients and/or carers should be warned that potentially severe psychiatric adverse reactions **may** occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 for pharmacokinetic interactions that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary.

Patient/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

Dexamethasone Tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Preterm neonates: Available evidence suggests long-term neurodevelopment adverse events after early treatment (< 96 hours) of premature infants with chronic lung disease at starting doses of 0.25mg/kg twice daily.

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.

4.5 Interaction with other medicinal products and other forms of interactions

Rifampin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone and aminoglutethimide enhance the metabolism of glucocorticoids and the therapeutic effects may be reduced.

Dexamethasone is a moderate inducer of CYP 3A4. Co-administration of dexamethasone with other drugs that are metabolized by CYP 3A4 (e.g., indinavir,erythromycin) may increase their clearance, resulting in decreased plasma concentrations.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.
The desired effects of hypoglycaemic agents (including insulin), antihypertensives and diuretics are antagonised by glucocorticoids.

The effects of anticholinesterases are antagonised by glucocorticoids in myasthenia gravis.

Concurrent use of potassium-depleting diuretics (e.g. acetazolamide, loop diuretics, thiazide diuretics or carbenoxolone) and glucocorticoids may result in severe hypokalaemia.

The efficacy of coumarin anticoagulants may be altered by concurrent glucocorticoid therapy and close monitoring of the International Normalised Ratio or prothrombin time is required.

The renal clearance of salicylates is increased by glucocorticoids and steroid withdrawal may result in salicylate intoxication.

Combination of corticosteroids with ulcer-inducing agents (e.g. NSAID's) enhances the risk of peptic ulceration.

4.6 Fertility, pregnancy and lactation

Pregnancy
Dexamethasone readily crosses the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intrauterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. **See also section 5.3 of the SmPC.**

When administered for prolonged periods or repeatedly during pregnancy, systemic glucocorticoids increase the risk of intra-uterine growth retardation (IUGR). There is no evidence for an increased incidence of IUGR following short-term treatment, such as prophylactic treatment for neonatal respiratory distress syndrome. In this case (to prevent respiratory distress syndrome), glucocorticoids are essential.

Patients with pre-eclampsia or fluid retention require close monitoring. Dexamethasone should, for maternal indications, not be used during pregnancy unless clearly necessary.
Adrenal suppression in the neonate following prenatal glucocorticoid exposure is to be expected.

Breast-feeding
No data are available on the transfer of dexamethasone into breast milk. Because corticosteroids are in general excreted into breast milk, and given the lack of experience, breast feeding is discouraged during Dexamethasone therapy.

As with all medicines, before prescribing systemic glucocorticoids in pregnancy or during lactation, the benefits of treatment should be weighed against the potential risks to both mother and child.

4.7 Effects on ability to drive and use machines

Glucocorticoids may cause mood changes (e.g. euphoria or depression) or visual disturbances. If affected, caution should be exercised in driving and operating machinery.

4.8 Undesirable effects

The incidence of predictable undesirable effects of glucocorticoids correlates with the dosage, timing of administration and duration of treatment. The clinician must balance the therapeutic effects of glucocorticoids with their risk for adverse effects, using the lowest possible effective doses for the shortest possible period of time, preferably by dosing in the morning on an alternate day dosing regimen. Early recognition and appropriate management of adverse effects can minimise the potential severe complications of glucocorticoid therapy.

A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood, and

suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations, and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%.

Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

Table 1: Adverse reactions of Dexamethasone

System organ class	Preferred Term(s) or Lower Level Terms Frequency not known*
Blood and lymphatic system disorders	Leucocytosis
Endocrine disorders	Hypothalamo-pituitary disorder, Adrenal suppression, Cushingoid appearance
Eye disorders	Papilloedema (in children with pseudotumour cerebri, usually after withdrawal), Glaucoma, Cataract subcapsular, Corneal thinning, Scleral thinning, Chorioretinopathy, Vision, blurred (see also section 4.4)
Gastrointestinal disorders	Gastric ulcer (haemorrhage), Duodenal ulcer (haemorrhage), dyspepsia, peptic ulcer perforation, Pancreatitis acute
General disorders and administration site conditions	Oedema, Impaired healing
Immune system disorders	Drug hypersensitivity, Anaphylactic reaction, Angioedema
Infections and infestations	Infection (aggravated), opportunistic infection, tuberculosis (reactivated), developing severe Varicella-Zoster Virus Infection, Eye infection viral exacerbated, Eye infection fungal exacerbated, Candidiasis
Injury, poisoning and procedural complications	(Spinal) fracture, Tendon rupture, Contusion
Investigations	Weight increased, Carbohydrate tolerance decreased, Intraocular pressure increased
Metabolism and nutrition disorders	Increased appetite, Diabetes mellitus inadequate control, Lipoprotein deficiency, Calcium deficiency, Sodium retention, Fluid retention, Hypokalaemia, Alkalosis hypokalaemic, in post-marketing experience tumour lysis syndrome (TLS) has been reported very rarely.
Musculoskeletal and connective tissue disorders	Growth retardation (infancy, childhood and adolescence), Osteoporosis, Osteonecrosis, proximal Myopathy
Nervous system disorders	Intracranial pressure increased (in children with pseudotumour cerebri, usually after withdrawal), Epilepsy aggravated
Psychiatric disorders	Nervousness, Euphoric mood, Drug dependence, Depression, Insomnia, Schizophrenia aggravated,
Reproductive system and breast disorders	Menstruation irregular, Amenorrhoea
Skin and subcutaneous tissue disorders	Dermatitis allergic, Hirsutism, Skin atrophy, Telangiectasia, Skin striae, Acne
Vascular disorders	Hypertension, Embolism

*The frequency of adverse reactions: not known (cannot be estimated from the available data).

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. Healthcare professionals are asked to report any suspected adverse reactions via: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2. Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

In animal experiments, the acute toxicity of dexamethasone has been shown to be rather low. Symptoms of acute overdosage that can occur are nausea and vomiting. If vomiting has not yet occurred this can be provoked. For the rest a symptomatic treatment is probably sufficient.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use, Glucocorticoids, ATC code: H02AB02.

Dexamethasone tablets contains as active ingredient dexamethasone, which is a synthetic glucocorticoid with approximately a 7 times higher anti-inflammatory potency than prednisolone and 30 times that of hydrocortisone.

Glucocorticoids are produced and secreted by the adrenal cortex and are an intrinsic part of the hypothalamus-pituitary-adrenal axis (HPA-axis). In physiological concentrations glucocorticoids, both naturally occurring (hydrocortisone or cortisone) or synthetic (like dexamethasone) exert a broad range of effects on multiple organ systems and tissues; they affect carbohydrate, protein, lipid and calcium metabolism and have effects on fluid and electrolyte balance and are important for support of normal cardiovascular structure and function and the normal function of skeletal muscle.

In target tissues glucocorticoids interact with specific receptor proteins to regulate, via the expression of glucocorticoid-responsive genes, protein synthesis. As a consequence of the time required for changes in gene expression and protein synthesis, most effects of glucocorticoids are not immediate, but become apparent after several hours. This fact is of clinical significance, because a delay generally is seen before beneficial effects of glucocorticoid therapy are observed.

Dexamethasone is therapeutically used mostly because of its anti-inflammatory and immunosuppressive properties. Dexamethasone has virtually no mineralocorticoid activity which makes it suitable for use in patients with cardiac failure or hypertension.

The RECOVERY trial (Randomised Evaluation of COVid-19 thERapY,)[1] 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.

Primary endpoint
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.

