Molnupiravir Mini-HTA for the treatment of COVID-19

Evidence Evaluation Center for Health Care Decisions - CEEDS

Global Institute of Clinical Excellence

Health and Innovation Chair

Contents

Título	Health Technology Assessment: Molnupiravir (Lagevrio) for the treatment of COVID-19
Code	23122021IHLMKCh
Requestor area	Public Health Committee
Request date	21/12/2021
First Reply	23/12/2021
Last Update	17/01/2022

Executive Summary

COVID-19 antiviral treatments are still in the early stages of development, considering that the disease was first identified in late 2019.

The cost of molnupiravir estimated from the U.S. government's published purchase price is $700 per 5-day treatment (Willyard, 2021).

The molnupiravir (lagevrio) mechanism has a high potential for long-term risk. This antiviral works by incorporating itself into viral RNA, creating errors, and preventing effective replication within days (Kabinger et al., 2021). Introducing/provoking mutations in a virus can lead to potentially dangerous changes, especially when poor adherence or total drug consumption cannot be guaranteed. Also, laboratory results showed a low frequency of mutations in human DNA in blood cells and spermatozoa. Its mechanism of action and the observed effects make its use unfeasible during pregnancy.

The evidence collected by Bernal et al. had a high risk of bias in the outcomes evaluated for its effectiveness (incidence of hospitalization for any cause (defined as ≥24 hours of

acute care in a hospital or any similar center or death up to day 29). Therefore, the recommendation for using Molnupiravir should be evaluated with caution, given that there is little evidence regarding its effectiveness and safety. Additionally, the only peer-reviewed study presents a low level of certainty of the evidence, and the risks appear to be higher than the potential benefits.

Methodology

We carried out a technology assessment following the methodological manual for health technology assessment Multicriteria Decision Analysis Matrix of the Global Institute for Clinical Excellence (IGEC).

The following are the steps used:

1. Identify the specific technology and use 2.
2. Elaborate the PICOTS
3. Elaborate on the CATWOE of the technology (Annex).
4. Establish the Search Equation (Annex)
5. Establish the incidence and prevalence of the problem to be solved by the technology. (Annex)
6. Establish the ethical evaluation of the use of the technology (Annex).
7. Establish the social evaluation of the use of the technology (Annex).
8. Establish the legal evaluation of the use of the technology (Annex).
9. Establish the environmental evaluation of the use of the technology (Annex).
10. Establish the impact of the technology on the quality of life of the patients (Annex).

11. Establish the Survival contributed by the technology to the patients. (Annex)
12. Establish the effect on caregiver/family well-being. (Annex)
13. We evaluate the studies using the GRADE methodology (Annex).

Background

Coronaviruses use an RNA-dependent RNA polymerase (RdRp) to replicate and transcribe their RNA genome (Kabinger et al., 2021).

RNA-dependent RNA polymerase of severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) is an essential target in the current drug development efforts to treat COVID-19 disease (Gordon et al., 2021).

Molnupiravir targets RdRp, suggesting a two-step model for the mechanism of molnupiravir-induced coronavirus RNA mutagenesis (Gordon et al., 2021).

It has been theorized that the strategy of action followed by the drug molnupiravir or NHC is that of lethal mutagenesis, also known as catastrophic viral error, which is the same as that of broad-spectrum antivirals that exploit the high mutation rate of viruses and low mutational tolerance of RNA viruses. Although lethal mutagenesis seems to be supported by some laboratory results, evidence still requires validation in animal and human studies (Menendez-Arias, 2021).

Technology description.

Molnupiravir or MK-4482/EIDD-2801 or NHC is a prodrug of the nucleoside derivative β-D-N4-hydroxycytidine (NHC) (Menendez-Arias, 2021), initially considered as a possible therapy for Venezuelan equine encephalitis virus at the non-profit company DRIVE (Drug Innovation Ventures at Emory) of Emory University, in Atlanta, then tested for influenza and respiratory syncytial virus. DRIVE licensed the compound to Ridgeback

Biotherapeutics, Miami, Florida, which tried to partner with several companies until Merck finally reached an agreement (Willyard, 2021).

