# Actualización en el Manejo de Infecciones Respiratorias Virales en UCI Adultos

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# Contenidos

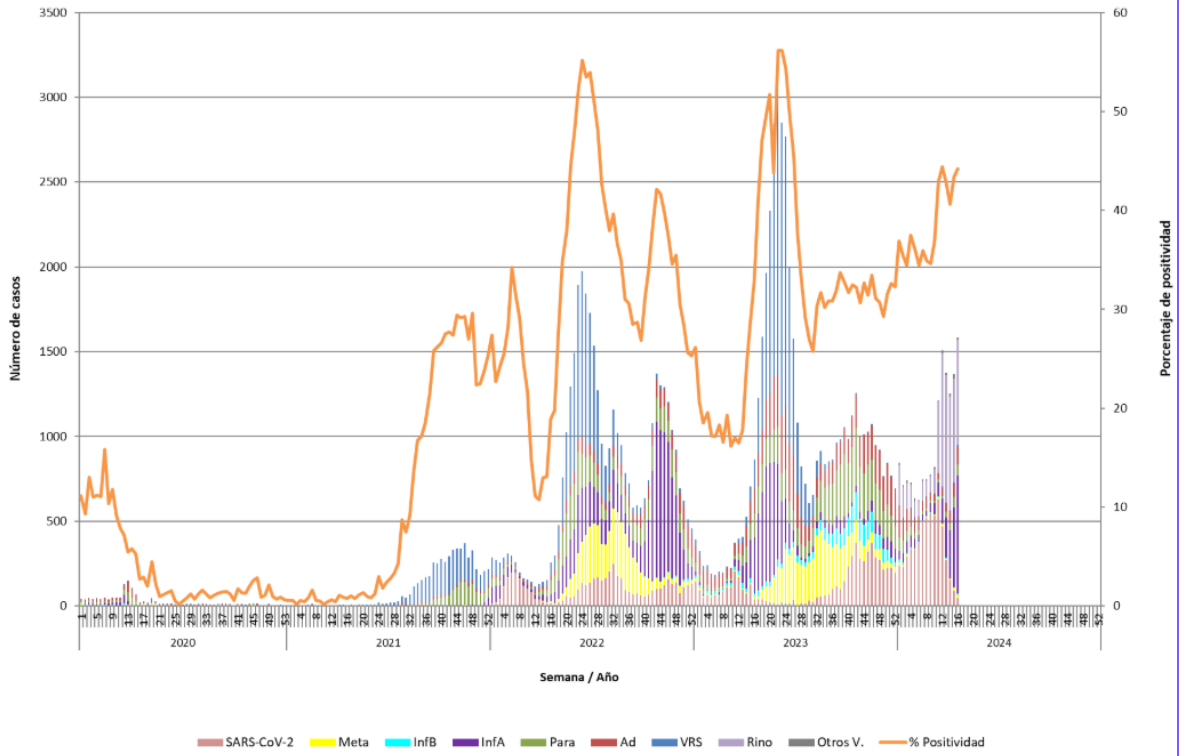
- Escenario actual
- Influenza
- COVID -19

# Escenario actual

# Informe de Circulación de Virus Respiratorios

| Virus | 2023 SE 1-16 | 2024 SE 1-16 |
|---|---|---|
| SARS-CoV-2 | 26,6% | 35,4% |
| Adenovirus | 25,1% | 8,5% |
| Influenza A | 17,8% | 15,7% |
| Parainfluenza | 12,5% | 3,9% |
| VRS | 10,2% | 0,5% |
| Influenza B | 5,3% | 0,6% |
| Metapneumovirus | 2,6% | 1% |
| Rinovirus | - | 33,1% |
| O.V.R | - | 1,4% |
| **Casos totales detectados** | **5.692** | **14.859** |

**Figura N°1.** Número de casos detectados de Virus Respiratorios por agente y porcentaje de positividad del total de las muestras analizadas, según semana epidemiológica. Chile 2020-2024.



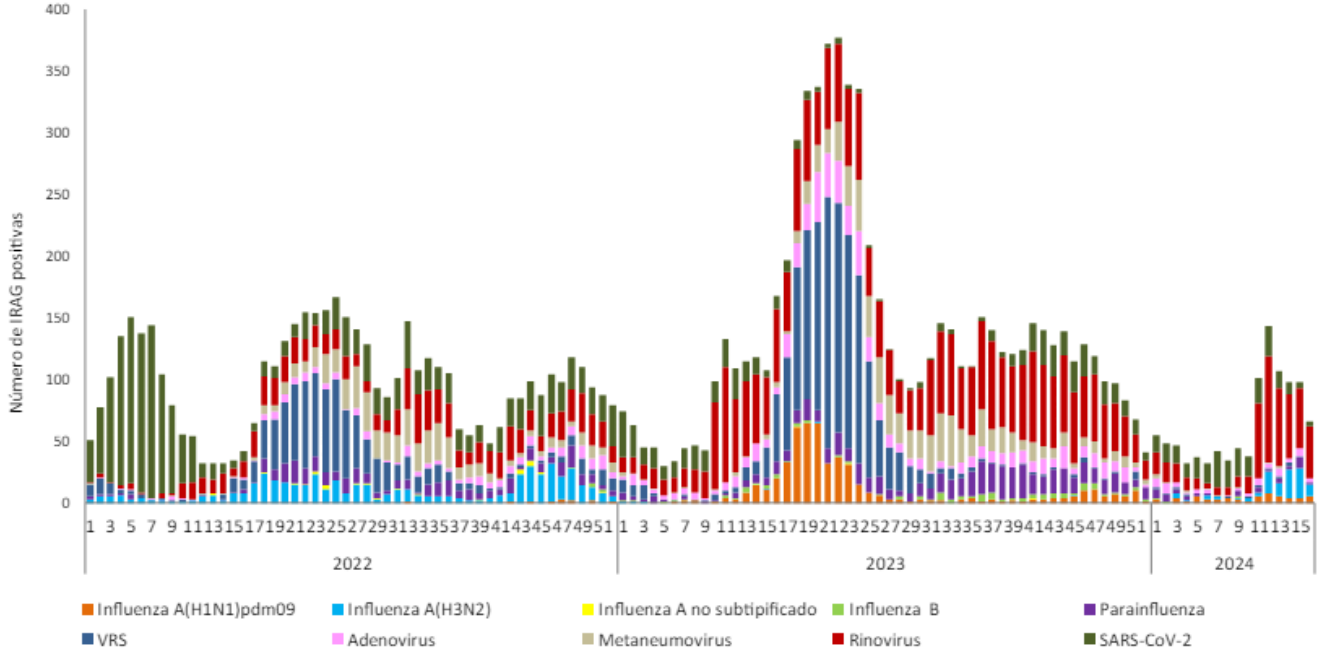

Casos de SARS-CoV-2 incorporados a partir de la SE N°1 del 2022. Rinovirus y otros virus respiratorios, incluidos a partir de la SE N°1 del 2024.

**Fuente:** Sección Virus Respiratorios y Exantemáticos. Departamento de Laboratorio Biomédico. Instituto de Salud Pública de Chile.

