

**ESSENTIAL MEDICINES LIST FOR  
MANAGEMENT OF PATIENTS ADMITTED TO  
INTENSIVE CARE UNITS WITH SUSPECTED  
OR CONFIRMED COVID-19 DIAGNOSIS  
(EML-ICU-COVID-19)**

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## ESSENTIAL MEDICINES LIST FOR MANAGEMENT OF PATIENTS ADMITTED TO INTENSIVE CARE UNITS WITH SUSPECTED OR CONFIRMED COVID-19 DIAGNOSIS

### OBJECTIVE

- ✚ Develop an essential medicines list (EML) to manage patients in intensive care units (ICUs) with suspected or confirmed COVID-19 diagnosis, which includes active ingredients with dosage form and concentration, and are preferably in the WHO Model Lists of Essential Medicines 2019; based on clinical presentations and symptoms identified and prioritized in World Health Organization (WHO) and Surviving Sepsis Campaign (SSC) guidelines<sup>1,3</sup> and the evidence presented in these guidelines.

***This List primarily includes drugs considered essential for treatment of clinical presentations most frequently seen in patients hospitalized in ICUs for COVID-19 infection and associated conditions.***

***It does not include most drugs commonly found in ICUs for treatment of signs and symptoms related to other pathologies or comorbidities or for stabilization of the ICU patient (e.g., insulin), except those that may be needed for treatment or support (e.g., neuromuscular blockers) of conditions owing to the infection.***

***Recommended pharmaceutical presentations may vary by country.***

***The List also does not include any specific drugs for treatment of COVID-19, since, at present, there is no high-quality scientific evidence supporting their use.***

***This List will be updated on the basis of the appearance of new evidence in this regard.***

## METHODOLOGY

Randomized controlled clinical trials (RCTs), meta-analyses, and evidence-based treatment guidelines from the last 10 years were identified in the Cochrane and MEDLINE biomedical databases (through PubMed) with respect to hospital treatment of the critically ill patient, in accordance with the aforementioned WHO and SSC guidelines.

For selected PICO (patient, problem, or population; intervention; comparison; outcome) questions, a pair of reviewers selected titles and abstracts found in the biomedical databases. For each PICO question, all potentially eligible studies were evaluated according to specified criteria.

Due to the recent COVID-19 pandemic, any direct or indirect publication that mentioned patient care in the crisis was also considered.

The WHO and SSC guidelines were used to identify the most important clinical presentations and symptoms in critically ill COVID-19 patients.

- 1- Treatment of patients with hypoxemic respiratory failure and respiratory distress syndrome.
- 2- Treatment of patients with hemodynamic deterioration and septic shock.
- 3- Treatment of complications in critically ill patients.

These treatments will be described in sections 1 and 2.

## ANALYSIS APPROACH

***Identification of therapeutic approaches and essential medicines for this situation. Selection criteria for Essential Medicines List for ICU-COVID-19. (EML-ICU-COVID-19)***

For each specific clinical situation, treatments and medicines were identified in the main WHO evidence-based treatment guidelines on the subject and systematic reviews and meta-analyses, as well as the latest studies that retrospectively analyzed the epidemiology and clinical development of this disease in different countries around the world.<sup>1-38</sup>



## RATIONALE FOR KEY MEDICINES INCLUDED IN THE EML-ICU-COVID-19, NOT DETAILED IN REFERENCE GUIDELINES

### **1. Treatment of patients with hypoxemic respiratory failure and respiratory distress syndrome**

#### ***Drugs for management of sedation, analgesia, delirium, and muscle relaxation in critically ill, mechanically ventilated ICU patients***

Sedation, analgesia, management of delirium, and muscle relaxation are an integral part of the management of critically ill patients in intensive care units (ICUs) and they are especially important in mechanically ventilated patients. A great number of patients infected with COVID-19 will need mechanical ventilation due to respiratory failure. An expert panel has recently recommended that patients diagnosed with coronavirus should be handled similarly to any other mechanically ventilated patient <sup>29</sup>.

The initial clinical practice guidelines recommended (with weak evidence) the use of diazepam or midazolam for rapid sedation in acutely agitated patients, lorazepam to manage the majority of patients requiring sedation, and propofol as the preferred sedative when rapid awakening is required (for neurological assessment or patient being extubated). Likewise, they recommended haloperidol as the drug of choice for treatment of delirium, a frequent symptom in critical care patients <sup>30</sup>.