Molnupiravir is a nucleoside analog, meaning that it mimics some of the components of RNA. When SARS-CoV-2 enters a cell, the virus needs to duplicate its RNA genome to form new viruses. Molnupiravir is incorporated into the emerging RNA strands and, once inside, wreaks havoc. The compound can change its configuration, sometimes mimicking the nucleoside cytidine and sometimes uridine (Willyard, 2021). Those RNA strands become defective blueprints for the next round of viral genomes. Wherever the compound is inserted, and conformational change occurs, a point mutation occurs (Gordon et al., 2021). When enough mutations accumulate, the viral population collapses. And because mutations accumulate randomly, it is difficult for viruses to develop resistance to molnupiravir, a supposed advantage for the compound (Willyard, 2021).La dosis recomendada en pacientes adultos es de 800 mg (cuatro cápsulas de 200 mg) por vía oral cada 12 horas durante 5 días, con o sin alimentos. El tratamiento debe iniciarse en los 5 días siguientes al inicio de los síntomas. (FDA, 2021).

PICOTS

Population: people over 18 years of age with COVID-19 disease.

Intervention: use of molnupiravir (lagevrio) for the treatment of COVID-|9

Comparator: standard medical care, other pharmacological therapies, non-pharmacological medical management.

Outcomes: Safety, Effectiveness, and Quality of Life.

Time: all outcomes up to a maximum of 1 year after treatment initiation

Settings: outpatient management only.

Integrative studies

As a result of the primary search performed, a systematic review on the efficacy and safety of molnupiravir in patients with COVID-19 by Singh et al. was found.

The quality of the evidence of the review by Singh et al. was critically low according to AMSTAR-2, based on the lack of detailed eligibility criteria, lack of an exhaustive literature search, lack of definition of terms or search strategy, and lack of risk of bias assessment of primary studies.

The systematic review by Singh et al. was carried out to evaluate the efficacy and safety of oral antiviral in patients with COVID-19. It included nine human studies. There were 2 phase I studies (NCT04392219, NCT04746183), one phase II study (NCT04405570), three phase III studies (NCT04575597, NCT04575597, NCT04575584), and three studies withdrawn due to futility. Most of the studies were conducted in patients with mild COVID-19 not requiring hospitalization. Studies withdrawn early included patients with moderate or severe COVID-19 and requiring hospitalization. The primary outcomes of the Phase, I and II studies were safety (tolerability, adverse events, toxicity) and time to viral RNA clearance in nasopharyngeal swabs (Singh et al.,2021).

The early phase studies (I and II) included in the review suggest that molnupiravir is tolerated in two doses of 50 to 800 mg/day for 5.5 days or single doses of up to 1600 mg, as well as twice-daily schedules of 200 mg, 400 mg and 800 mg for five days. Virus clearance time was shorter with molnupiravir (14 days versus 27 days with placebo, $p<0.05$), there was less viral isolation in treated patients. Regarding the adverse events reported in the primary studies included in Singh et al., headache, diarrhea, insomnia, and increased alanine aminotransferase (ALT). In a phase II study, serious adverse

events were reported, three patients were receiving molnupiravir (2 patients with 400 mg and one patient with 800 mg), two patients had decreased oxygen saturation, one case of stroke, and one case of acute respiratory failure. The death occurred in one patient in the placebo group (Singh et al.,2021).

Clinical Trials

We found only one randomized, controlled study included in the clinical evaluation at the review. We found six other studies, only one with available results but with a small sample size and only evaluating the safety and tolerability of the drug. Recruitment was terminated based on positive efficacy results from a planned interim analysis conducted when 50% of the target enrollment had been followed through day 29. Therefore, the study (n = 1433) did not achieve the target sample size (n = 1550). Additionally, the primary outcomes described in the article generally reflect those of the registry, with the omission of the percentage of participants who discontinued the study intervention due to an adverse event (Bernal et al., 2021).

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Table of Types of Clinical Studies Included in the Molnupiravir Health Technology Assessment