# Informe epidemiológico SE nº16 -2024: vigilancia centinela ETI e IRAG de influenza y otros virus respiratorios

**Figura 3. Casos de IRAG según virus respiratorios y semana epidemiológica en hospitales centinelas**

**IRAG. Chile, 2022 – 2024 (SE 16)**



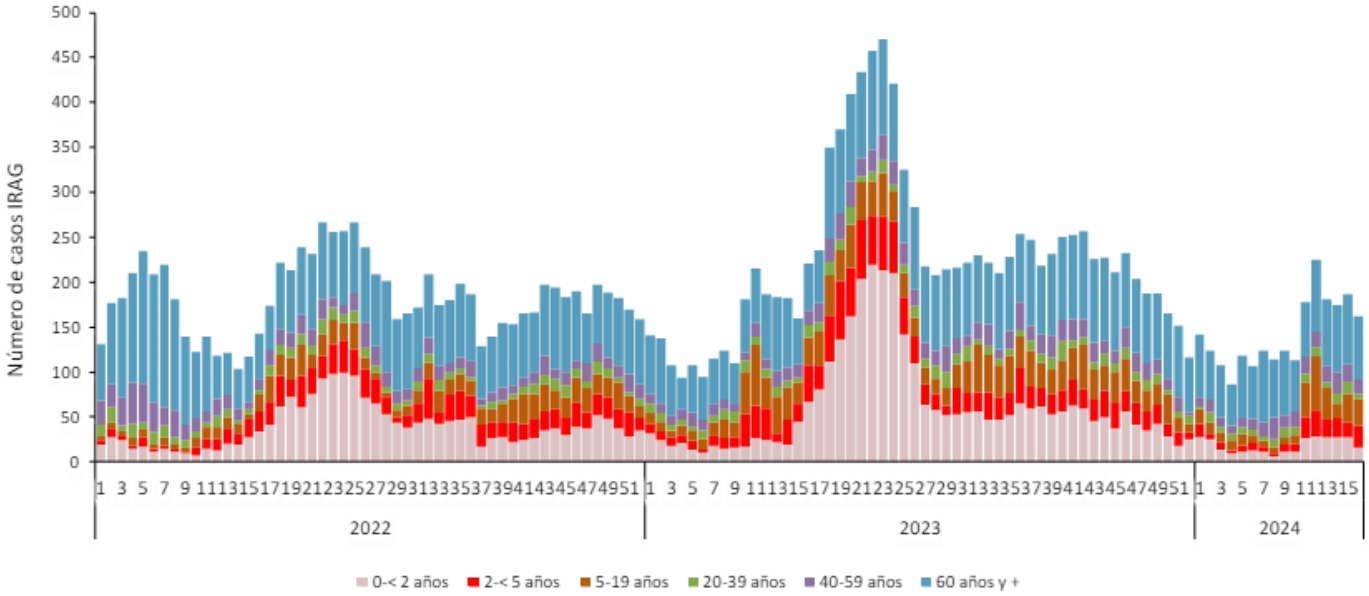

**Fuente: Vigilancia centinela IRAG. Depto. Epidemiología MINSAL**

Casos de IRAG en Hosp. centinelas hasta la SE 16, 2024:

- Total: 2.263 IRAG
- Un 92% posee una muestra para análisis virológico con una positividad global acumulada del 90% para virus respiratorios.

# Informe epidemiológico SE nº16 -2024: vigilancia centinela ETI e IRAG de influenza y otros virus respiratorios

**Figura 4. Distribución total de casos IRAG en Hospitales centinela IRAG según grupos de edad y semana de ocurrencia. Chile, años 2022- 2024 SE 16.**




**Fuente: Vigilancia centinela IRAG. Depto. Epidemiología MINSAL**

Grupos etarios predominantes de casos de IRAG hasta la SE 16, 2024:

- > 60 años (47%)
- 5 a 19 años (14%)
- < 2 años (13%)

# Informe epidemiológico SE nº16 -2024: vigilancia centinela ETI e IRAG de influenza y otros virus respiratorios

**Tabla 2. Indicadores de gravedad intrahospitalaria de casos de la vigilancia centinela IRAG según agentes virales involucrados. Chile, SE 16, 2024.**

| 2024 (SE 1-16) | IA (H1N1) pdm09 | IA H3N2 | IB | IA Sin subtipificación | VRS | SARS- CoV-2 | % Influenza | % VRS | % SARS-CoV-2 |
|---|---|---|---|---|---|---|---|---|---|
| IRAG | 58 | 104 | 3 | 0 | 17 | 254 | - | - | - |
| IRAG en UCI | | | 40 | | 4 | 66 | 24% | 24% | 26% |
| Letalidad | | | 9 | | 0 | 18 | 5% | 0% | 7% |
| > 60 años | | | 86 | | 0 | 143 | 52% | 0% | 56% |
| 40-59 años | | | 23 | | 0 | 24 | 14% | 0% | 9% |
| 20-39 años | | | 10 | | 0 | 14 | 6% | 0% | 6% |
| 5-19 años | | | 23 | | 2 | 20 | 14% | 12% | 8% |
| 2-<5 años | | | 13 | | 5 | 11 | 8% | 29% | 4% |
| 0-<2 años | | | 9 | | 10 | 42 | 5% | 59% | 17% |

Fuente: Vigilancia centinela IRAG. Depto. Epidemiología MINSAL

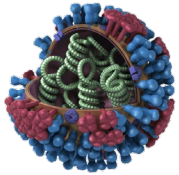
Para la SE 16 un 7,2% del total de ingresos a UCI correspondieron a IRAG.

**Influenza :** 165 casos confirmados durante el 2024 hasta la SE 16, con 40 casos ingresados a camas críticas y 9 fallecidos .

**SARS-CoV-2:** 254 casos confirmados durante el 2024 hasta la SE 16 con 66 casos ingresados a camas críticas y 18 fallecidos .

# Influenza

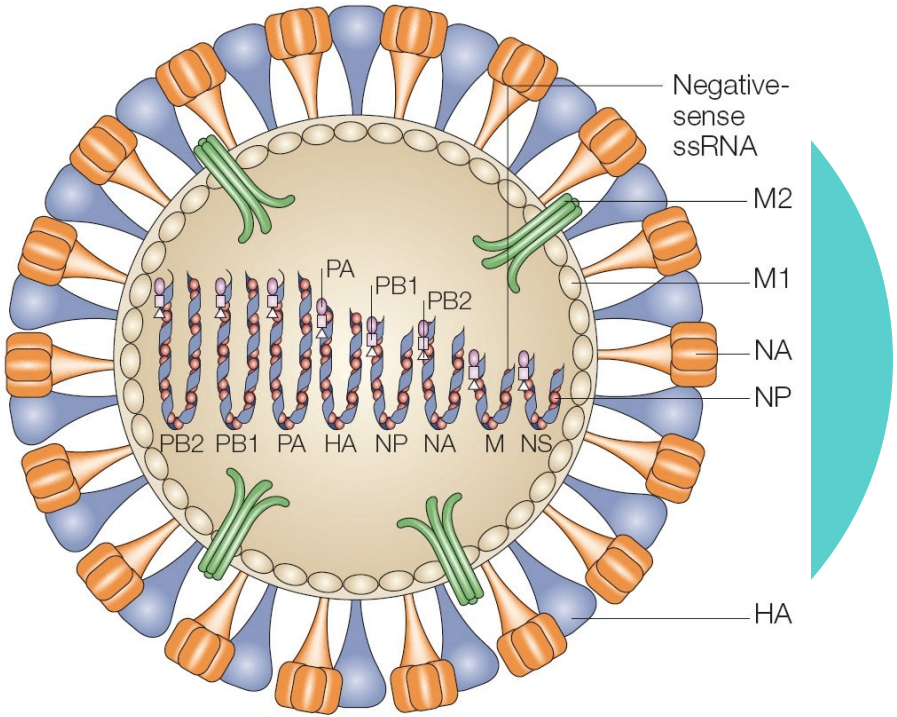
# Definiciones



- Enfermedad viral transmisible, que afecta el tracto respiratorio superior e inferior.
- Los síntomas son de origen abrupto y suelen ser autolimitados.
  - Fiebre alta (39-40°), tos, dolor de garganta, fatiga, cefalea, mialgias y secreción nasal.
- Grupos de alto riesgo: puede progresar a neumonía e incluso a muerte.
  - Niños, adultos mayores, enfermos crónicos, inmunodeprimidos y embarazadas.

- Período de incubación: 1 a 4 días, en promedio 2.
- Período de transmisibilidad: -2 días antes de los síntomas, hasta aprox. +5 días después de aparición de síntomas.
  - Grupos de alto riesgo, excluyendo embarazadas, pueden transmitir el virus durante un período más prolongado.