Benzodiazepines and haloperidol have been, and continue to be, the most commonly used drugs in many ICUs for sedation or treating delirium, respectively. However, more recent clinical practice guidelines suggest the use of propofol or dexmedetomidine over benzodiazepines for treatment of sedation in critically ill mechanically ventilated adults<sup>31-32</sup> and suggest not routinely using haloperidol or atypical antipsychotics in treatment of delirium, clarifying that both groups of antipsychotics can be used for short periods in select patients. Dexmedetomidine is not a drug included in the WHO EML 2019, which is why including other therapeutic options was considered, despite the limited evidence.

The use of neuromuscular relaxants in mechanically ventilated patients is associated with better oxygenation; prevents ventilator dyssynchrony; and decreases airway pressure, potential pulmonary injuries, and barotrauma. Different guidelines agree on the need for using neuromuscular blockers in the management of adult patients with acute respiratory distress syndrome (ARDS) <sup>29,33</sup>. In adults with COVID-19 and mild to moderate ARDS, the most recent guidelines suggest using boluses of muscle relaxants on demand instead of continuous infusion and suggest limiting intravenous (IV) infusion to no more than 48 hours in the following cases: patients with persistent ventilator dyssynchrony, patients who require very deep sedation, patients ventilated in a prone position, and patients with persistently high plateau pressure in the airway<sup>29</sup>. The most important clinical trial used as a basis for



the recommendations was carried out with cisatracurium<sup>34</sup>. Atracurium is a muscle relaxant that is closely related structurally to cisatracurium with similar pharmacodynamic and pharmacokinetic characteristics, but is less costly. Both cisatracurium and atracurium are metabolized by plasma mechanisms independent of the liver and renal function does not affect their elimination. Vecuronium, which is considered an alternative, can present greater pharmacokinetic changes in patients with deterioration in liver and renal function<sup>35</sup>. As present options, given their inclusion in the WHO EML, atracurium and vecuronium will be included.

Succinylcholine, a short-acting depolarizing relaxant, is reserved for when emergency orotracheal intubation in the ICU is necessary<sup>36</sup>.

Opioids continue to be a cornerstone of pain management and sedation/analgesia in the mechanically ventilated patient. Clinical practice guidelines rate morphine and fentanyl as the best evaluated and most recommended opioids for management of critically ill patients<sup>29-31</sup>.

- *Conclusions: A list of essential medicines for management of sedation, analgesia, delirium, and muscle relaxation in critically ill patients in the ICU should include:*
- *Benzodiazepine sedatives: midazolam and lorazepam.*
- *Nonbenzodiazepine sedatives: propofol.*
- *Antipsychotics: haloperidol.*
- *Neuromuscular relaxants: succinylcholine, atracurium, or vecuronium.*
- *Opioids: morphine and fentanyl.*

## **2. Patients who deteriorate hemodynamically and present septic shock**

Reported prevalence of shock in adult COVID-19 patients varies greatly (from 1% to 35%), and based on epidemiological data from China is 5%,<sup>6</sup> which is why it is necessary to identify the best therapeutic options to treat it.

### ***Parenteral solutions***

Cardiac dysfunction in COVID-19 patients is frequent (7% to 23%)<sup>7-10</sup>. Good management of fluid administration reduced mortality (RR 0.59, 95% CI: 0.42 to 0.83) and duration of ICU stay among critically ill patients<sup>11</sup>. Comparison between restriction or free administration of fluids in patients with septic shock is not conclusive in terms of mortality (RR 0.87; 95% CI: 0.69 to 1.10) or serious adverse events (RR 0.91; 95% CI: 0.78 to 1.05)<sup>12</sup>. However, all the results evaluated seem to favor using conservative fluid therapy with administration of low volumes of fluid,<sup>13</sup> avoiding administration of large volumes of fluid or albumin<sup>14</sup>.