Title	Study Type	Participants	Objective	Methods	Outcomes	Observation
Bernal et al. (2021)	A phase 3, double-blind, randomized and placebo-controlled	1443	to evaluate the efficacy and safety of treatment with molnupiravir initiated within five days of the onset of signs or symptoms in non-hospitalized, unvaccinated adults with laboratory-confirmed mild-to-moderate Covid-19 at least one risk factor for severe Covid-19 disease. .	1,433 participants were randomized; 716 were assigned to receive molnupiravir, and 717 received a placebo. Trial participants were randomly assigned to receive 800 mg of molnupiravir or placebo twice daily for five days. The primary efficacy endpoint was the incidence of hospitalization or death at day 29; the incidence of adverse events was the primary safety endpoint. A planned interim analysis was performed when 50% of the 1,550 participants (target enrollment) had been followed through day 29.	The risk of hospitalization for any cause or death through day 29 was lower with molnupiravir (28 of 385 participants [7.3%]) than with placebo (53 of 377 [14.1%]) (difference, -6.8 percentage points; 95% confidence interval, -11.3 to -2.4; P=0.001). In the analysis of all participants who had been randomized, the percentage of participants who were hospitalized or died by day 29 was lower in the molnupiravir group than in the placebo group (6.8% [48 of 709] vs. 9.7% [68 of 699]; difference, -3.0 percentage points; 95% confidence interval, -5.9 to -0.1). The subgroup analyses were broadly consistent with these overall results; in some subgroups, such as patients with evidence of prior SARS-CoV-2 infection, those with a low baseline viral load, and those with diabetes, the point estimate of the difference favored placebo. One death was reported in the molnupiravir group and 9 in the placebo group through day 29. Adverse events were reported in 216 of 710 participants (30.4%) in the molnupiravir group and 231 of 701 (33.0%) in the placebo group.	El intervalo de confianza de la reducción del riesgo absoluto es amplio (0,1% - 5,9%), por lo que el NNT puede estar entre 17 y 1000.) El nivel de certeza de la evidencia a partir del sistema GRADE fue entre baja y muy baja,que incluye las dimensiones de: riesgo de sesgo, inconsistencia, evidencia indirecta, imprecisión (Tabla GRADE)

Other studies found but not used on this document

Title	Status	Results	Conditions	Interventions	URL
Efficacy and Safety of Molnupiravir (MK-4482) in Hospitalized Adult Participants With COVID-19 (MK-4482-001)	Ended	No available	Coronavirus Disease (COVID-19)	Drug: Molnupiravir|Drug: Placebo	https://ClinicalTrials.gov/show/NCT04575584
Efficacy and Safety of Molnupiravir (MK-4482) in Non-Hospitalized Adult Participants With COVID-19 (MK-4482-002)	Active, not recruiting	No available	Coronavirus Disease (COVID-19)	Drug: Molnupiravir|Drug: Placebo	https://ClinicalTrials.gov/show/NCT04575597
Study of MK-4482 for Prevention of Coronavirus Disease 2019 (COVID-19) in Adults (MK-4482-013)	Recruiting	No available	Coronavirus Disease (COVID-19)	Drug: Molnupiravir|Drug: Placebo	https://ClinicalTrials.gov/show/NCT04939428
The Safety of Molnupiravir (EIDD-2801) and Its Effect on Viral Shedding of SARS-CoV-2 (END-COVID)	Recruiting	No available	SARS-CoV 2	Drug: EIDD-2801|Drug: Placebo	https://ClinicalTrials.gov/show/NCT04405739
COVID-19 First In Human Study to Evaluate Safety, Tolerability, and Pharmacokinetics of EIDD-2801 in Healthy Volunteers	Completed	Results available	Coronavirus	Drug: EIDD-2801|Drug: Placebo	https://ClinicalTrials.gov/show/NCT04392219
A Safety, Tolerability, and Efficacy of Molnupiravir (EIDD-2801) to Eliminate Infectious Virus Detection in Persons With COVID-19	Completed	No available	SARS-CoV 2	Drug: EIDD-2801|Drug: Placebo (PBO)	https://ClinicalTrials.gov/show/NCT04405570
AGILE (Early Phase Platform Trial for COVID-19)	Recruiting	No available	Covid19	Drug: CST-2: EIDD-2801|Drug: CST-2: Placebo|Drug: Nitazoxanide|Drug: VIR-7832|Drug: VIR-7831|Drug: CST-5: Placebo	https://ClinicalTrials.gov/show/NCT04746183

Source: information extracted from each of the studies

Clinical Outcomes

The clinical outcomes on which we focused this technology assessment demonstrated effectiveness in decreasing hospitalizations, mortality, and adverse events.

In the study by Bernal et al., the primary efficacy endpoint was the incidence of all-cause hospitalization (defined as ≥24 hours of acute care in a hospital or any similar facility) or death through day 29 in the modified intention-to-treat population.

Effectiveness of the use of technology

The estimated effectiveness in the Bernal et al. study is 30%.