# Estructura

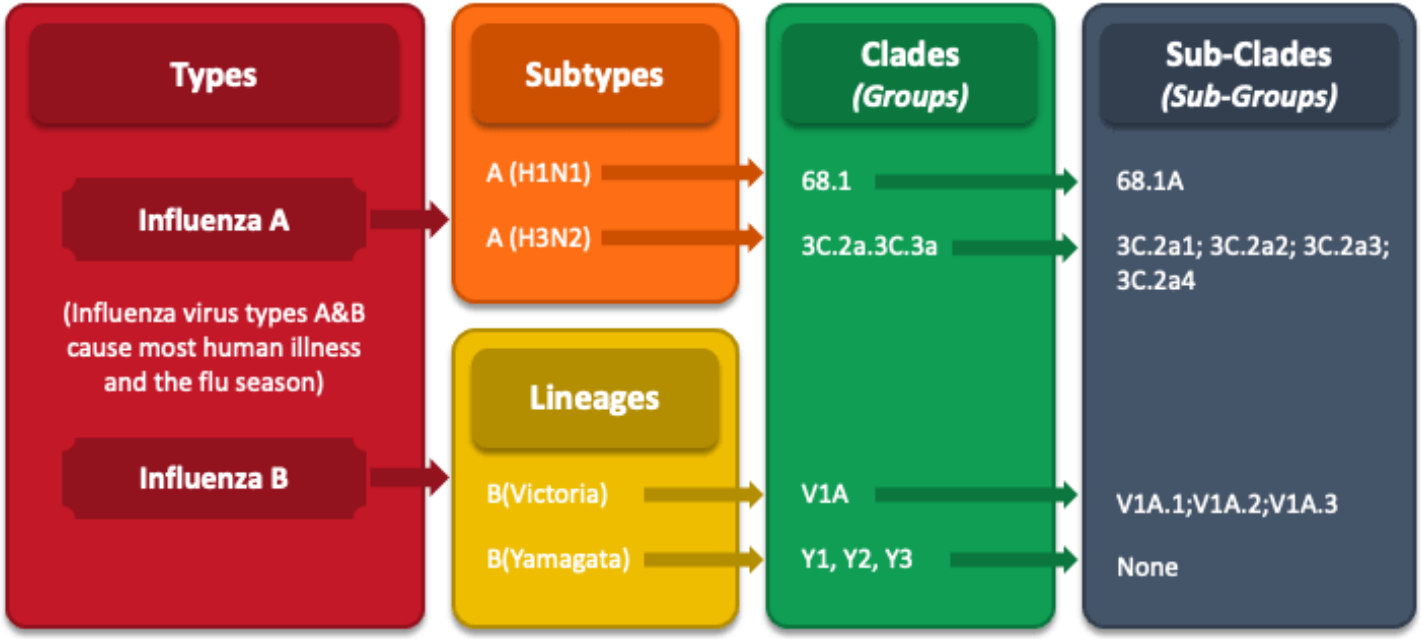



Las partículas virales son pleomórficas .
Envoltura :

- Formada por MP de la célula huésped .
- Pose M2 proteína integral de membrana .
- Contiene glicoproteínas virales hemaglutininas (HA) y neuraminidasas (NA)
    - **NA : degrada el ácido siálico de las glicoproteínas y glicolípidos usados como receptores para la infección viral .**

Al interior posee nucleocápside formada por proteína M1 que contiene el genoma viral .

# Tipos de virus de la Influenza



# Manejo Farmacológico

TABLE 4

**Treatment of Influenza**

| Drug/formulation | Cost* | Dosages | FDA-approved indications | Contraindications and precautions |
|---|---|---|---|---|
| Oseltamivir (Tamiflu), available as oral capsules or suspension | $50 to $100 ($160 to $310) depending on dosage | Adults and children 13 years and older: 75 mg 2 times per day for 5 days<br>Children:<br>2 weeks to < 12 months of age (any weight): 3 mg per kg 2 times per day for 5 days<br>< 33 lb (15 kg): 30 mg 2 times per day for 5 days<br>33 to 50 lb (15 to 23 kg): 45 mg 2 times per day for 5 days<br>> 50 to 88 lb (23 to 40 kg): 60 mg orally 2 times per day for 5 days<br>> 88 lb (40 kg): adult dosage | Prevention of influenza A and B in patients 12 months and older<br>Treatment of uncomplicated acute influenza A and B in patients 2 weeks and older who have been symptomatic for no more than 48 hours | Contraindicated in people with serious hypersensitivity to oseltamivir or any component of the product<br>Potential adverse effects include nausea, vomiting, and allergic reactions (e.g., rash, facial swelling)<br>May use during pregnancy; preferred drug for influenza treatment; consider increased dose in pregnant women who are hospitalized with influenza complications; risk of embryo-fetal toxicity not expected based on human data |
| Zanamivir (Relenza), available as powder for inhalation<br>Intravenous formulation available only as an emergency investigative new drug | NA ($65) | Adults and children 7 years and older:<br>10 mg 2 times per day for 5 days (2 doses should be taken on the first day of treatment, provided there is at least 2 hours between doses; on subsequent days, doses should be about 12 hours apart at approximately the same time each day) | Prevention of influenza A and B in patients 5 years and older<br>Treatment of uncomplicated acute influenza A and B in patients 7 years and older who have been symptomatic for no more than 48 hours | Contraindicated in people with milk allergy, underlying reactive airway disease (e.g., asthma, chronic obstructive pulmonary disease), or history of allergic reaction to zanamivir or any component of the product<br>Potential adverse effects include headaches, diarrhea, nausea, vomiting, allergic reaction, nasal symptoms, bronchitis, cough, sinusitis, dizziness, fever, chills, arthralgia, and articular rheumatism; serious and sometimes fatal cases of bronchospasm have occurred<br>May use during pregnancy; risk of embryo-fetal toxicity not expected based on human data |
| Peramivir (Rapivab), available as solution for injection | $1,000 | Adults and children 13 years and older: single dose of 600 mg<br>Children 2 to 12 years of age: single dose of 12 mg per kg (up to 600 mg) | Treatment of uncomplicated acute influenza A and B in patients 2 years and older who have been symptomatic for no more than 48 hours | Contraindicated in people with serious hypersensitivity or anaphylaxis to peramivir or any component of the product<br>Potential adverse effects include diarrhea, nausea, vomiting, and neutropenia<br>Weigh risks and benefits during pregnancy; no human data available; no known risk of embryo-fetal toxicity based on animal data at 8 times the recommended human dose; possible risk of embryo-fetal toxicity with continuous intravenous infusion based on limited animal data |
| Baloxavir (Xofluza), available as oral tablets | NA ($160) | Adults and children 12 years and older:<br>88 to 174 lb (40 to 79 kg): single dose of 40 mg<br>≥ 175 lb (80 kg): single dose of 80 mg | Treatment of uncomplicated acute influenza in patients 12 years and older who have been symptomatic for no more than 48 hours | Contraindicated in people with a history of hypersensitivity to baloxavir or any component of the product<br>Potential adverse effects include diarrhea, bronchitis, nasopharyngitis, headache, and nausea<br>Avoid use during pregnancy; no human data available; no known risk of fetal harm based on animal data at 5 and 7 times the maximum recommended human dose |

FDA = U.S. Food and Drug Administration; NA = not available.

*—Estimated retail cost for one treatment course based on information obtained at http://www.goodrx.com (accessed September 12, 2019). Generic price listed first; brand name in parentheses.

Gaitonde, D. Y., Moore, F. C., & Morgan, M. K. (2019). Influenza: diagnosis and treatment. American family physician, 100(12), 751-758.

Adamantanos (amantadina y rimantadina ) no se recomiendan, porque no son activos contra la influenza B, y la mayoría de las cepas de influenza A han mostrado resistencia al adamantano durante los últimos 10 años.

