

SELECTION CRITERIA OF PROMISING COVID-19 THERAPEUTICS

According to the EU Strategy on COVID-19 Therapeutics, on scanning for candidate therapeutics activity to establish the EU's therapeutics portfolio (and more specifically a broader portfolio of ten potential promising candidates by October 2021), the expert sub-group on COVID-19 Therapeutics (under the European expert group on SARS-CoV-2 variants) defines the selection criteria, template and ranking system for inclusion of the different therapeutics in this portfolio.

The ranking of promising therapeutics according to the selection criteria will be done by the expert subgroup, within the Template for selecting promising COVID-19 therapeutics according to selection criteria, provided for this activity (Appendix I).

The criteria for selecting promising COVID-19 therapeutics, with description, are listed below:

Selection criteria	Description
Diverse portfolio approach	Diverse portfolio approach is applied to cover the whole spectrum of COVID-19 and all COVID-19 product categories of new or repurposed medicinal products, in line with the EU Strategy on COVID-19 Therapeutics and the Document defining the categories of products most needed in the EU: - Coverage of the whole spectrum of COVID-19: Pre-exposure and post-exposure prophylaxis in high-risk patient; Treatment of acute COVID-19 in (high-risk) outpatients (mild/moderate COVID-19) and hospitalised patients (moderate/severe/critical COVID-19); Treatment of Long COVID-19; - Coverage of all product categories of new or repurposed medicinal products (i.e., Antiviral medicinal products; Immunomodulators; Other medicinal products).
Soundness of scientific approach and technology used (pharmacological rationale)	Available evidence of potential role of medicinal product in the COVID-19 setting suggests potential therapeutic activity and is supportive of the proof of principle, from non-clinical studies (in vitro and in vivo used animal models) or early clinical studies related to appropriate mechanism of action, safety and efficacy of new medicinal products; or for repurposed medicinal products, already known evidence is available from existing use, relevant to the whole spectrum of COVID-19
Stage of development	Progress in development of medicinal product is achieved from non-clinical studies to late phase clinical trials or regulatory process, reflecting the need to enable promising medicines to reach patients in the European Union (EU) as soon as possible
Availability of relevant clinical outcome results from clinical trial(s)*	Relevant clinical evidence of medicinal product is announced by manufacturer or is published as preprint or in scientific journals, relevant to the whole spectrum of COVID-19, from living systematic reviews/meta-analysis, platform trials (to generate robust and interpretable evidence that would allow prompt definition of which investigational or repurposed medicinal products are effective and safe for the treatment of COVID-19) or phase 2 or 3 non-platform trials, based on the certainty of evidence and effect size
Absence of (new) major identified safety issues (that would question the appropriateness of the	Adverse events (AEs) and serious AEs of medicinal product are consistent with the mechanism of action and are manageable across the whole spectrum of COVID-19, with absence of (new) major identified safety issues that would question the appropriateness of the product in the proposed indication

product in the proposed indication)	
Unmet need** and/or therapeutic added value	Unmet need and/or therapeutic added value of medicinal product is achieved
Efficacy against new SARS-CoV-2 variants (relevant only for some product categories)***	Medicinal product is relevant for those variants of concern with clear evidence available indicating a significant impact on transmissibility, severity and/or immunity that is likely to have an impact on the epidemiological situation in the EU/EEA
Suitability of the product for the particular healthcare setting****	Related to route of administration, treatment regimen, formulation, target populations in the context of proposed indication, medicinal product is suitable for outpatients setting or for hospitalised patients according to disease severity
Intention to engage at an early stage with EMA to obtaining scientific advice (with the intention to apply for an EU marketing authorisation for the candidate therapeutics)	Medicinal product received scientific advice from EMA early in the development process (important for ensuring that developers can submit well-prepared applications and make use of the rapid procedures EMA has put in place for COVID-19 treatments)
Candidate therapeutics already within the regulatory process (EMA rolling review process, or use endorsed after Article 5(3) review, or in EMA's marketing authorization process or FDA's EUA granted for the product)	Potential COVID-19 medical product is currently undergoing evaluation by EMA /medicinal product under rolling review, as regulatory tool that EMA uses to speed up the assessment of a promising medicine or vaccine during a public health emergency; or use endorsed after Article 5(3) review to support national decision-making on the possible use of these medicines before a formal authorisation is issued; or medicinal product is under marketing authorisation evaluation/, or medicinal product already received emergency use authorisation (EUA) from FDA

*Relevant clinical effectiveness outcome results:

For *pre- or post-exposure prophylaxis*, related to clinical outcomes: Number of patients infected with SARS-COV-2; Number of patients progressed to COVID-19; Number of patients progressed to mild/moderate COVID-19; Number of patients progressed to severe/critical COVID-19; All-cause mortality; Viral negative conversion (D7);

For *mild/moderate COVID-19 (outpatients)*, related to clinical outcomes: Clinical improvement; Number of patients progressed to COVID-19 related hospitalisation; Number of patients with ≥ 1 COVID-19 related medically attended visit (emergency room visits, urgent care visits, or telehealth/physician office visits); Viral negative conversion (D7);

For *moderate/severe/critical COVID-19 (hospitalised)*, related to clinical outcomes: All-cause mortality; Clinical improvement; WHO Clinical Progression Score level 7 or above /i.e., Mechanical ventilation +/- additional organ support (ECMO, vasopressors or dialysis) OR death/; Duration of hospitalisation;

For *Long COVID-19*, related to clinical outcomes: Clinical improvement (related to 4 different syndromes: Pulmonary symptoms; Cardiovascular symptoms; Fatigue, cognitive and neuropsychiatric symptoms; Other organ impairments); QoL; Number of patients progressed to COVID-19 related re-hospitalisation; Number of patients with ≥ 1 COVID-19 related medically attended visit (emergency room visits, urgent care visits, or telehealth/physician office visits); All-cause mortality

**No active treatment available for condition; current treatment is suboptimal, e.g., existing treatment has challenging adherence or delivery; new treatment has the potential to provide substantial additional benefits over existing treatment options; new treatment targets different aspects of the condition

***Scoring will be provided only if relevant for product category

****Route of administration, treatment regimen, formulation, target populations in the context of proposed indication (e.g. outpatient settings: oral or nasal; s.c. before IV; use in ICU)