According to the study by Bernal et al. (2021) published in New England, Molnupiravir (Lagevrio) was evaluated in a previously young population at increased risk of severe COVID-19. The mean age of participants was 43 years (range 18-90), and 17% were older than 60 years. Not enough is known about efficacy in the elderly, especially those over 75 years of age. The number of people at increased risk was mainly obese (75%), but relatively few high-risk patients, such as active oncologic morbidity, chronic kidney disease, COPD, cardiac pathology, or diabetes mellitus.

Reviewing the Number Needed to Treat (NNT), this was high based on the interim analysis results and adjusted upward to ~34 (n=1,433) based on the complete data set. In other words, an average of 34 people need to be treated to prevent one hospitalization or death. Similar studies in the past have shown that it is usual to multiply the NNT by a factor of ten to arrive at a realistic estimate that considers actual use in clinical practice. In addition, the NNT in vaccinated persons will be even higher, calling into question the added clinical value of Lagevrio in areas with vaccination coverage above 50%. The absolute risk reduction confidence interval is wide (0.1% - 5.9%), so the NNT may be

between 17 and 1000. In addition, the statistical significance of the results is low (p=0.02), and it is impossible to evaluate possible forms of bias, as all details of the study by Bernal et al. are not found.

According to the FDA analysis, it is difficult to identify specific subsets of vaccinated participants who are most likely to benefit from molnupiravir, or the particular subsets of vaccinated participants who are most likely to benefit from molnupiravir. In addition, some immunocompromised patients may not have a robust immune response following vaccination and, therefore, may represent a subset of vaccinated individuals more likely to benefit from molnupiravir. However, immunocompromised patients may experience prolonged viral shedding after COVID-19, given the higher spike protein mutations observed in Part 1 of the MK 4482-001 MK-4482-002 trials (FDA, 2021).

Quality of Life

In the study by Bernal et al., no results of quality-of-life measurements were found.

Given the above, we cannot state with sufficient certainty that molnupiravir positively impacts patients' quality of life with COVID-19.

Adverse Reactions

In the Bernal et al. study, the primary safety endpoint was the incidence of adverse events. Safety outcomes, including percentages of participants with adverse events, were assessed in the safety population, which consisted of all participants who had been randomized and had received at least one dose of molnupiravir or placebo. In addition, participants were evaluated for any post-treatment baseline platelet level below 50,000 per microliter and possible drug-induced liver injury based on prespecified changes in liver enzymes (Bernal et al., 2021).

According to the results published by Bernal et al., the secondary efficacy variables they used were based on the WHO 11-point clinical progression scale and patient-reported Covid-19 signs and symptoms up today 29. Improvement (i.e., decrease) and progression of Covid-19 signs and symptoms were defined as any reduction and worsening, respectively, of baseline symptom severity (Bernal et al., 2021).

In the results reported by Bernal et al., the percentage of participants with at least one adverse event was similar in the two groups (30.40% in the molnupiravir group and 33.0% in the placebo group), as was the percentage of participants with adverse events that the investigators considered related to the trial regimen (8.0% vs. 8.4%). Deaths due to adverse events, none of which were considered by the investigators to be related to the trial regimen, were reported less frequently in the molnupiravir group than in the placebo group. For example, after day 29, three additional deaths occurred due to adverse events in the placebo group, compared with one different end reported in the molnupiravir group and compared with one additional death in the molnupiravir group (Bernal et al., 2021). In addition, one participant in the molnupiravir group and one in the placebo group met the prespecified criteria of a post-baseline platelet count below 50,000 per microliter; the low platelet count in the molnupiravir-treated participant was reported on day 12 and was not considered to be treatment-related (Bernal et al., 2021).

About in vitro mutagenicity, a low frequency of human DNA mutations was demonstrated in blood cells and spermatozoa; in laboratory results reported to FDA in vivo, alterations in hemoglobin results of low and moderate severity were found (FDA, 2021).

Molnupiravir was found in the breast milk of rats (FDA, 2021).

Given the mechanisms of action of molnupiravir and the observed results make its use unfeasible during pregnancy or lactation.

Molnupiravir, according to data submitted to the FDA, may affect bone and cartilage development. In rats' chronic study (3 months), abnormal bone (growth plate) and cartilage formation were observed. In addition, delayed and incomplete ossification was observed in fetuses in embryo-fetal development (EFD) studies in rats and rabbits. Systemic exposures in pregnant rats and rabbits were approximately 8 and 7 times, respectively, the mean clinical exposure to NHC at 800 mg Q12H.