# Manejo Farmacológico

FDA-approved antivirals currently being used for the treatment of influenza

| Characteristic | Oseltamivir | Zanamivir | Peramivir | Baloxavir |
|---|---|---|---|---|
| Activity | IAV and IBV | IAV and IBV | IAV and IBV | IAV and IBV, including NAI-resistant strains |
| Antiviral target | Neuraminidase | Neuraminidase | Neuraminidase | Endonuclease |
| Mechanism of action | Impairs virus release | Impairs virus release | Impairs virus release | Blocks viral transcription |
| Administration/duration | Oral | Inhaled | Intravenous | Oral |
| Treatment | Any age | 7 yrs and older | 6 mo and older | 12 yrs and older |
| Prophylaxis | 3 mo and older | 5 yrs and older | Not recommended | Postexposure prophylaxis 12 yrs and older |
| Plasma half-life (h) | 6–10 | 2.5–5.1 | 12–24 | 79.1 h |
| Peak time (h) | 3–4 | 1–2 | 2–4 | 3.5–4 h |
| $C_{max}$[a] (ng/mL) | 259 | 39 | 34 | 68.9 for 40 mg, 82.5 for 80 mg |
| Protein binding (%) | 3 | <10 | <30 | 93–94 |
| Clearance | 99% kidneys | Urine and feces, unabsorbed | 90% renal | Feces and urine |
| Pro(s) | Impairs release of both IAV and IVB | Impairs release of both IAV and IVB, can be inhaled | Impairs release of both IAV and IVB | Blocks transcription from IAV and IVB |
| Cons | Should be given within the first 48 h of symptom onset | Should be given within the first 48 h of symptom onset | Should be given within the first 48 h of symptom onset | Cannot be given with dairy products, calcium-fortified beverages, or laxatives and antacids |
| | Dose adjustment is required for renal dysfunction | Not to be used in patients with allergies to lactose, asthma, or COPD | Diarrhea, bronchitis, nausea, and sinusitis | Diarrhea, bronchitis, nausea, and sinusitis |
| | Nausea, vomiting, and dizziness | Bronchospasm, bronchitis, cough, sinusitis | | |
| Resistance marker(s) | H275Y (H1N1, H1N1 pandemic), R292K (H7N9) | R294K (H7N9) | H275Y (H1N1) | I38T (H1N1 pandemic, H3N2) |

Kumari, R., Sharma, S. D., Kumar, A., Ende, Z., Mishina, M., Wang, Y., … & Sambhara, S. (2023). Antiviral approaches against influenza virus. Clinical microbiology reviews, 36(1), e00040-22.

RESEARCH Open Access

# Effectiveness of oseltamivir treatment on clinical failure in hospitalized patients with lower respiratory tract infection

Timothy L. Wiemken[1,4*], Stephen P. Furmanek[2], Ruth M. Carrico[2], Paula Peyrani[2,4], Daniel Hoft[1], Alicia M. Fry[3] and Julio A. Ramirez[2]

**Abstract**

**Background:** Influenza is associated with excess morbidity and mort
for treatment of influenza infection, and each require initiation as ea
efficacy difficult to estimate in the hospitalized patient with lower r
learning methods, we re-analyze data from a randomized trial of os
clinical failure in hospitalized patients with lower respiratory tract in

**Methods:** This was a secondary analysis of the Rapid Empiric Treatr
average treatment effects (CATE) and 95% confidence intervals were
cal and demographic variables. RETOS was a multicenter, randomize
with lower respiratory tract infections in Kentucky from 2009 throug
respiratory tract infection were randomized to standard of care or st
after hospital admission but within 24 h of enrollment. After random
arm per package insert. The primary outcome was clinical failure, a
clinical improvement within 7 days, transfer to intensive care 24 h a
30 days.

**Results:** A total of 691 hospitalized patients with lower respiratory trac
only subgroup of patients with a statistically significant CATE was those with laboratory-confirmed influenza infection with a 26% lower risk of clinical failure when treated with oseltamivir (95% CI 3.2–48.0%).

**Conclusions:** This study suggests that addition of oseltamivir to standard of care may decrease clinical failure in hospitalized patients with influenza-associated lower respiratory tract infection versus standard of care alone. These results are supportive of current recommendations to initiate antiviral treatment in hospitalized patients with confirmed or suspected influenza as soon as possible after admission.

*Trial registration* Original trial: Clinical Trials.Gov; Rapid Empiric Treatment With Oseltamivir Study (RETOS) (RETOS); ClinicalTrials.gov Identifier: NCT01248715 https://clinicaltrials.gov/ct2/show/NCT01248715

**Keywords:** Tamiflu, Flu, Heterogenous treatment effects, Causal forest

↓ falla clínica
↓ tiempo de alivio de síntomas
↓ riesgo de complicaciones del tracto respiratorio inferior
↑ aparición de náuseas y vómitos

# Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials

*Lancet* 2015; 385: 1729–37
Published Online January 30, 2015
http://dx.doi.org/10.1016/S0140-6736(14)62449-1

*Joanna Dobson, Richard J Whitley, Stuart Pocock, Arnold S Monto*

## Summary

**Background** Despite widespread use, questions remain about the efficacy of oseltamivir in the treatment of influenza. We aimed to do an individual patient data meta-analysis for all clinical trials comparing oseltamivir with placebo for treatment of seasonal influenza in adults regarding symptom alleviation, complications, and safety.

**Methods** We included all published and unpublished Roche-sponsored randomised placebo-controlled, double-blind trials of 75 mg twice a day oseltamivir in adults. Trials of oseltamivir for treatment of naturally occurring influenza-like y outcomes were eligible. We also searched Medline, PubMed, Trials, and the ClinicalTrials.gov trials register for other relevant ted on Nov 27, 2014). We analysed intention-to-treat infected, y outcome was time to alleviation of all symptoms analysed with os and Mantel-Haenszel methods to work out complications,

4328 patients. In the intention-to-treat infected population, we oms for oseltamivir versus placebo recipients (time ratio 0·79, alleviation were 97·5 h for oseltamivir and 122·7 h for placebo . For the intention-to-treat population, the estimated treatment ined highly significant (median difference –17·8 h). In the lower respiratory tract complications requiring antibiotics more 95% CI 0·42–0·75; p=0·0001; 4·9% oseltamivir *vs* 8·7% placebo, risk difference –3·8%, 95% CI –5·6 to –2·2) and also fewer admittances to hospital for any cause (RR 0·37, 95% CI 0·17–0·81; p=0·013; 0·6% oseltamivir, 1·7% placebo, risk difference –1·1%, 95% CI –1·4 to –0·3). Regarding safety, oseltamivir increased the risk of nausea (RR 1·60, 95% CI 1·29–1·99; p<0·0001; 9·9% oseltamivir *vs* 6·2% placebo, risk difference 3·7%, 95% CI 1·8–6·1) and vomiting (RR 2·43, 95% CI 1·83–3·23; p<0·0001; 8·0% oseltamivir *vs* 3·3% placebo, risk difference 4·7%, 95% CI 2·7–7·3). We recorded no effect on neurological or psychiatric disorders or serious adverse events.

**Interpretation** Our findings show that oseltamivir in adults with influenza accelerates time to clinical symptom alleviation, reduces risk of lower respiratory tract complications, and admittance to hospital, but increases the occurrence of nausea and vomiting.

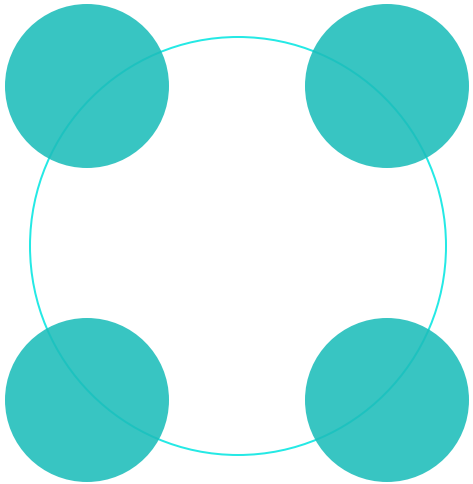
# Perlas Farmacoterapéuticas OS

## Actividad PK/PD

AUC dependiente
$AUC_{0-24}$ >14,000 ng*h/ml

## Dosis en Falla Renal

Alta tasa de excreción renal (98%)
<30 mL /min: 75 mg/día
<10 ml/min: 30 mg/día o 75 mg c/48h
HDLi : 75 mg + 30 mg post -HDL



## Dosis estándar vs Dosis altas

Dosis más altas no se asociaron con una mejoría en los desenlaces clínicos.

