SUMMARY OF THE COMMISSION ON HUMAN MEDICINES AD HOC MEETING HELD ON THURSDAY 24 DECEMBER 2020 AT 15:00 VIA VIDEOCONFERENCE

PAPERS/ OTHER ITEMS

Dose interval discussion for BNT162b2

The Commission considered the issue of extending the interval between the first and second dose for the BNT162b2 vaccine following a request from the Department of Health and Social Care (DHSC), in the context of the Regulation 174 authorisation[1], for advice on whether the timing of the second dose of BNT162b2 could be extended to provide operational flexibility to enable a large proportion of the population to receive a first dose. The Commission discussed a slide presentation of statistical analyses relating to the vaccine efficacy (VE) of a single dose. The Commission noted that an analysis conducted by Pfizer showed that vaccine efficacy (VE) in the study for the period from the second dose to 7 days after the second dose was 90.5% (95% CI 61.0, 98.9). This was considered to be a good estimate of the efficacy around 21-28 days after the first dose as the second dose would not be expected to have taken effect in this period. Results from the MHRA analysis of raw data from the interim analysis showed VE of 91% (CI 63, 98) in the period from day 14 after the first dose to when dose 2 was given. Results from an independent analysis by Public Health England of the full Pfizer dataset were also discussed. These showed VE of 89% (CI 74, 97) from day 15 to day 21 after dose 1 and 91% from day 15 to 28. The Commission noted the consistency of these various analyses and agreed that the available data support VE from a single dose of around 90% after 21-28 days, with no suggestion of a decline in protection towards the end of that period. There was little information available from the studies to provide information on longer dosing intervals than 28 days, but it was felt that there was no biologically plausible reason why there would be a rapid decline from this point, and immunological principles and experience with other types of vaccines suggest that immunogenicity may be improved with more prolonged intervals between doses in the primary immunisation series.

AZD1222 Deployment Model (for information)

A summary of the deployment models in place for all four home countries for the AZD1222 Vaccine was presented to the Commission. The Commission heard that each model contains a roving element to enable distribution of the vaccine to care homes and the housebound.

AZD1222 Quality Update

An updated summary of the quality data under assessment for the AZD1222 vaccine was provided to the commission by the MHRA team.

The Commission discussed aspects around the manufacture of the vaccine and discussed some aspects in detail such as the in-use shelf-life of the product and the stability of the product in transport.

The Commission noted that all batches tested by the National Institute for Biological Standards and Control (NIBSC) met specifications.

The Commission heard that the quality data reviewed support the use of the vaccine under Regulation 174 approval.

[1] Regulation 174 of the Human Medicines Regulations 2012 provides for the supply of a medicinal product on a temporary basis in response to a public health emergency which may cause harm to human beings. The spread of COVID-19 is considered to meet this criterion.

AZD1222 Non-Clinical Update – Reproductive Toxicity Focus

The Commission heard an updated summary of the non-clinical data under assessment for the AZD1222 vaccine.

The Commission discussed the current reproductive toxicity data and agreed that precautionary wording should go into the information for healthcare professionals (HCPs)/ information for UK recipients.

The Commission reviewed the wording around pregnancy which has been discussed at the EWG and agreed that the precautionary wording was appropriate.

The Commission considered whether to issue advice in the information for HCPs / information for UK recipients concerning the use of contraception following administration of the AZD1222 vaccine. The Commission agreed that the information for HCPs / information for UK recipients should make clear that pregnancy is not an absolute contraindication to receiving the AZD1222 vaccine.

The Commission agreed that information supplied on use of all COVID-19 vaccines in pregnant or breastfeeding women should be aligned where the data allow this. The Commission agreed to revisit the wording at the subsequent CHM meeting.

AZD1222 Clinical Update

The Commission heard an updated summary of the clinical data for the AZD1222 vaccine.

The Commission heard the discussion from the Vaccine Benefit Risk Expert Working Group (EWG) on the age of the target population for the vaccine and noted that the EWG concluded that the indication should include those aged 18 years of age and older without specifying an upper age limit. The Commission agreed it was appropriate to describe in the information for HCPs / information for UK recipients the small proportion of patients aged >65 enrolled in the clinical trial. The Commission heard that more data in elderly patients are expected in January 2021.

The Commission noted the EWG recommendation that a dosing interval of between 4 – 12 weeks could be justified based on the available data and would give flexibility in scheduling vaccination programmes. The Commission noted that there was evidence for protection after a single dose for up to 12 weeks, but that data were limited beyond 12 weeks.

The Commission discussed potential adverse events associated with the vaccine.

The Commission agreed to include a warning in section 4.4 of the information for HCPs regarding the possibility of neuroinflammatory disorders.

The Commission noted that the vaccine contains polysorbate 80 and agreed that the standard contraindication and warning in sections 4.3 and 4.4 of the information for HCPs regarding hypersensitivity/anaphylaxis was adequate.
The Commission agreed on the wording in the information for HCPs / information for UK recipients regarding symptomatic use of paracetamol.

AZD1222 Risk Management Plan Update

The Commission heard that a comprehensive plan has been put in place by Public Health England (PHE) to evaluate vaccine effectiveness, failures and exposure in pregnant women.