No data were found to verify safety in children under 18 years of age, and there are concerns regarding use, given the potential for impairment of bone development.

Conclusions:

a) Molnupiravir Treatment has FDA approval for Emergency use only; the given approval does not imply support for its clinical effectiveness.

b) In the GRADE evaluation done to Bernal et al.'s study (see annex), we identified serious methodological flaws which prevent inferring conclusions favorable to the use of molnupiravir.

c) The recommendation to use molnupiravir in any subgroup of patients should be analyzed with caution due to the low level of certainty of the evidence in patients with COVID-19.

d) The use of molnupiravir in pregnant or lactating women or children under 18 years of age is not recommended under any circumstances. If a pregnant woman inadvertently receives the drug, an active search for fetal alterations during pregnancy should be performed.

e) Molnupiravir was not studied in the COVID-19 vaccinated population.

f) The effect of a 30% decrease in hospitalization with the use of molnupiravir was obtained in populations with a predominance of SARS-CoV-2 delta variant, which had a high potential for hospitalization and death. In the case of variants with a lower potential for hospitalization and death, an even lower effect can be inferred from their mechanism of action. For example, if we were faced with a variant with a hospitalization and death rate eight times lower than that of the study, we would have an NNT of 80,000 to obtain a positive effect on one patient. This would imply a non-hospitalized patient cost of = 80,000* $700, i.e. US$56,000,000.

In vaccinated populations with a lower risk of hospitalization and death, using molnupiravir to obtain one patient benefit would imply a cost about six times higher. In a previously vaccinated population, the combination of a more benign variant implies a theoretical NNT of more than 200,000.

g) The risk of mutations capable of maintaining the virus viable in patients with suboptimal consumption (below the recommended doses) is low. Still, the risk exists and should be especially considered in countries with problems of continuity of access to drugs.

Cite as

Evidence Evaluation Center for Health Care Decisions (CEEDS). (2022), Health Technology Assessment: Molnupiravir for the treatment of COVID-19.

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Annexes

GRADE: EVIDENCE EVALUATION TABLE

Question: Oral Molnupiravir compared to placebo for outpatients with COVID-19 (Mild to moderate with 1 risk factor for the development of severe disease by Covid-19)
Setting: Outpatient
Reference: Jayk Bernal, A., Gomes da Silva, M. M., Musungaie, D. B., Kovalchuk, E., Gonzalez, A., Delos Reyes, V., Martín-Quirós, A., Caraco, Y., Williams-Diaz, A., Brown, M. L., Du, J., Pedley, A., Assad, C., Strizki, J., Grobler, J. A., Shamsuddin, H. H., Tipping, R., Wan, H., Paschke, A., Butterton, J. R., … MOVe-OUT Study Group (2021). Molnupiravir for Oral Treatment of Covid-19 in Non-hospitalized Patients. The New England journal of medicine, 10.1056/NEJMoa2116044. Advance online publication. https://doi.org/10.1056/NEJMoa2116044

Certainty Evaluation							Patient number		Effect		Quality of Evidence	Importance
№ Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations	Molnupiravir oral	placebo	Relative (95% CI)	Absolute (95% CI)		
Incidence of all-cause hospitalization (defined as ≥24 hours of acute care in a hospital or similar facility) participants in the modified intention-to-treat population.												
1	Randomized Controlled Trial	Very serious [a,b,c,d]	Not serious	Not serious	Not serious	None	28/385 (7.3%)	53/377 (14.1%)	**RR 0.52** (0.33 to 0.80)[e]	**7 minus per 100** (from 9 minus to 3 less)	⊕⊕◯◯ Low	CRITICAL
Incidence of hospitalization for any cause (defined as ≥24 hours of acute care in a hospital or similar facility) participants in the fully randomized modified intention-to-treat population.												
1	Randomized Controlled Trial	Very serious [a,b,c,d]	Not serious	serious[f]	serious[g]	None	48/709 (6.8%)	68/699 (9.7%)	**RR 0.70** (0.49 to 0.99)[e]	**Three minus per 100** (from 5 minus tp 0 less)	⊕◯◯◯ Very Low	IMPORTANT
Incidence of only Covid-19-related hospitalizations or deaths												
1	Randomized Controlled Trial	Very serious [a,b,c,d]	Not serious	serious[f]	very serious [h]	None	45/709 (6.3%)	64/699 (9.2%)	**RR 0.69** (0.48 to 1.00)[e]	**Three minus per 100** (from 5 to 0 less)	⊕◯◯◯ Very Low	CRITICAL
Incidence of adverse events in the safety population (≥1 adverse event.												
1	Randomized Controlled Trial	serious[b,d]	Not serious	serious[f]	very serious [h]	None	216/710 (30.4%)	231/701 (33.0%)	**RR 0.92** (0.79 a 1.08)[e]	**Three minus per 100** (from 7 to 3 plus)	⊕◯◯◯ Very Low	CRITICAL
Death												
1	Randomized Controlled Trial	serious[b,d]	Not serious	serious[f]	serious[g]	None	2/710 (0.3%)	12/701 (1.7%)	**RR 0.16** (0.04 a 0.73)[e]	**One minus per 100** (from 2 to 0 less)	⊕◯◯◯ Very Low	CRITICAL