## Dosis en ARC

>130 mL/min, requieren dosis más altas.

Ann Phys. 2014 . DOI : 10.1177/ 1060028014535362 Fphar . 2020 . DOI : 10.3389/fphar .2020.00786 Am J Respir Crit Care Med . 2023. DOI : 10.1164/rccm .202207-1393OC

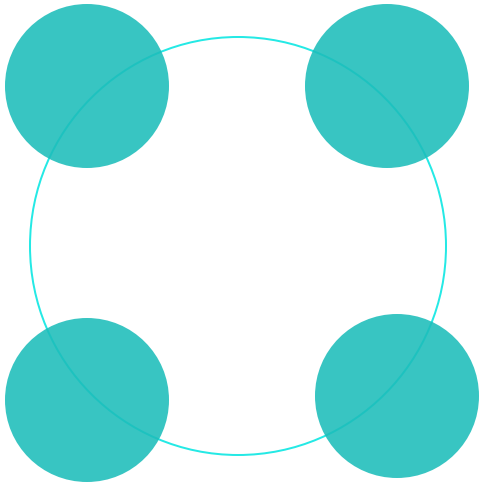
# Perlas Farmacoterapéuticas OS

## Dosis/Duración en IC con influenza

Dosis altas muestran beneficios limitados.
Duración prolongada (10 d) limita el rebote viral

## Dosis en obesos

Exposición sistémica a oseltamivir carboxilato no se ve reducida en obesos con dosis estándar



## Dosis en ECMO y TRRC

- ECMO vv : 150 mg c/12h
- TRRC: 75 mg c/12h

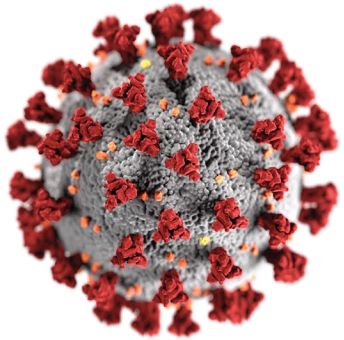
## Duración en UCI con influenza

Considerar 10 días en:
- Neumonía, VMI, FOM
Independiente del estado de inmunosupresión

Br J Clin Pharm . 2021. DOI : 10.1111/bcp .14523 CMAJ . 2010. DOI :10.1503/cmaj .092127 J Med Virol . 2023. DOI : 10.1002/jmv .29010 Br J Clin Pharm . 2016. DOI :10.1111/bcp .12892 Am J Respir Crit Care Med . 2023. DOI : 10.1164/rccm .202207-1393OC

# COVID -19

# Definiciones

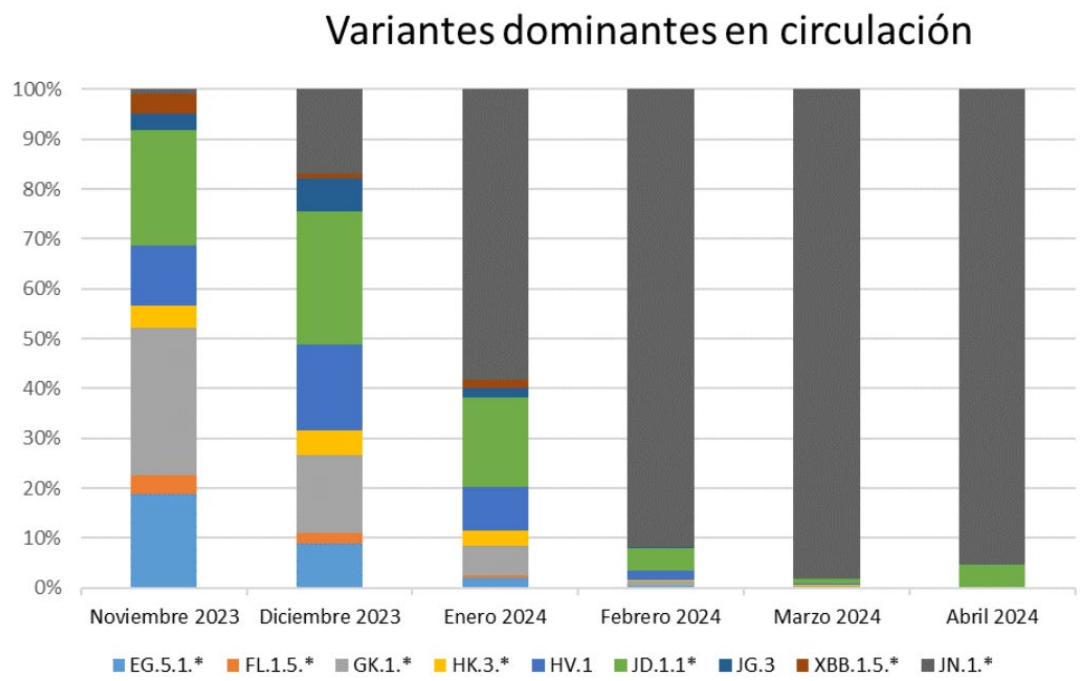


- COVID-19 es una enfermedad infecciosa causada por el virus SARS-CoV-2, de la familia de los coronavirus.

- La enfermedad puede presentarse de forma leve o **progresar a enfermedades críticas**: insuficiencia respiratoria hipoxémica, SDRA, shock séptico, enfermedad tromboembólica, disfunción renal y hepática, disfunción cardíaca, enfermedad del SNC y exacerbación de comorbilidades subyacentes .

# Informe de Circulación de Virus Respiratorios SE 16, 2024

**Figura N°7**: Variantes predominantes de SARS-CoV-2 en Chile, noviembre 2023 a abril 2024*.

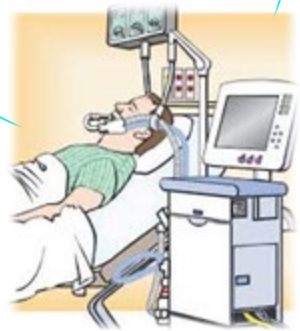



*Información hasta la SE N°16 del 2024.

**Fuente:** Sección Virus Respiratorios y Exantemáticos; Subdepartamento de genómica y Genética Molecular; Departamento Laboratorio Biomédico Nacional y de Referencia. Instituto de Salud Pública de Chile.

- Vigilancia genómica de SARS-CoV-2, durante mes de abril demuestra un **incremento de la circulación de JN.1*,** desplazando a las variantes recombinantes predominantes registradas en los últimos meses (EG.5.1*, GK.1* y JD.1.1*).

# Perspectiva Farmacológica



| 01 | 02 | 03 | 04 |
|---|---|---|---|
| Sedoanalgesia | BNM | Corticoides | Terapias dirigidas |

Elevada complejidad farmacoterapéutica

# Sedoanalgesia y BNM

## Paciente COVID -19

Requerirá VM prolongada.

