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Covid-19: regulatory steps taken by AIFA in relation to the pharmacological treatment of the desease.

SARS-CoV-2, which causes COVID-19 disease, is a virus that belongs to the Coronavirus family and, even though it is very similar to the SARS spread between 2002 and 2003, is a pathogen new to the world.

Nowadays, indeed, there are no specific treatments authorized by the Italian Medicines Agency - AIFA. - for COVID-19. In addition to that, nowadays there are no vaccines for the prevention of such disease.

In this context, in front of such epidemic emergency, the disease has been mainly treated with supportive therapies: antipyretics, hydration and ventilatory support devices, if necessary.

At the same time, the entire world - and Italy is in the front line - is trying to test the efficacy and safety of some drugs already available for the treatment of other diseases.

In order to do so, AIFA's regulatory intervention was deemed necessary: for this purpose AIFA has set up a specific crisis unit and has taken various initiatives within the framework of the national legislation previously in force and the emergency one.

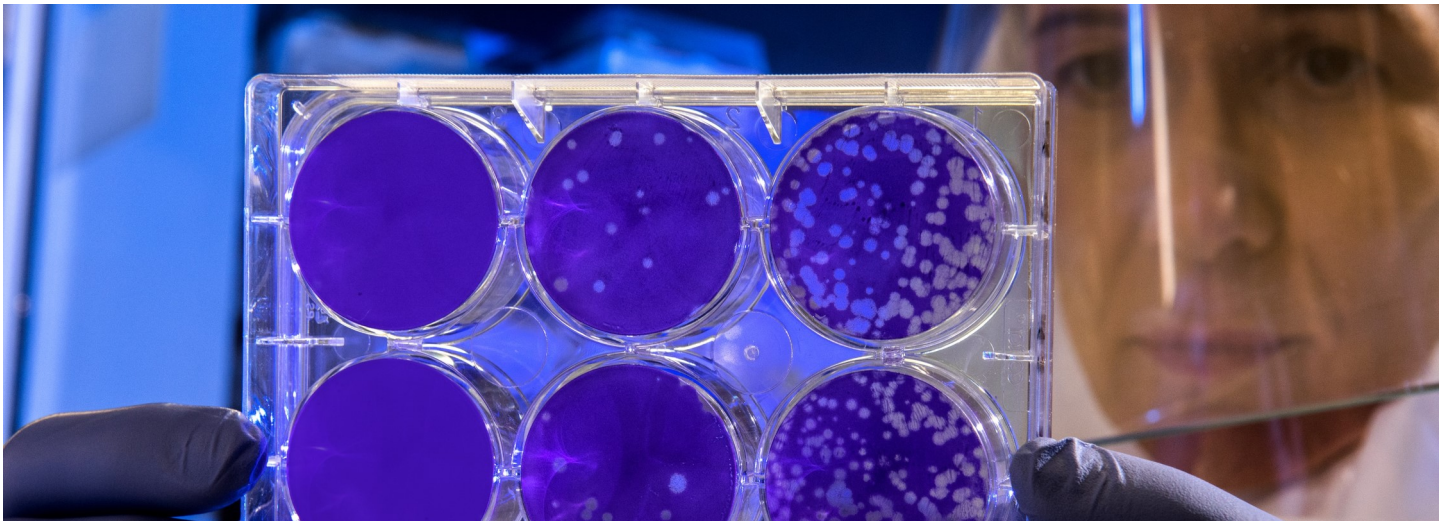
USE OF OFF-LABEL MEDICINES

First of all, the possible authorisation of off-label use of certain medicinal products (i.e.the medicine is being used in a manner not specified in the marketing authorisation's approved packaging label):

- Chloroquine and Hydroxychloroquine: two anti-malaria medicines with potential antiviral efficacy;
- Lopinavir/Ritonavir and, alternatively to the latter, Darunavir in combination with Cobicistat or Ritonavir: such medicines are used to treat HIV infection.

The use of these drugs is an exception to the ordinary regulation of off-label drugs pursuant to Law no. 648/96, which ordinarily enables the NHS to provide medicines off label only with the support of completed research studies during phase II aimed at demonstrating proper efficacy and an acceptable risk profile.

Initially, it was also envisaged the temporary inclusion, for three months, in the list of off-label medicinal products available under Law 648/96 the drug Interferon beta 1-a. However, this decision was subsequently revoked by AIFA itself "*for incompatibility with the available formulation in relation to the intended use*".



ACCESS TO MEDICINES BY WAY OF CLINICAL TRIALS AND COMPASSIONATE USE

By way of clinical trials and compassionate use, a further initiative concerns access to certain medicines.

In particular, such access concerns the following medicines:

- Remdevisir: this is an experimental molecule of Gilead Sciences with potential antiviral efficacy;
- Tocilizumab: this is a monoclonal antibody already used in the treatment of other diseases such as rheumatoid arthritis and that the pharmaceutical manufacturer, Roche, has decided to supply to Regions free of charge upon request;
- Favipiravir (trade name Avigan): this is an antiviral medicine developed by the Japanese group Fujifilm Toyama Chemical and authorised in Japan (but not in Europe and the United States) since March 2014 for the treatment of various forms of *influenza* caused by new or re-emerging *influenza* viruses;
- Lopinavir/Ritonavir (see above).

With respect to such initiative, through Article 17 of the "Cura Italia" Decree (D.L. n. 18 of March 17, 2020) a simplified, accelerated and centralised procedure has been introduced, pivoting on the AIFA Technical Scientific Commission (CTS) and on the Ethics Committee of IRCCS Spallanzani, indicated as the Single National Ethics Committee.

Such procedure, as an exception to the ordinary one, allows the rapid adoption of national and uniform protocols for the beginning of clinical trials and for a compassionate usage in patients with serious medical conditions and without valid therapeutic alternatives.

Moreover, with specific reference to clinical trials, the European Medicines Agency - EMA - has urged the EU scientific community to give priority to large randomised and controlled multicentre trials, which are more likely to generate the necessary evidence of efficacy to allow the rapid development and approval of potential treatments against COVID-19.

The concern is that individual clinical trials are not able to generate the data required to draw strong conclusions.

Therefore, the aim that should move the scientific community is a harmonised approach to data collection, involving all Member States. Plus, from this point of view, it is important to point out that, in the Italian context, the abovementioned Article 17 of the "Cura Italia" Decree has entrusted AIFA with the task of evaluating all clinical trials on medicines for patients with COVID-19. In addition to that, AIFA is making a continuous effort to make public and update all the data collected.

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