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Certainty Evaluation							Patient number		Effect		Quality of Evidence	Importance
№ Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations	Molnupiravir oral	placebo	Relative (95% CI)	Absolute (95% CI)		

IC: Confidence Interval; **R.R.:** Relative Risk

Explanations

a. Randomization (Low Risk): Eligible participants were randomized in a 1:1 ratio using a centralized interactive response technology system to receive molnupiravir (800 mg administered in four 200 mg capsules) or an identical placebo, administered orally twice daily for five days. Randomization was stratified into four blocks according to the onset of signs or symptoms (≤3 days vs. >3 days).
b. Intervention deviations: (some considerations) quote, "Participants and investigators will not know treatment assignments until all actively enrolled participants have undergone the 7-month follow-up visit." Data on outcomes are not reported for all randomized participants; in the absence of mortality status, data at day 29 was imputed as hospitalization or death (Lack of information could depend on the actual value of the outcome.).
c. The efficacy analysis was performed using a modified ITT analysis (i.e., not all participants initially randomized in the study were included).
d. The groups differed in terms of the sex of the participants. The results of a post hoc analysis adjusted for participant sex (the only baseline factor potentially unbalanced between groups) were consistent with those of the primary analysis, with the risk of hospitalization or death through day 29 being lower by 2.8 percentage points (95 % CI, -5.7 to 0.1) with molnupiravir over placebo; however, there was no difference between groups
e. The R.R. was calculated by the authors of the GRADE table based on the following data published in the study
f. Estimates may change over longer follow-up. For example, the population included in the RCT may not represent all persons with mild to moderate COVID 19 with one risk factor for developing severe disease.
g. Wide confidence intervals
h. The confidence interval limits include an increase or decrease in the effect.

PICOTS

What is the problem to be solved by the proposed technology?	COVID-19
What is the intervention (technology) to be evaluated?	Molnupiravir for the treatment of COVID-19
What are the comparators for the technology to be evaluated? If none, write None.	Standard medical care, other pharmacological therapies, non-pharmacological medical management.
What are the Results you are evaluating or looking for? If you do not have them predetermined, write "No results specified."	Effectiveness, safety
Is there a specific time frame ? If yes, please indicate which one, otherwise enter "No predefined time frame."	No preset time frame
What is the target environment for the technology?	Outpatient

CATWOE

What is the technology under analysis?	molnupiravir para el tratamiento del COVID-19
Who are the direct beneficiaries of the technology?	men and women over 18 years old
And how does its use affect beneficiaries?	Decreases viral load eliminates the virus at the end of treatment. Avoids hospitalizations by 30%,
Who will implement the technology?	Primary care and emergency physicians, while its use was tested in the first five days.
What needs to be impacted for technology success?	The learning curve, technology acquisition, verification of delivery costs, safety of care, early diagnosis, patient follow-up. Active exclusion of patients at low, medium, and high risk of pregnancy.

What is the purpose of the technology?	Decrease hospitalizations and deaths due to COVID-19.
What is the global vision of using or not using technology?	Pandemic control.
What are the broader impacts of using or not using technology?	Cease virus transmission.
Who owns the technology being investigated?	Merck
What role will the owner of the investigated technology play in its implementation, evaluation, monitoring?	monitoring, encouragement of the use
What are the demands and constraints external to the System in which the technology will be deployed?	In ambulatory consultation. Service costs.