Comparisons of types of solutions to replace or expand volume that can be administered<sup>i</sup> intravenously (balanced crystalloid solutions vs. 0.9% saline solution) for resuscitation of critically ill patients do not report significant differences in mortality (OR 0.91, 95% CI: 0.83 to 1.01) or acute renal injury (OR 0.92; 95% CI: 0.84 to 1.00)<sup>15</sup> among treatments. However, the data suggest a potential benefit of balanced crystalloid solutions for resuscitation of patients with COVID-19 and shock. When availability of balanced crystalloid solutions is limited, sodium chloride 0.9% saline solution continues to be a reasonable alternative. When crystalloids were compared against colloids in critically ill patients with COVID-19 and shock, statistically significant differences in mortality were not observed (RR 0.97; 95% CI: 0.86 to 1.09) at 1 and 3 months. However, risk of renal damage and need for transfusion is greater with colloids (RR 1.30, 95% CI: 1.14 to 1.48)<sup>16</sup>.

***In conclusion, use of balanced crystalloid solutions such as Ringer's lactate, or in its absence, sodium chloride 0.9% solutions, is recommended to replace fluids, with restrictive administration, in critically ill COVID-19 patients. Avoid the use of hypotonic solutions.***

### ***Vasoactive drugs***

Given the absence of direct evidence in patients with COVID-19 and shock, indirect evidence from critically ill patients in general can guide the therapeutic decision-making process in these cases.

In adults with COVID-19 and shock, norepinephrine is recommended as the first choice (norepinephrine compared with vasopressin or epinephrine in this type of patient does not show significant differences with regard to mortality, although epinephrine was associated with greater tachycardia and excess lactate production<sup>1,17</sup>). If norepinephrine is not available, use vasopressin or adrenaline as first choice<sup>1</sup>.

In adults with COVID-19 and shock with evidence of cardiac dysfunction and persistent hypoperfusion despite resuscitation with fluids and norepinephrine, it is suggested adding dobutamine<sup>1,18, 19, 20</sup> without first attempting to increase the dose of norepinephrine.

<sup>i</sup> Crystalloid solutions are defined as those containing water, electrolytes, and/or sugars in different proportions and osmolarities. With respect to plasma, they can be hypotonic, hypertonic, or isotonic. These solutions include sodium chloride 0.9% hydrosaline (sodium 154 mEq / osmolarity 308 mOsm/L), Ringer's (148 mEq sodium / osmolarity 310 mOsm/L), Ringer's lactate (sodium 130 mEq / lactate 28 mEq / and osmolarity 272 mOsm/L), 5% dextrose in saline solution (glucose 50 g / sodium 154 mEq / and osmolarity 560 mOsm/L), and 5% dextrose in water (glucose 50 g and osmolarity 253 mOsm/L). Colloidal solutions such as dextran are plasma expanding agents that contain suspended high-molecular-weight particles that do not cross capillary membranes so they are capable of increasing plasma osmotic pressure and retaining water in the intravascular space. Human albumin has also been used as a plasma expander at 5% or 25%, prepared in isotonic solution. Administration of albumin 25% solution increases intravascular volume by five times with regard to the volume of albumin given in 30 to 60 minutes.



For children with COVID-19 and septic shock with organ dysfunction, the SSC<sup>2</sup> guidelines recommend both epinephrine and norepinephrine, which were evaluated in comparison with dopamine. But the decision to select one or the other as first choice, with no clinical trials comparing them, is suggested to be based on the patient's pathophysiological condition (preference for epinephrine to treat myocardial dysfunction and low cardiac output and for norepinephrine to increase vascular resistance) and on local factors.

***Therefore, it is recommended to start with norepinephrine in critically ill patients with COVID-19 and cardiogenic or septic shock who need hemodynamic support. In the absence of norepinephrine, vasopressin or adrenaline can be used. If there is evidence of cardiac dysfunction or persistent hypoperfusion, dobutamine can be used.***

***With regard to the vasoactive agent for children with septic shock, there is no strong recommendation, but the SSC<sup>2</sup> guidelines suggest choosing epinephrine or norepinephrine in accordance with the patient's pathophysiological condition (preference for epinephrine to treat myocardial dysfunction and low cardiac output and for norepinephrine to increase vascular resistance) and local factors.***

### **Corticosteroids**

- **In adults**

The evidence on use of glucocorticoids for Acute Respiratory Distress Syndrome (ARDS-COVID-19) is disputed. The SSC<sup>1</sup> guidelines recommend not using systemic glucocorticoids in adult patients with COVID-19 and respiratory failure (without ARDS). In patients with ARDS, they suggest the use of systemic glucocorticoids<sup>1</sup>.

