CAPSULAS
Boletín de información jurídica

Special Edition | Faus & Moliner Abogados | December 2020

Approval process for COVID-19 vaccines

On the occasion of the grant of the marketing authorization to Comirnaty®, the vaccine developed by BioNTech and Pfizer

Background

On Monday, 21 December, the European Medicines Agency (EMA) issued its opinion in favour of granting a marketing authorization for the Covid-19 vaccine developed by BioNTech and Pfizer. In recent weeks, especially following the approvals by the Food & Drug Administration (FDA) in the United States and the Medicines & Healthcare Regulatory Agency (MHRA) in the UK, we have heard and read a lot about vaccine approval processes.

The aim of this CAPSULAS is to clarify some doubts regarding the approval process of these vaccines, from our legal perspective and applying the rigor that we try to use in our daily activity.

Comirnaty® is an authorized medicine

European pharmaceutical law clearly states that no medicinal product may be placed on the market in a Member State without the competent authority of that Member State granting a marketing authorization under Directive 2001/83/EC or without the European Commission granting a valid authorization throughout the European Union in accordance with Regulation (EC) 726/2004.

However, there are two situations in which the supply or distribution of unauthorised medicines could be allowed.

Firstly, there are the situations of compassionate use, foreseen in Article 5.1. of Directive 2001/83/EC. A Member State may permit the supply of an unauthorised medicinal product with a view to meeting special needs, always in accordance with the prescription of a recognised physician for an individual patient under the direct personal responsibility of that physician.

Secondly, we may refer to cases where a Member State temporarily permits the distribution of unauthorised medicinal products in response to the alleged or confirmed spread of a pathogen or chemical agent, toxin, or nuclear radiation capable of causing damage. This option is referred to in Article 5.2 of Directive 2001/83/EC.

Corminaty® is not in either of those two cases because is a medicinal product which has obtained a marketing authorization after being evaluated by the EMA. The authorization granted to Comirnaty® is an authorization known as conditional authorization.

Conditional marketing authorizations

Anyone who may think that conditional authorizations is a tool specifically aimed to validate the process of authorization of Covid-19 vaccines is wrong. The possibility of granting conditional marketing authorizations has been contemplated in European Community pharmaceutical law for many years, stated under Regulation (EC) 507/2006, the provisions of which have also been incorporated into Article 14bis of Regulation (EC) 726/2004.

It would also be wrong to state that the process of granting a conditional authorization is a lax or untransparent process. During the period from 2006 to 2016, a total of 30 conditional authorizations were granted, of which only 2 were withdrawn for commercial reasons not related to the safety or efficacy of the product; and none have been suspended or revoked. Between 2017 and 2020, EMA has issued more than 20 opinions in favour of granting conditional authorizations.

On the other hand, EMA has always maintained a policy of sharing relevant information in a very transparent manner. On 11 December the EMA hosted a stakeholders public meeting on development and authorization of COVID-19 vaccines in the EU.

When can a conditional authorization be granted?

In accordance with Article 14bis of Regulation (EC) 726/2004 a conditional authorization may be granted to meet uncovered medical needs. It is understood that there are "uncovered medical needs" when there is no satisfactory method of diagnosis, prevention or authorised treatment in the European Union for a disease or, when such method exists, the medicinal product to be authorized constitutes a substantial therapeutic advance for those concerned.

On the other hand, on a general level, the granting of a conditional authorization implies that the applicant has submitted complete preclinical or pharmaceutical data but does not yet have all the clinical data normally required. Notwithstanding this, conditional authorization may also be granted where complete preclinical or pharmaceutical data have not been provided in emergency situations in response to public health threats. However, in all cases, the EMA must confirm that the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required and should also find that the applicant is likely to be able to submit the complete data.

In addition, the granting of a conditional marketing authorization is subject to the fulfillment of specific obligations which must be indicated in the summary of product characteristics and which will be reviewed annually by the EMA. Among these specific obligations, the marketing authorization holder shall complete ongoing studies, or develop further studies, in order to confirm that the risk-benefit ratio is favorable. Specific obligations related to the collection of pharmacovigilance data may also be imposed. In addition to this, EU law contemplates that the EMA must disclose to the public the specific obligations and the timetable for their fulfilment.

A key element of conditional marketing authorizations is their temporary aim. A conditional marketing authorization has an initial validity period of one year, but the system is oriented towards its conversion into an ordinary authorization after the submission of the complete data. European pharmaceutical law also foresees (Article 14.8 of Regulation (EC) 726/2004) the granting of exceptional authorizations when the applicant can demonstrate that, for objective and verifiable reasons, it cannot provide complete data on the efficacy and safety of the medicinal product under normal conditions of use. In these cases, it is normal that the marketing authorization holder may never be able to provide the complete data.

