HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
20 JANUARY 2021

The legally binding text is the original French opinion version

dexamethasone
DEXAMETHASONE MYLAN 20 mg/5 ml solution for injection in vials
DEXAMETHASONE MYLAN 4 mg/1 ml solution for injection in vials

New indication

Key points

Favourable opinion for reimbursement in the treatment of SARS-CoV-2 19 coronavirus infection (COVID-19) in adult and adolescent patients (aged 12 years and older with body weight at least 40 kg) who require supplemental oxygen therapy.

What therapeutic improvement?

Therapeutic improvement in management.

Role in the care pathway?

The management of COVID-19 patient is detailed in the French High Council for Public Health (HCSP) report of 25 November 2020 and is based on supportive and preventive treatments:

- Appropriate oxygen therapy,
- Analgesics and antipyretics,
- Prevention of the thrombotic risk,
- Antibacterial antibiotics in the event of arguments in favour of co-infection.

Corticosteroid therapy is an integral component of the standard of care according to national (HCSP) and international (WHO) guidelines.

No other specific immunomodulatory or antiviral treatment is currently recommended outside of clinical trials.

Role of the medicinal product in the care pathway

DEXAMETHASONE MYLAN and KRKA for injection are the first dexamethasone-based medicinal products to have obtained a specific MA in the treatment of COVID-19 in adult and adolescent patients who require supplemental oxygen therapy. The recommended dosage regimen, in accordance with the RCP, is 6 mg per day intravenously for a maximum of 10 days, depending on the patient's clinical condition.

Oral or IV dexamethasone is the first-line treatment for hospitalised patients with COVID-19 receiving oxygen therapy. At present, it is the only curative medicinal product having demonstrated a benefit in terms of reducing mortality in hospitalised patients with COVID-19 requiring supplemental oxygen.

The Committee points out that systemic corticosteroid therapy, including with dexamethasone, is not recommended in COVID-19 patients not requiring supplemental oxygen, since the available data has not demonstrated a benefit in this clinical situation. It should be noted that corticosteroid therapy may be detrimental at early stages of the disease not requiring supplemental oxygen.

In addition, the Committee highlights the fact that data in patients aged over 70 years is limited, as well as the lack of clinical data in special populations (pregnant women, children) and data relative to optimisation of the treatment regimen in terms of dose and duration based on patient characteristics (age, weight, etc.).

Special recommendations

The Committee would like new presentations better suited to the dosage regimens to be made available, particularly a 6 mg/ml strength and an oral form.

The Committee points out that demonstration of the value of dexamethasone in COVID-19 is the fruit of academic clinical research work.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ SARS-CoV-2 is an acute viral disease that is potentially life-threatening, primarily in its severe form, following complications. It is a major public health problem of global concern due to its contagiousness, its severity and its impact on healthcare system organisation and, in particular, intensive care units.

◗ DEXAMETHASONE MYLAN (dexamethasone) is a curative medicinal product.

◗ The efficacy/adverse effects ratio of DEXAMETHASONE MYLAN (dexamethasone) is high in adult and adolescent patients (aged 12 years and older with body weight at least 40 kg) with COVID-19 who require supplemental oxygen therapy.

◗ There are other therapeutic alternatives, such as proprietary medicinal products containing dexamethasone and other glucocorticoids.

◗ It is a first-line treatment that is an integral component of the standard of care.

Public health impact

Considering:

- the severity, contagiousness and impact on healthcare organisation, particularly in intensive care units, and the Public Health Emergency of International Concern (PHEIC),
- the major medical need to have access to effective, well-tolerated medicines in the treatment of SARS-CoV-2 infection due to the absence of any available curative treatment,
- the fact that DEXAMETHASONE MYLAN (dexamethasone) provides a partial response to the identified medical need due to an impact on morbidity and mortality and on the care and life pathway of treated patients (reduction in length of hospital stay and more frequent hospital discharge),
- an expected impact on the organisation of care (transfers to intensive care units and hospital discharge),

In view of the data currently available, DEXAMETHASONE MYLAN (dexamethasone) is likely to have an impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of DEXAMETHASONE MYLAN (dexamethasone) is substantial in the indication extension to include treatment of: "SARS-CoV-2 2019 coronavirus infection (COVID-19) in adult and adolescent patients (aged 12 years and older with body weight at least 40 kg) who require supplemental oxygen therapy".

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the new indication and at the MA dosage.

Clinical Added Value

Considering:

- **demonstration of the superiority of the addition of dexamethasone (6 mg once daily orally or IV for 10 days) to usual care compared to usual care alone on terms of reducing all-cause mortality at D28 (primary endpoint) in hospitalised patients requiring supplemental oxygen, in an English academic study (RECOVERY):**
  - **with a clinically relevant effect size on the relative reduction of the risk of death of 17% (HR = 0.83 [0.75; 0.93]; p < 0.001),**
  - **with an impact on hospital discharge within 28 days (secondary endpoint): 67.2% versus 63.5% (HR = 1.10 [1.03; 1.17]);**
- **data from the WHO meta-analysis supporting the value of systemic corticosteroid therapy, in particular dexamethasone, in patients with critical forms of COVID-19 in the terms of reduced mortality (OR = 0.66 [0.53; 0.82]; p < 0.001);**
- **the already established use of systemic corticosteroid therapy in the treatment of severe forms of COVID-19, the only treatment to have demonstrated an impact on reducing mortality in COVID-19;**

the Committee considers that the proprietary medicinal product DEXAMETHASONE MYLAN (dexamethasone) provides moderate clinical added value (CAV III) in the treatment of COVID-19 in adult and adolescent patients (aged 12 years and older with body weight at least 40 kg) who require supplemental oxygen therapy.