There are no data on the use of steroids in patients with COVID-19 and shock, but *indirect* evidence comparing therapy with low-dose corticosteroids to no corticosteroids in critically ill patients in shock did not show significant differences in short-term (RR 0.96; 95% CI: 0.91 to 1.02) or long-term (RR 0.96; 95% CI: 0.90 to 1.02) mortality, although times for resolution of shock and duration of hospital stay were shorter with corticosteroids<sup>21-23</sup>.

There are studies that hold that glucocorticoids should be avoided in these patients since they can be detrimental in cases of viral pneumonia and ARDS from influenza<sup>24</sup>. They would only be indicated in limited cases of severe community-acquired bacterial pneumonia<sup>25</sup>.

A systematic review in March 2020 (reported by PAHO) assessed the results of the latest Cochrane systematic review (2019)<sup>23</sup> and those of a broad multicenter clinical trial done in 2020<sup>37</sup>. The results of this meta-analysis suggest that systemic corticosteroids can potentially improve mortality, duration of mechanical ventilation, and days free of mechanical ventilation. However, hyperglycemia and an uncertain effect on muscle weakness were





observed. These results contradict the previous systematic review<sup>23</sup>, which did not find benefits for mortality or duration of mechanical ventilation.

- **In children**

No high-quality investigations currently support or refute the routine use of adjunctive glucocorticoids for pediatric septic shock or other sepsis-associated organ dysfunction. A clinical trial is in progress to examine the potential risks and benefits of adjunctive hydrocortisone for septic shock refractory to fluids and vasoactive-inotropic agents in children.

Only in situations where a child presenting with septic shock or other sepsis associated with organ dysfunction is known to also have had acute or chronic corticosteroid exposure, hypothalamic-pituitary-adrenal axis disorders, congenital adrenal hyperplasia, or other corticosteroid-related endocrinopathies, or has recently been treated with ketoconazole or etomidate; is prescription of stress-dose hydrocortisone indicated, with or without evaluation of the adrenal axis<sup>2, 38</sup>.

***Although there is evidence concerning the use of corticoids in acute respiratory distress syndrome without viral infection, there is insufficient evidence on the use of corticoids in refractory shock in adult COVID-19 patients for a recommendation to be made.***

***Given the above discussion, hydrocortisone is included conditionally in the present list, without being a current recommendation, pending additional evidence. A typical regimen in septic shock is IV administration of hydrocortisone by infusion or intermittent dosing<sup>1</sup>.***

***For septic shock or other organ dysfunction in children with COVID-19, there is no quality evidence that supports or refutes corticosteroid use.***

***Corticoids should only be used in very particular conditions: if the child had previous acute or chronic exposure to corticosteroids, hypothalamic-pituitary-adrenal axis disorders, congenital adrenal hyperplasia, or other corticosteroid-related endocrinopathies, or has recently been treated with ketoconazole or etomidate. In these cases, prescription of stress-dose hydrocortisone is indicated, with or without evaluation of the adrenal axis<sup>2</sup>.***

### ***Treatment with antimicrobials***

***There is no clear evidence concerning the best treatment choices for COVID-19-associated infections and the proposed list is based on guidelines and***





***recommendations in situations with this type of infection (such as ventilator-associated pneumopathies, sepsis, etc.) in other conditions. The list of proposed antimicrobials is for reference only and should be adapted to guidelines and to the sensitivity of local pathogens to treatments. Only a few of the most common options for treatment of infections in ICU patients are included.***

There are no controlled clinical trials evaluating the use of empiric antimicrobials in COVID-19 patients or other coronaviruses. As a result, the recommendations are based on extrapolation of data from other viral pneumonias that can have bacterial superinfection, in particular viral influenza pneumonias<sup>1</sup>.

In a critically ill COVID-19 patient, secondary bacterial pulmonary infection is frequent (both from harm caused by the virus, and from mechanical-ventilation-associated infection)<sup>3</sup>. The symptoms of secondary bacterial infection in COVID-19 patients may be similar to those of the underlying viral infection, making diagnosis difficult. This is reflected indirectly in the high rates of IV antibiotics administered in Wuhan: 53% with non-severe disease and >90% of hospitalized or ICU patients<sup>1, 7-8</sup>.