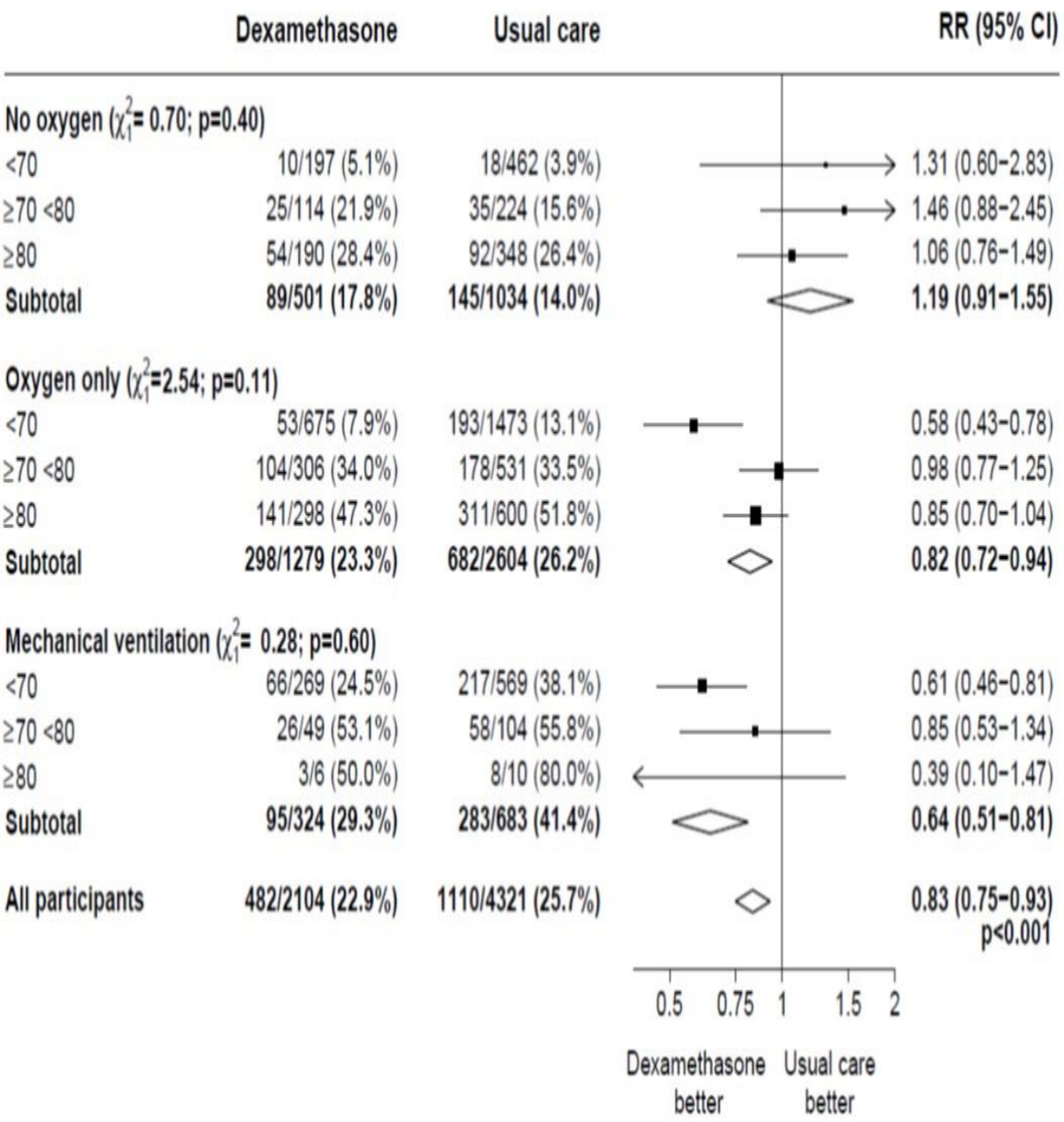
[1] www.recoverytrial.net

Safety

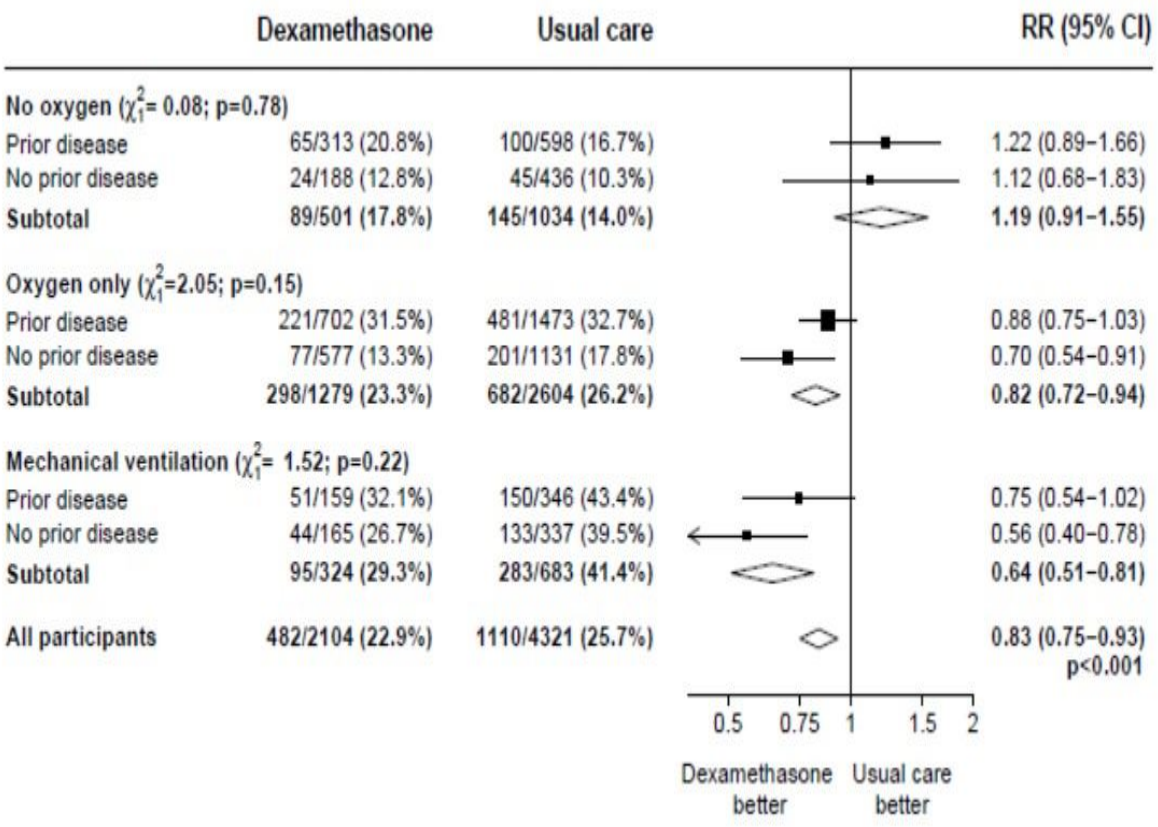
There were four serious adverse events (SAEs) related to study treatment: two SAEs of hyperglycaemia, one SAE of steroid-induced psychosis and one SAE of an upper gastrointestinal bleed. All events resolved.

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

Absorption
After ingestion, dexamethasone is rapidly and well (around 80%) absorbed. Peak plasma levels are reached between 1 and 2 hours after ingestion.

Distribution
Dexamethasone is bound (up to 77%) by plasma proteins, mainly albumin. There is high uptake of dexamethasone by the liver, kidney and adrenal glands.

Biotransformation and Elimination
Metabolism in the liver is slow and excretion is mainly in the urine, largely as unconjugated steroids. The plasma half-life is 3.0-4.5 hours but, as the effects significantly outlast plasma concentrations of steroids, the plasma half-life is of little relevance and the use of the biological half-life is more applicable. The biological half-life of dexamethasone is 36-54 hours. Therefore Dexamethasone is especially suitable in conditions where continuous glucocorticoid action is desirable.

5.3 Preclinical safety data

In animal studies, cleft palate was observed in rats, mice, hamsters, rabbits, dogs and primates; not in horses and sheep. In some cases these divergences were combined with defects of the central nervous system and of the heart. In primates, effects in the brain were seen after exposure. Moreover, intra-uterine growth can be delayed. All these effects were seen at high dosages.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol
Potato starch
Magnesium stearate
Lactose monohydrate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C. Store in the original package (to protect from light).

6.5 Nature and contents of container

White, cylindrical wide mouth containers with screw caps made of high density polyethylene (HDPE) with a child resistant polypropylene screw cap, containing 100 or 500 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Aspen Pharma Trading Limited
3016 Lake Drive
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1691/014/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1978

Date of last renewal: 29 November 2007

10 DATE OF REVISION OF THE TEXT

June 2022