## Peor escenario

- IOT y VMI
- Sedación Profunda SAS 1 -2
- BNM en infusión continua

## Desenlaces PC

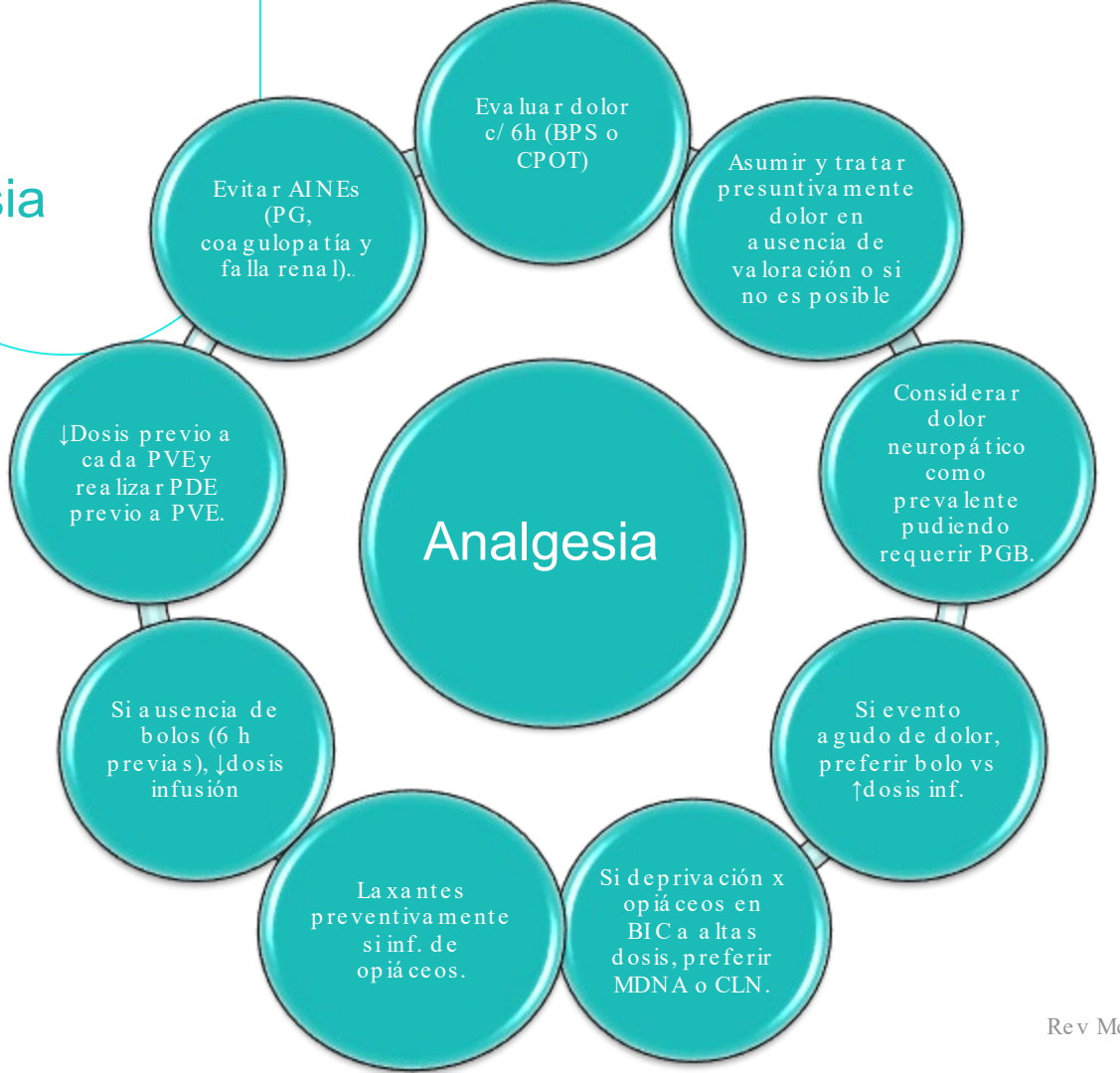
- Estadía en UCI
- Estadía hospitalaria
- Días de VMI
- Delirium y mortalidad

# Paquete ABCDEF

Optimizar el manejo del dolor, evitar la sedación profunda, reducir el delirio, acortar la duración de la VM, minimizar la debilidad adquirida en UCI y fomentar la participación del paciente y la familia en los procesos de atención en esta unidad.

| | |
|---|---|
| A | Assess, prevent and manage pain |
| B | Both SAT and SBT |
| C | Choice of analgesia and sedation |
| D | Delirium: asses, prevent and manage |
| E | Early Mobility and exercise |
| F | Family engagement and empowerment |

# Tips Analgesia

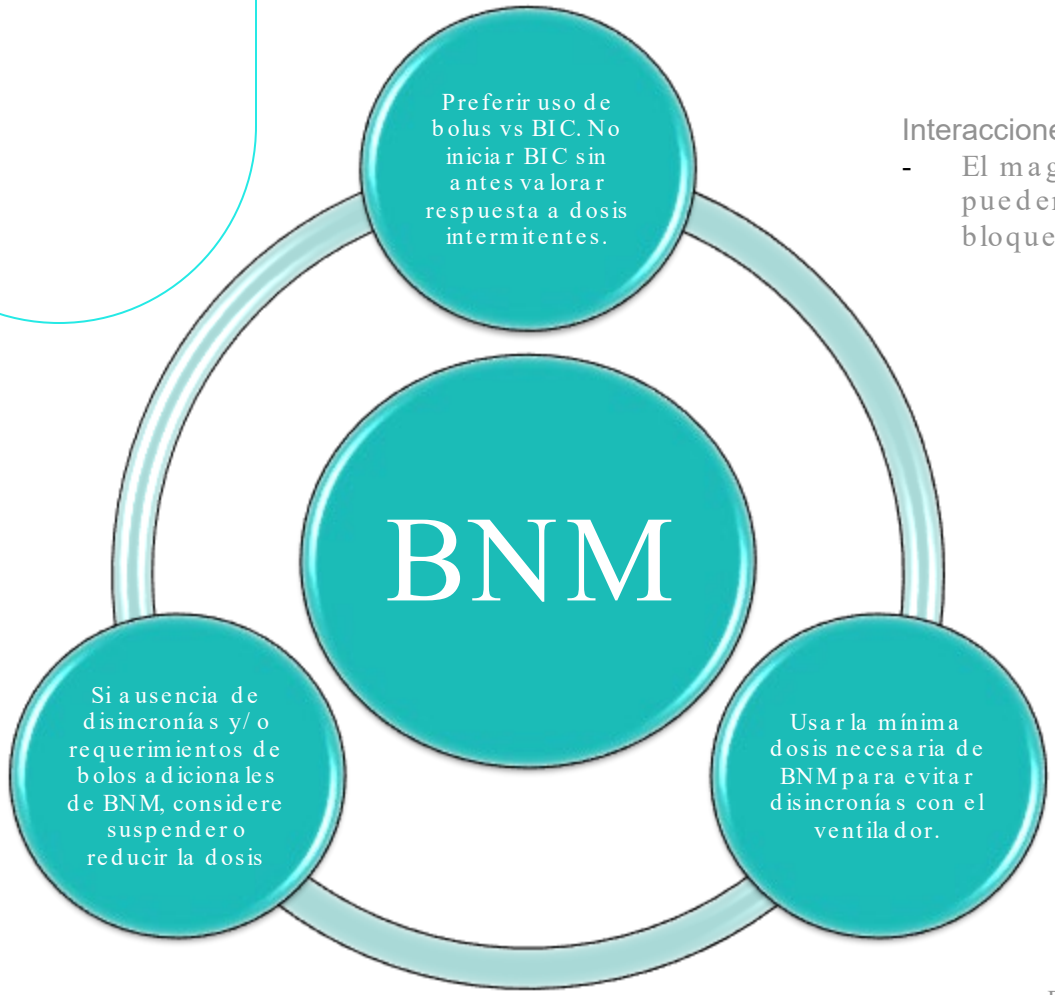



Rev Med Chile 2021; 149: 559-569

# Tips Sedación


Rev Med Chile 2021; 149: 559-569

# Tips BNM




Interacciones relevantes:

- El magnesio, la fenitoína y el litio pueden prolongar la duración del bloqueo no despolarizante.