Sepsis requires administration of empiric antimicrobials to treat the responsible pathogens within the first hour after diagnosis<sup>3,5</sup>.

Empiric antibiotic treatment in adults should be based on clinical diagnosis, time elapsed between the patient's admission to the hospital and diagnosis of sepsis, and local epidemiological data on antimicrobial sensitivity (community-acquired pneumonia, healthcare-associated pneumonia).

Since the vast majority of patients with severe sepsis and septic shock have one or more forms of immunocompromise, the initial empiric regimen should be broad enough to cover most pathogens isolated in healthcare-associated infections. Broad-spectrum carbapenem (e.g., meropenem, imipenem/cilastatin) or a combination of broad-spectrum penicillin/ beta-lactamase inhibitors (e.g., piperacillin/tazobactam) should be considered. Third or fourth generation cephalosporins can also be used, especially as part of a multidrug regimen<sup>26</sup>.

Risk factors for invasive *Candida spp.* infections include immunocompromised status (neutropenia, chemotherapy, transplant, diabetes mellitus, chronic liver failure, chronic renal failure), prolonged invasive vascular devices (hemodialysis catheters, central venous catheters), total parenteral nutrition, necrotizing pancreatitis, recent surgery (particularly abdominal), prolonged administration of broad-spectrum antibiotics, prolonged hospital/ICU admission, and colonization. If the risk of sepsis from *Candida spp.* justifies empiric antifungal therapy, the selection of the specific agent should be tailored to the severity of illness, the local pattern of the most prevalent *Candida* species, and any recent exposure to antifungal drugs. Empiric use of liposomal formulations of amphotericin B is a reasonable recommendation in these patients<sup>26</sup>.



In pediatric COVID-19 patients, an estimated 20% present coinfection with *Mycoplasma pneumoniae*, although this percentage has not been clearly established<sup>27</sup>.

In light of ongoing local circulation of seasonal influenza, consider therapy with a neuraminidase inhibitor for treatment of influenza patients at risk of severe disease<sup>3</sup>.

*For this reason, and taking into account that antimicrobial sensitivity patterns vary at the local level, we recommend adding the following drugs to the list for treatment of complications from superinfection in the critically ill COVID-19 patient: amikacin, amoxicillin-clavulanate/ampicillin-sulbactam, amphotericin B, ceftazidime, ceftriaxone, meropenem/imipenem-cilastatin, piperacillin-tazobactam, vancomycin and oseltamivir<sup>28</sup>.*



## ESSENTIAL MEDICINES LIST FOR TREATMENT OF PATIENTS ADMITTED TO INTENSIVE CARE UNITS WITH SUSPECTED OR CONFIRMED COVID-19 DIAGNOSIS

MEDICINE	DOSAGE FORM AND CONCENTRATION
<b>DRUGS FOR FEVER</b>	
paracetamol	Injection: 10 mg/ ml in 10 ml ampoule or 50-100 ml vial.
<b>MEDICINAL GASES</b>	
oxygen	Inhalation. For use in management of hypoxemia.
<b>DRUGS FOR ANALGESIA</b>	
fentanyl	Injectable: 50ug/ ml in 5 ml ampoule.
morphine	Injection: 10 mg (sulfate or chlorhydrate) in 1 ml ampoule.
<b>DRUGS FOR SEDATION</b>	
haloperidol	Injection: 5 mg in 1 ml ampoule.
lorazepam	Parenteral formulation: 2 mg/ ml in 1 ml ampoule; 4 mg/ml in 1 ml ampoule.
midazolam	Injection: 1mg/ ml and 5mg/ ml.
propofol	Injection: 10 mg/ ml in 20 ml ampoule.
<b>MUSCLE RELAXANTS</b>	
atracurium*	Injection: 10 mg/ ml (besilate) in 5 ml ampoule.  *vecuronio powder for injection: 10 mg (bromide) in vial, as option according to local availability.
succinylcholine	Injection: 50 mg (chloride)/ ml in 2 ml ampoule.
<b>SEDATION ADJUNCTS</b>	
atropine	Injection: 1 mg (sulfate) in 1- ml ampoule.
<b>ANTIMICROBIALS</b> <b>(Not directly related to treatment of COVID-19. Attached for reference. See note on use according to local guidelines)</b>	
amikacin	Injection: 250 mg (as sulfate)/ ml in 2- ml vial.
amoxicillin + clavulanic acid*	Powder for injection: 500 mg (sodium) + 100 mg (as potassium salt); 1000 mg (sodium) + 200 mg (as potassium salt) in vial.  *Ampicillin sulbactam 1.5 g (ampicillin 1 g/sulbactam 0.5 g); 3 g (ampicillin 2 g/sulbactam 1 g) as alternative according to local availability.
amphotericin B	Powder for injection: 50 mg in vial (as sodium deoxycholate or liposome complex).