The Commission heard that AstraZeneca have proposed four studies in their Risk Management Plan (RMP) to look at effectiveness, use in immunodeficient groups, severe underlying disease, and pregnant and breastfeeding women. AstraZeneca have also put in place an enhanced active surveillance programme to enrol patients at first vaccination and follow them up for 2 years. AstraZeneca have also proposed a pregnancy registry and an effectiveness plan. The Commission heard that further details are expected in 2021.

PROCEDURAL ITEMS

In addition, the Commission completed its usual procedural business including the need to observe the confidentiality of the meeting, to declare interests, apologies, announcements and approval of minutes of previous meetings. Professor Ralston, Professor Friedland, Professor Gilson, Professor Lachmann, Professor Macleod, Dr Mann, Professor Meredith, Dr Misbah, Professor Patel, Professor Sir Munir Pirmohamed, Professor Price, Professor Turner and Professor Weir declared non-personal, non-specific or other interests in one or more agenda items and the appropriate action was taken.

i. A list of Commissioners and invited experts who attended the meeting is at **Annex A**.

ii. Medicines Healthcare products Regulatory Agency staff may be present for all or part of the meetings or for specific items.

iii. The meeting started at 15:00 on Thursday 24th December 2020 and finished at 17:10.

The next meeting will take place on Tuesday 29th December 2020 at 15:30.

USEFUL WEBSITE LINKS

Drug Safety Update:

https://www.gov.uk/drug-safety-update

Members' declaration of interests:
https://www.gov.uk/government/publications/human-medicines-regulations-2012-advisory-bodies-annual-report-2019

European Medicines Agency updates:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/landing/news_and_events.jsp&murl=menus/news_and_events/news_and_events.jsp&mid=WC0b01ac0580022519

MHRA Website:
https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

Yellow Card Website:

http://yellowcard.mhra.gov.uk/

Information is being withheld, under Section 43 of the Freedom of Information Act 2000, on the grounds that information regarding the issue under consideration and advice from the CHM remains confidential at the date of this summary and will remain so until a final decision has been taken. Any request for future information should be made direct to the MHRA (via info@mhra.gov.uk) and will be considered in accordance with the FOI Act.

ANNEX A

MEMBERSHIP OF THE COMMISSION ON HUMAN MEDICINES

Chair

Professor Stuart Ralston MB ChB MD FRCP FMedSci FRSE FFPM (Hon)
Professor of Rheumatology, University of Edinburgh, Western General Hospital, Edinburgh

Members

Ms Susan Bradford
Lay Representative

Professor Jamie Coleman MD MA (Med Ed) FRCP FBPhS
Professor in Medical Education / Consultant Clinical Pharmacologist, University of Birmingham

Dr Jamie Fraser BSc MB ChB MRCGP
GP Partner, Southside Surgery, Inverness

Professor Jonathan S Friedland MA PhD FRCP FRCPE FRCPI FESCMID FMedSci
Deputy Principal, St. George's, University of London

Professor Richard J C Gilson MD FRCP
Professor of Sexual Health & HIV Medicine, Director of the UCL Centre for Clinical Research in Infection & Sexual Health & Deputy Director of the UCL Institute for Global Health

Professor Malcolm R Macleod BSc MBChB MRCP PhD FRCP (Edin)
Professor of Neurology and Translational Neurosciences, University of Edinburgh and Honorary Consultant Neurologist, NHS Forth Valley

Dr Rebecca Mann BMBS FRCPCH
Consultant Paediatrician, Taunton and Somerset NHS Foundation Trust

Professor Sarah Meredith
Professor of Clinical Trials, MRC Clinical Trials Unit at UCL, Institute of Clinical Trials and Methodology, University College London

Dr Siraj Misbah MBBS (Hons) MSc FRCP FRCPath
Consultant Clinical Immunologist, Lead for Clinical Immunology, Oxford University Hospitals

Professor Poulam Patel MD, PhD, MBBS, FRCP
Professor of Clinical Oncology, Academic Unit of Clinical Oncology, University of Nottingham

Professor Sir Munir Pirmohamed MB ChB (Hons) PhD FRCP FRCP (Edin) FBPhS, FFPM (Hon) FMedSci
David Weatherall Chair of Medicine, University of Liverpool, NHS Chair of Pharmacogenetics, Director of the Wolfson Centre for Personalised Medicine, Director of the MRC Centre for Drug Safety Science

Professor Shirley Price MSc PhD FBTS FRSB ERT FHEA FRSC MBPharmacol Soc
Emerita Professor of Toxicology, University of Surrey
Visiting Professor of Toxicology, University of Hertfordshire

Professor Marc Turner MBBS PhD MBA FRCP FRCPath FHEA
Professor of Cellular Therapy; Medical Director Scottish National Blood Transfusion Service (SNBTS)

Professor Christopher Weir BSc (Hons) PhD MSc FRSS C.Stat
Personal Chair in Medical Statistics and Clinical Trials, Usher Institute, University of Edinburgh

Dr Martin Wilson MB ChB, MPhil (Glasgow), FRCP(Edin)
Consultant Physician in Care of the Elderly, Raigmore Hospital, Inverness

Invited Experts

Professor Kevin M G Taylor BPharm PhD FRPharmS
Chair of the British Pharmacopoeia Commission and Professor of Clinical Pharmaceutics, UCL School of Pharmacy, London

Mrs Helen M Ward MSc, BSc (Hons), Senior Fellow HEA, RGN, RCN Nurse Practitioner, PGCEA, PG Cert NMP, Queens Nurse, Advanced Nurse Practitioner