Comirnaty® is not an exceptional authorization but a conditional authorization.

The situation in the US, UK and Switzerland

On December 10, it was announced that the FDA had authorized the use of the vaccine developed by BioNTech and Pfizer, placing itself among the first countries to give green light to it. FDA approval is known as an "Emergency Use Authorization", regulated in section 564 of the Federal Food, Drug, and Cosmetic Act. Under this standard, the FDA may allow unauthorized drugs to be used in emergencies, to treat serious illnesses or events caused by pathogens, chemicals, toxins or nuclear radiation. The State of Emergency was declared on March 27, 2020 by the U.S. Secretary of Health and Human Services.

Does this mean that the approval granted by the FDA is somewhat worse than the conditional authorization granted by the European Commission? People could point out that the vaccine developed by BioNTech and Pfizer is not authorized in the USA, that it is simply allowed to be used exceptionally because the country is under State of Emergency; and then jump into the conclusion that the regulatory situation of the vaccine in the European Union is stronger than in the USA. From our point of view, this position may be correct but it would not be complete nor fair. The FDA's evaluation of the vaccine has been supported by the results of the same studies that EMA has evaluated, 44,000 people have participated on the studies; and the conditions that the FDA has imposed to allow the use of the vaccine in the U.S. do not seem to be any different from those stated by the EMA.

In the United Kingdom, a marketing authorization has not been granted. Instead, UK authorities have acted under the rule which allows MHRA to approve the use of an un authorised product in a state of emergency. The MHRA, on its website, clearly states that "this medicinal product does not have a UK marketing authorization but has been given authorization for temporary supply". Here too, someone could argue that the regulatory situation of the vaccine in the UK is less robust than the situation in the EU, but we still think that this position could be called into question. The basic information on the vaccine in the United Kingdom (a document analogous to our summary of product characteristics) is very similar to the one approved by the EMA, and the conditions imposed on Pfizer/BioNTech in terms of monitoring and permanent updating of available information are also equivalent to those stated in the European Union.

As for Switzerland, Swissmedic authorized the vaccine developed by BioNTech and Pfizer on 19 December, noting that it was the first authorization granted in the world by the ordinary procedure. Swissmedic welcomed the issue of this authorization within two months of receiving the application thanks to a continue evaluating procedure ("rolling procedure"). At first glance, someone might think that the authorization granted by Swissmedic is stronger than the one granted by the European Commission, but that assessment would also be incorrect. In Europe, the EMA has also followed a continuous evaluation procedure, and Swissmedic has declared that, as a condition to obtain this authorization, Pfizer/BioNTech had been required to comply with obligations very similar to those imposed in the European Union.

Special conditions imposed to Corminaty® in the EU

The authoization granted to Pfizer/BioNTech includes several specific obligations among which we highlight the following:

- The release of each manufactured batch shall be performed by an official laboratory for the control of medicinal products or a laboratory designated by a Member State having been deemed necessary to protect public health (Article 114 Directive 2001/83/EC).

- A Periodic Safety Report (PSUR) must be submitted within 6 months and an updated version of the Risk Management Plan should be submitted whenever the EMA requires it.

- Additional data will be submitted from January 2021, and the final results of the clinical trials currently underway, in December 2023.

Conclusion

Over the next few days, during Christmas holidays meetings (even if they are held in virtual form), all of us who are in one way or another close to the activity of the pharmaceutical industry run the risk of being asked about the approval of Covid-19 vaccines many times. We hope we have provided some useful information to respond to some of your queries. From a legal point of view, the issue is quite clear: we are dealing with highly regulated administrative procedures, managed by independent agencies with the support of reputable professionals and with a lot of transparency, much more transparency than the one seen in other areas (try to find information on how licenses are granted in other sectors).

On a more scientific level, simply note that the results of the Pfizer/BioNTech vaccine trials were published in the New England Journal of Medicine (NEJM) on December 10. Among the 21,720 participants receiving the vaccine, only 8 cases of Covid-19 appeared (none of them very serious); while among the 21,728 who received placebo, 162 positives were detected; without unexpected side effects. Clearly, these are primary results, but the NEJM editorial statements are conclusive: "The trial results are impressive enough to hold up in any conceivable analysis. This is a triumph". On the other hand, a journal as prestigious as the British Medical Journal publishes in one of its Editorials on December 17 (BMJ 2020;371:m4838) that "The scientific achievements since SARS-CoV-2 was identified first less than year ago give grounds for optimism within a reasonable timeframe we should, globally, be able to successfully manage this pandemic". Evidently, there are still very important questions and challenges to be solved, especially those related to logistics and equity in access to vaccines; but above all it is worth highlighting that we are much better off than we were a few months ago. Merry Christmas and our best wishes for 2021.