BRITISH PHARMACOLOGICAL SOCIETY

23 April 2020

Our position: medicines and COVID-19

Medicines have been prominent in discussions about the COVID-19 pandemic. There is an urgent need to develop effective treatments to reduce morbidity and mortality from the disease, but it is important that we do not compromise the rigour of our scientific approaches. It is also important to always consider the benefit-risk ratio of different treatments which may vary depending on whether the therapeutic is used prophylactically or in those who are severely ill and ventilated on intensive care units.

We are working with our members to understand the evolving situation. Please see below for our current view of the key issues relating to medicines development and use, which we will monitor on a regular basis:

1) Approval of treatments must be expedited safely

There are currently no medicines in any country that have regulatory approval for the treatment of COVID-19 infections. Treatments currently under investigation to treat COVID-19 infection, and the pathologies arising from this infection, include licenced medicines and products under investigation for other conditions that may be effective (repurposed) for use in COVID-19 infection. There are also completely new products in development. The potential advantage of using an already licenced medicine, or one that is part-way through clinical trials is that there will be existing knowledge about the safety profile and so, it should take less time to get these approved for treating patients. However, it remains important to use pharmacological principles to define the safe and effective doses and treatment protocols for COVID-19 patients for all potential treatments - irrespective of whether these are new or repurposed.

The large-scale international trials that are currently underway will be critical in understanding whether treatments are likely to work safely. It is crucial that hospitals and associated healthcare staff are allowed and supported to recruit patients to such trials in a timely manner, reducing bureaucracy whilst ensuring Good Clinical Practice standards are upheld. This seems to be happening effectively at the moment as evidenced by the fact that the RECOVERY trial managed to recruit over 4000 patients in 4 weeks, and is in fact, the fastest recruiting trial ever undertaken in the NHS. The Society welcomes the swift action of regulators (such as the MHRA) and other organisations who are working to safely expedite trials.

2) Standards and guidance for clinical research relating to COVID-19 are urgently needed to ensure trial data are meaningful

Currently, many studies that are running are not of high enough quality to generate meaningful data. Standards and guidelines to support properly designed and appropriately powered studies are urgently needed.

A particular challenge is the data arising from compassionate use studies. Compassionate use is defined as the use of an unlicensed therapy to treat a patient because there are no other treatments available. Compassionate use, however, often leads to poor quality data and should be treated with extreme caution with regard to efficacy and safety of drugs. We therefore strongly support the UK Government's view that wherever possible patients should be entered into clinical trials.

However, it is likely that some patients will be treated on a compassionate use basis. Given the pressing need for high quality research and that large-scale studies will take longer to report, the Society supports the WHO guidelines on compassionate use if assessment within the context of a clinical trial is not possible. Standards that specifically focus on how to run high quality, small-scale studies are particularly needed to ensure that they have the best chance of informing treatment protocols.

A further complication is that the COVID-19 disease state may be thought of in two phases: the initial viral infection/replication stage and the later 'cytokine storm' immune phase that is only experienced by a subset of patients but is the major cause of fatalities. It is important that patient groups are well-defined in any study.

Useful standards and guidelines are likely to include randomisation of treatment protocol, stratification of different patient populations and the use of appropriate clinical endpoints. The Society and our journals are currently working with experts to help define these parameters and we will update this page when the guidance is available.

3) Comprehensive pharmacovigilance and pharmacoepidemiology are needed to inform medication use during the COVID-19 pandemic

The Society recognises that concerns have been raised about the use of certain medications in the COVID-19 pandemic. Comprehensive pharmacovigilance and pharmacoepidemiology are of utmost importance when seeking to understand how this new virus may affect the risk of using medicines. Concerns have been raised about the following medications:

- Ibuprofen (a non-steroidal anti-inflammatory drug used to relieve pain and inflammation; NSAID)
- ACE (angiotensin converting enzyme) inhibitors and angiotensin receptor blockers, both used to treat high blood pressure and cardiac diseases
- Corticosteroids (anti-inflammatory medicines used for conditions including as asthma, and chronic obstructive pulmonary disease (COPD) and ulcerative colitis)
- Immunosuppressants, as used for example in the treatment of autoimmune conditions such as rheumatoid arthritis

The Commission on Human Medicines (an advisory body of the Medicines & Healthcare products Regulatory Agency; MHRA) and the National Institute for Health and Care Excellence (NICE) were asked to review the evidence on these medicines. These organisations are publishing rapid guidelines and evidence summaries to support the management of chronic conditions during the COVID-19 pandemic as soon as their reviews are completed.

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Regarding ibuprofen, a rapid evidence summary report was released on 14 April 2020 relating to acute use of NSAIDs. NHS England released a clinical commissioning policy on the topic alongside this report. The Society previously set out our position on the use of ibuprofen as it relates to COVID-19 on 18 March 2020, stating that 'there is no consistent evidence to suggest that ibuprofen worsens the disease', and we support the NHS guidance. We will continue to regularly review the emerging guidelines on this and for other medications.

Patients should not stop taking medication for long-term conditions unless on the advice of a healthcare professional. Stopping or changing medicines for chronic health conditions without appropriate advice can be harmful. Now more than ever, people can look after their own health and support the NHS by following both official guidance and that of their doctor.

Clinical pharmacologists are experts in interpreting the overall balance of risks and benefits of using medicines and are among those working with NICE, the MHRA and NHS England to support the safe and effective use of medicines during the COVID-19 pandemic.