ceftazidime	Powder for injection: 250 mg or 1 g (as pentahydrate) in vial.
ceftriaxone	Powder for injection: 250 mg; 500 mg; 1g in vial.
meropenem*	Powder for injection: 500 mg (as trihydrate); 1 g (as trihydrate) in vial. * Optionally: Imipenem + cilastatin 250 mg/250 mg, 500 mg/500 mg, as alternatives to local availability.
piperacillin + tazobactam	Powder for injection: 2 g (as sodium salt) + 250 mg (as sodium salt); 4 g (as sodium salt) + 500 mg (as sodium salt) in vial.
vancomycin	Powder for injection: 250 mg (as chlorhydrate) in vial.
<b>GLUCOCORTICOIDS (controversial evidence, will be updated when specific studies have been published)</b>	
hydrocortisone*	Powder for injection: 100 mg, 500 mg (as sodium succinate) in vial.  *methylprednisolone powder for injection: 500 mg as alternative according to local availability.
<b>VASOACTIVE DRUGS</b>	
dobutamine	Injection: 5, 10, 25, 50, & 100 mg (as chlorhydrate) in 20 ml ampoule.
epinephrine* (adrenaline)	Injection: 1 mg (as chlorhydrate or tartrate) in 1- ml ampoule. Injection: 100 micrograms/ ml (as tartrate or chlorhydrate) in 10- ml ampoule.  First in children.  *Injectable vasopressin solution: 20 units/ml as alternative according to local availability.
norepinephrine* (noradrenaline)	Injection: 1 mg /ml in 4- ml ampoule.  *as first choice
<b>VOLUME EXPANDERS (CRYSTALLOIDS)</b>	
Ringer's lactate	Ringer with sodium lactate, compound solution. Injectable.
normal saline solution	Injectable solution: 0.9% isotonic (equivalent to Na <sup>+</sup> 154 mmol/L, Cl <sup>-</sup> 154 mmol/L).
<b>DRUGS FOR COINFECTION WITH INFLUENZA VIRUS</b>	
oseltamivir*	Capsule: 30 mg; 45 mg; 75 mg (as phosphate). Oral powder: 12 mg/ ml. * Severe illness due to suspected or confirmed coinfection with influenza virus in critically ill hospitalized patients.
<b>ANTICOAGULANTS</b>	
enoxaparin	Injection: ampoule or prefilled syringe 20 mg/0.2 ml; 40 mg/0.4 ml; 60 mg/0.6 ml; 80 mg/0.8 ml; 100 mg/1 ml; 120 mg/0.8 ml; 150 mg/1 ml.  *Alternatives are limited to nadroparin and dalteparin.
sodium heparin	Injection: 1000 IU/ ml; 5000 IU/ ml in 1- ml ampoule.



<b>ANTACIDS</b>	
omeprazole	Powder for injection: 40 mg in vial.
ranitidine	Injection: 25 mg/ ml (as chlorhydrate) in 2- ml ampoule.
<b>ANTIEMETICS</b>	
metoclopramide	Injection: 5 mg (chlorhydrate)/ ml in 2-ml ampoule.
ondansetron	Injection: 2 mg/ ml in 2- ml ampoule (as chlorhydrate).
<b>ANTISEPTICS AND DISINFECTANTS</b>	
alcohol for hands	Solution: containing isopropyl (isopropanol) alcohol 75% or ethanol 80% volume/volume.
chlorhexidine	Solution: 5% (digluconate).
iodopovidone	Solution: 10% (equivalent to 1% available iodine).
<b>BRONCHODILATORS</b>	
ipratropium bromide	Inhalation (aerosol): 20 micrograms/dose.
salbutamol	Inhalation (aerosol): 100 micrograms (as sulfate) per dose. Injection: 50 micrograms (as sulfate)/ ml in 5- ml ampoule.

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