INCIDENCE, PREVALENCE, MORBIDITY, AND MORTALITY

What is the disease that the technology will solve?	COVID-19
What is the technology under evaluation?	Molnupiravir for the treatment of COVID-19
What is the incidence of the health problem to be solved with the technology?	As of December 22, 2021, there are 5112719 confirmed cases in Colombia, of which 12806 are active.
What is the prevalence of the health problem to be solved with the technology?	Variable, today 12806 active cases
What is the mortality of the health problem to be solved with the technology?	Variable, today, December 22, 45 deaths.
What is the morbidity of the health problem to be solved with the technology?	Hospitalization and death.

SEARCH STRATEGY

((("molnupiravir"[Supplementary Concept] OR "molnupiravir"[All Fields]) AND ("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "covid 19 vaccines"[All Fields] OR "covid 19 vaccines"[MeSH Terms] OR "covid 19 serotherapy"[All Fields] OR "covid 19 serotherapy"[Supplementary Concept] OR "covid 19 nucleic acid testing"[All Fields] OR "covid 19 nucleic acid testing"[MeSH Terms] OR "covid 19 serological testing"[All Fields] OR "covid 19 serological testing"[MeSH Terms] OR "covid 19 testing"[All Fields] OR "covid 19 testing"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR (("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication]))) AND ((y_10[Filter]) AND (booksdocs[Filter] OR clinicaltrial[Filter] OR meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR review[Filter] OR systematicreview[Filter]))

QUALITY OF LIFE

¿Cuál es la tecnología en evaluación?	Molnupiravir para tratamiento de COVID-19
Are QOL, O.S., PFS, W.B. C.G. being evaluated with which comparators?	Not established in the literature
What is the impact of technology on patients' quality of life?	Not established, high risk of bias in existing data. Not reported
Which scale was used for the evaluation of patients' quality of life?	Not established
What is the total Survival contributed by the technology to patients?	30%
What is the Survival Free of Disease Progression (SLPE) or Disease-Free Survival?	Not evaluated
To what extent does technology improve caregiver well-being?	Not evaluated

POLITICAL, ECONOMIC, SOCIAL, ENVIRONMENTAL, AND ETHICAL

What is the name of the technology to be evaluated?	Molnupiravir
Is the proposed technology change similar to something previously implemented or existing?	Yes
Is the current government ideologically opposed to the incorporation of this technology?	No
Does the current government have a price control strategy that may prevent access to technology?	No
Does the government have a regulatory initiative underway or planned in the short term (less than two years) for the technology or a broader category that includes it?	No
If you have answered yes to any of the above questions, please explain why	
Is the current macroeconomic context favorable to the introduction of new technology?	Yes
Explain in a paragraph your justification of the previous answer (remember to include as the following variables employment, price level, exchange rate, and interest rate)	.
Does the adoption of technologies imply a change in customs or ingrained beliefs?	No
Does the use of technology go against a belief or custom?	No
Is the use of technology acceptable to local elites?	Yes
Is the use of technology acceptable to non-elite groups?	Yes
Does the technology of interest replace an existing one?	No
If the above answer is yes, please indicate which one(s) it replaces	Supplements symptomatic management of COVID-19
Does the technology under evaluation complement an existing technology?	Yes
If the above answer is yes, please indicate which technology(ies) it complements.	Dexamethasone, oxygen.
How do you think this technology affects other existing technologies? Write your concept.	May decrease the use of other medications and use of the emergency department.
Does the use of technology imply a change in legislation?	No
Does the use of technology contravene a law or regulation?	No

Does the implementation of the technology require a regulatory change?	No
Does the implementation of technology violate the principle of patient autonomy?	No
Does the implementation of the technology violate the principle of patient benefit?	No
Does the implementation of the technology violate the principle of patient nonmaleficence?	No
Does the implementation of the technology harm any patients?	No
Does the implementation of the technology harm any individuals? (obligatorily individuals other than patients are judged).	No
Does the implementation of the technology violate the principle of patient justice?	No
Is the technology reusable?	No
How many times can the technology be reused after disinfection if the technology is reusable?	Zero
What materials make up the technology? you can choose more than one	Med
Are there mechanisms in place in the organization to dispose of technology once it has completed its useful life?	Yes
Can the use of technology induce the violation of the value of Compassion?	No