Rev Med Chile 2021; 149: 559-569

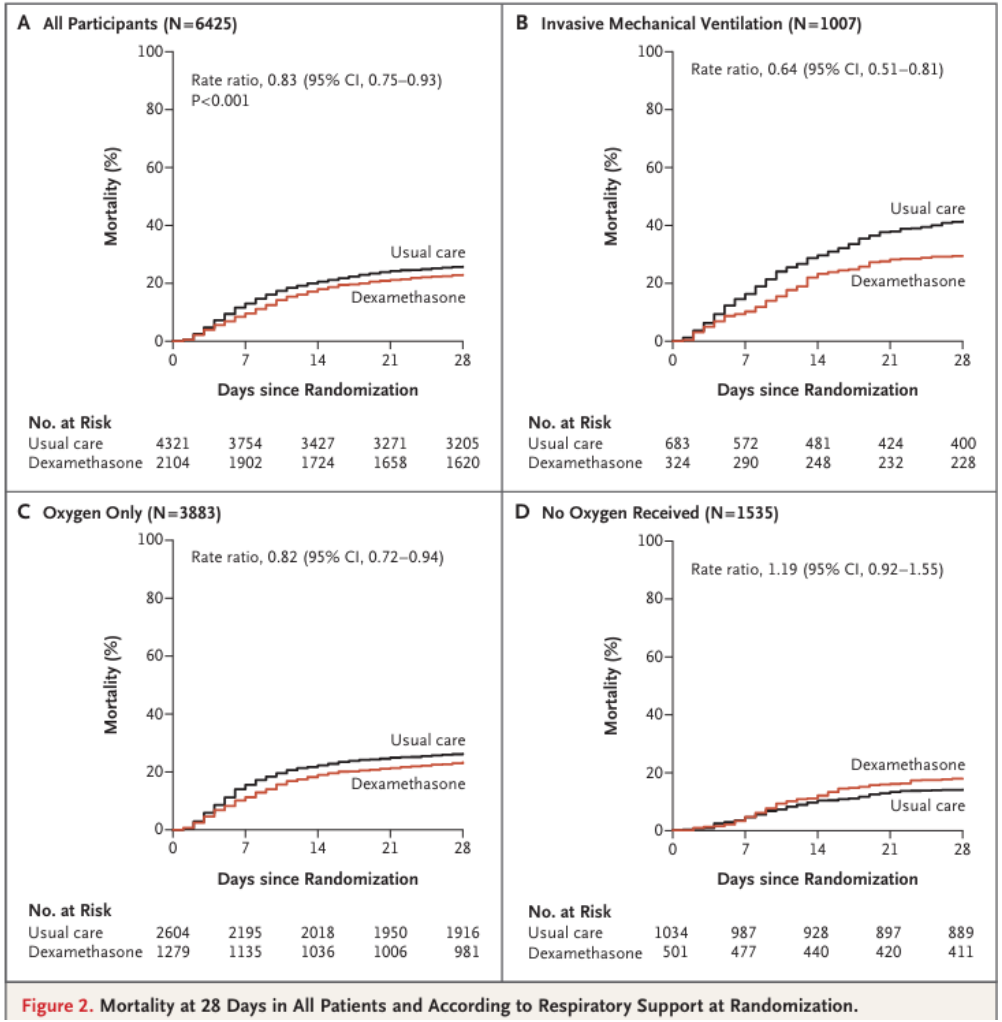



**Figure 2.** Mortality at 28 Days in All Patients and According to Respiratory Support at Randomization.

# Corticoides

- En pacientes hospitalizados con Covid - 19, uso de DEX resultó en una menor mortalidad a 28 días entre aquellos que recibían VMI u oxígeno, pero no entre aquellos que no recibían asistencia respiratoria .
- Dosis altas de DEX aumentaron el riesgo de muerte e hiperglicemia en comparación con el uso de dosis estándar .

DEX 6 mg IV o VO/día durante hasta 10 días o hasta el alta hospitalaria, lo que ocurra primero

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Lancet 2023; 401: 1499 –507

# Terapias dirigidas

Table 2c. Therapeutic Management of Hospitalized Adults With COVID-19

| Disease Severity | Recommendations for Antiviral or Immunomodulator Therapy | | Recommendations for Anticoagulant Therapy |
|---|---|---|---|
| | Clinical Scenario | Recommendation | |
| **Hospitalized for Reasons Other Than COVID-19** | Patients with mild to moderate COVID-19 who are at high risk of progressing to severe COVID-19[a] | See Therapeutic Management of Nonhospitalized Adults With COVID-19.[b] | For patients without an indication for therapeutic anticoagulation:<br>• **Prophylactic dose of heparin**, unless contraindicated **(AI)**; **(BIII)** for pregnant patients |
| **Hospitalized but Does Not Require Supplemental Oxygen** | All patients | The Panel **recommends against** the use of **dexamethasone (AIIa)** or other systemic corticosteroids **(AIII)** for the treatment of COVID-19.[c] | |
| | Patients who are at high risk of progressing to severe COVID-19[a] | **Remdesivir**[d] **(BIIb)** for patients who are immunocompromised; **(BIII)** for other high-risk patients | |
| **Hospitalized and Requires Conventional Oxygen**[e] | Patients who require minimal conventional oxygen | **Remdesivir**[d,f] **(BIIa)** | For nonpregnant patients with D-dimer levels above the ULN who do not have an increased bleeding risk:<br>• **Therapeutic dose of heparin**[h] **(CIIa)**<br>For other patients:<br>• **Prophylactic dose of heparin**, unless contraindicated **(AI)**; **(BIII)** for pregnant patients |
| | Most patients | Use **dexamethasone plus remdesivir**[f] **(BIIa)**. If remdesivir cannot be obtained, use **dexamethasone (BI)**. | |
| | Patients who are receiving dexamethasone and who have rapidly increasing oxygen needs and systemic inflammation | Add 1 of the following immunomodulators:[g]<br>*Preferred*<br>• **PO baricitinib (BIIa)**<br>• **IV tocilizumab (BIIa)**<br>*Alternatives (Listed in Alphabetical Order)*<br>• **IV abatacept (CIIa)**<br>• **IV infliximab (CIIa)** | |
| **Hospitalized and Requires HFNC Oxygen or NIV** | All patients | **Dexamethasone** should be administered to all patients **(AI)**. If not already initiated, promptly add 1 of the following immunomodulators:[g,i]<br>*Preferred*<br>• **PO baricitinib (AI)**<br>*Preferred Alternative*<br>• **IV tocilizumab (BIIa)**<br>*Additional Alternatives (Listed in Alphabetical Order)*<br>• **IV abatacept (CIIa)**<br>• **IV infliximab (CIIa)**<br>Add remdesivir to 1 of the options above in certain patients (for examples, see footnote).[j] | For patients without an indication for therapeutic anticoagulation:<br>• **Prophylactic dose of heparin**, unless contraindicated **(AI)**; **(BIII)** for pregnant patients<br>For patients who start on a therapeutic dose of heparin in a non-ICU setting and then transfer to the ICU, the Panel recommends switching to a **prophylactic dose of heparin**, unless there is another indication for therapeutic anticoagulation **(BIII)**. |
| **Hospitalized and Requires MV or ECMO** | All patients | **Dexamethasone** should be administered to all patients **(AI)**. If the patient has not already received a second immunomodulator, promptly add 1 of the following (listed in alphabetical order):[i,k]<br>• **PO baricitinib**[i] **(BIIa)**<br>• **IV tocilizumab**[i] **(BIIa)**<br>See footnote k for a discussion on the use of remdesivir. | |

Manejo terapéutico de adultos hospitalizados según la gravedad de su enfermedad y sus necesidades de oxígeno .

Varios estudios sugieren una alta tasa de complicaciones tromboembólicas en pacientes hospitalizados con COVID - 19, sobre todo si son pacientes críticos .

Key: CDC = Centers for Disease Control and Prevention ; Ct = cycle threshold ; ECMO = extracorporeal membrane oxygenation ; ED = emergency department ; HFNC = high - flow nasal cannula ; Hgb = hemoglobin ; ICU = intensive care unit ; IL = interleukin ; IV = intravenous ; JAK = Janus kinase ; MV = mechanical ventilation ; NIV = noninvasive ventilation ; the Panel = the COVID - 19 Treatment Guidelines Panel; PLT = platelet count ; PO = oral; RT-PCR = reverse transcription polymerase chain reaction ; SUBQ = subcutaneous ; ULN = upper limit of normal

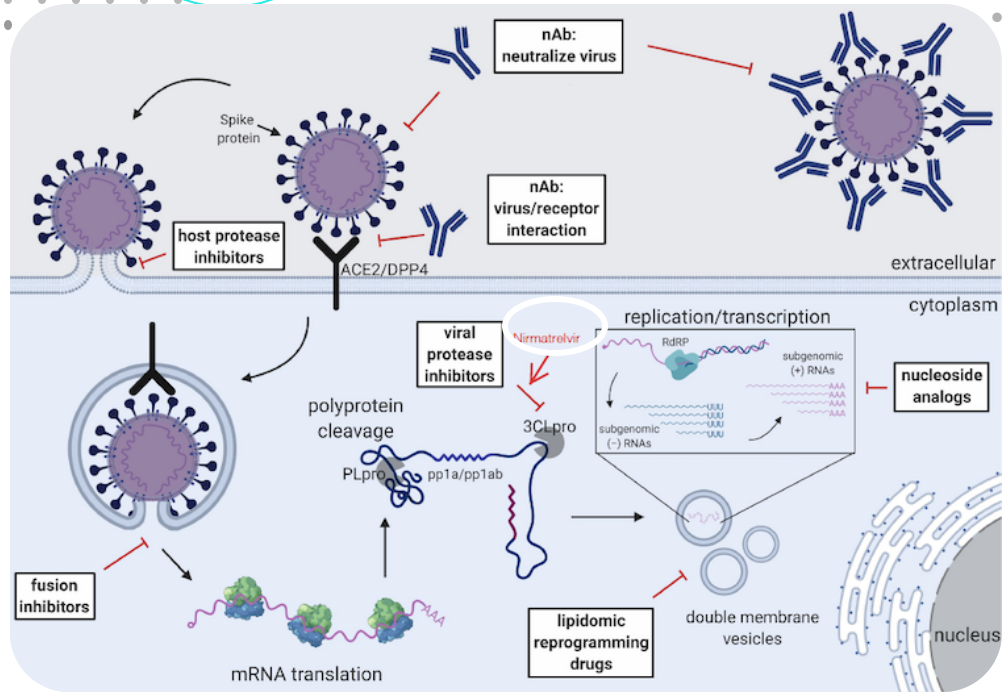
https://www.covid19treatmentguidelines.nih.gov /

| Drug Name | Dosing Regimen | Comments |
|---|---|---|
| **Abatacept** | Abatacept 10 mg/kg actual body weight (up to 1,000 mg) administered as a single IV dose | • No adjustment based on eGFR |
| **Baricitinib** | BAR dose is dependent on eGFR; duration of therapy is up to 14 days or until hospital discharge, whichever comes first. | • eGFR ≥60 mL/min/1.73 $m^2$: BAR 4 mg PO once daily<br>• eGFR 30 to <60 mL/min/1.73 $m^2$: BAR 2 mg PO once daily<br>• eGFR 15 to <30 mL/min/1.73 $m^2$: BAR 1 mg PO once daily<br>• eGFR <15 mL/min/1.73 $m^2$: **Not recommended**. |
| **Dexamethasone** | DEX 6 mg IV or PO once daily for up to 10 days or until hospital discharge, whichever comes first | • If DEX is not available, an equivalent dose of another corticosteroid may be used.<br>• For more information, see Systemic Corticosteroids. |
| **Heparin** | Therapeutic dose of SUBQ LMWH or IV UFH | • Administer for 14 days or until hospital discharge (whichever comes first) unless there is a diagnosis of VTE or another indication for therapeutic anticoagulation. |
| | Prophylactic dose of SUBQ LMWH or SUBQ UFH | • Administer for the duration of the hospital stay. |
| **Infliximab** | Infliximab 5 mg/kg actual body weight administered as a single IV dose | • No adjustment based on eGFR |
| **Remdesivir** | RDV 200 mg IV once, then RDV 100 mg IV once daily for 4 days or until hospital discharge, whichever comes first | • If the patient is hospitalized for reasons other than COVID-19, the treatment duration is 3 days. For more information, see Therapeutic Management of Nonhospitalized Adults With COVID-19.<br>• If the patient progresses to more severe illness, complete the course of RDV.<br>• For a discussion on using RDV in patients with renal insufficiency, see Remdesivir. |
| **Sarilumab** | Use the single-dose, prefilled syringe (**not** the prefilled pen) for SUBQ injection. Reconstitute sarilumab 400 mg in 100 cc 0.9% NaCl and administer as an IV infusion over 1 hour. | • In the United States, the currently approved route of administration for sarilumab is SUBQ injection. In the REMAP-CAP trial, the SUBQ formulation was used to prepare the IV infusion. |
| **Tocilizumab** | Tocilizumab 8 mg/kg actual body weight (up to 800 mg) administered as a single IV dose | • In clinical trials, a third of the participants received a second dose of tocilizumab 8 hours after the first dose if no clinical improvement was observed. |
| **Tofacitinib** | Tofacitinib 10 mg PO twice daily for up to 14 days or until hospital discharge, whichever comes first | • eGFR <60 mL/min/1.73 $m^2$: tofacitinib 5 mg PO twice daily |

Key: BAR = baricitinib; DEX = dexamethasone; eGFR = estimated glomerular filtration rate; IV = intravenous; LMWH = low-molecular-weight heparin; NaCl = sodium chloride; PO = oral; RDV = remdesivir; SUBQ = subcutaneous; UFH = unfractionated heparin; VTE = venous thromboembolism

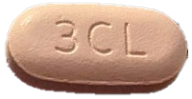
https://www.covid19treatmentguidelines.nih.gov/

# PAXLOVID
# (Nirmatrelvir /Ritonavir)



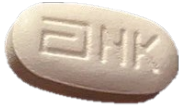

Antiviral compuesto por 2 inhibidores de proteasa .

Indicado en el tratamiento de la infección por SARS-CoV-2 no severa, en pacientes que cumplen con algunos criterios que los clasifican como población de alto riesgo de progresar a enfermedad grave .




## Nirmatrelvir

Impide replicación viral inhibiendo a la proteasa 3CLpro del SARS-CoV-2.




## Ritonavir

Potencia actividad de nirmatrelvir mediante inhibición del CYP3A4.

# Población objetivo

| | |
|---|---|
| Criterio 1 | ⩾65 años + Comorbilidad severa (Enf. pulmonar cónica avanzada, Enf. Hepática crónica con cirrosis, Enf. Cardiovascular descompensada o severa, obesidad mórbida). Independiente de vacunación. |
| Criterio 2 | ≥12 años + Inmunosupresión. (Neutropénicos, trasplantados, usuarios anticuerpos monoclonales anti CD-20, tto. Inmunosupresor, PPVI en etapa avanzada de la enfermedad, cáncer activo). Independiente de vacunación. |
| Criterio 3 | Entre 12 y 65 años + Comorbilidad severa. Protección incompleta de vacunación. |

- Pacientes ambulatorios u hospitalizados con diagnóstico COVID-19 confirmado, que no requieren oxígeno suplementario.
- Inicio de síntomas ≤5 días.
- Infección por SARS-CoV-2 no severa.

# Criterios de exclusión

- <12 años.
- Peso <40 kg.
- Insuficiencia renal grave (incluyendo pacientes en diálisis).
- Insuficiencia hepática grave (Child -Pugh Clase C)
- Hipersensibilidad
- Interacciones farmacológicas graves.
- Personas en tratamiento de tuberculosis.
- **Embarazo/lactancia: No se dispone de información sobre la seguridad de Paxlovid

# Posología

| | |
|---|---|
| **Dosis estándar** | 300 mg nirmatrelvir + 100 mg ritonavir c/12h x 5 días |
| **VFGe 30-59 ml/min/1.73m2** | 150 mg nirmatrelvir + 100 mg ritonavir c/12h x 5 días |
| **Insuficiencia hepática leve a moderada ( Child-Pugh Clase A o B)** | No requiere ajuste de dosis. |

# Conclusiones

- Patologías prevalentes en intensivos, frecuentemente requieren VM, estadías prolongadas .
- Polimedicados .
- Medicamentos de alto riesgo .
- Terapias antivirales dirigidas no tan disponibles en Chile.