Message

From: Personal Data [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D21258C9254E4E32942F15C21EE78F6F-Personal Data
Sent: 19/02/2020 08:42:05
To: Van Tam, Jonathan [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d29c846fc8fa4678b419c6f0dc3836f3-JVanTam]
Subject: RE: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

From Chris - yes probably.

From: Van Tam, Jonathan <Jonathan.VanTam@dhsc.gov.uk>
Sent: 18 February 2020 17:25
To: Personal Data @dhsc.gov.uk>
Subject: FW: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

Also further question for Chris in yellow I don't know answer to but he will?

Imagine hydroxyQ is bioactive in same way?

From: Glover, Kathryn <kathryn.glover@dhsc.gov.uk>
Sent: 18 February 2020 17:21
To: Van Tam, Jonathan <Jonathan.VanTam@dhsc.gov.uk>; Willett , Keith <keith.willett@nhs.net>; I&S I&S
Cc: Personal Data @dhsc.gov.uk>; Personal Data @officeforlifesciences.gov.uk>; Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk>; RIDGE, Keith (NHS ENGLAND & NHS IMPROVEMENT - X24 <PD @nhs.net>; Covid-19spoc <Covid-19spoc@dhsc.gov.uk>; PD PD @dhsc.gov.uk>; Whitty, Chris <Chris.Whitty@dhsc.gov.uk>; Lovell, Helen <helen.lovell@dhsc.gov.uk>; Personal Data @phe.gov.uk
Subject: RE: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

Amended to include a further question below:

Department of Health & Social Care

Kathryn Glover
Deputy director – EU exit, medicines supply
(job share with Helen Lovell – please copy all emails to helen.lovell@dhsc.gov.uk)

South Wing, Floor 3, 39 Victoria St, London SW1H 0EU
E: kathryn.glover@dhsc.gov.uk T: I&S / Personal Data

Please note I work Monday to Wednesday.

From: Glover, Kathryn
Sent: 18 February 2020 17:13
To: Van Tam, Jonathan <Jonathan.VanTam@dhsc.gov.uk>; Willett , Keith <keith.willett@nhs.net>; I&S I&S @nhs.net>
Cc: Personal Data @dhsc.gov.uk>; Personal Data @officeforlifesciences.gov.uk>; Personal Data Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk>; PD (NHS ENGLAND & NHS IMPROVEMENT - X24 PD @nhs.net>; Covid-19spoc <Covid-19spoc@dhsc.gov.uk>; PD

PD l@dhsc.gov.uk>; Whitty, Chris <Chris.Whitty@dhsc.gov.uk>; Lovell, Helen <helen.lovell@dhsc.gov.uk>;
PD s@phe.gov.uk
Subject: RE: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)
Importance: High

JVT PD

Sarah has now spoken to all suppliers of Kaletra and chloroquine. Stock levels in the UK are sufficient for BAU demand. Production lead times for Kaletra and its generic equivalents are 4-6 months. The production site for chloroquine tablets has closed as the product is soon to be divested. If high volume is required, Alliance will investigate reopening production, however they don't currently have API. Further details for all products/ suppliers are attached.

Listed below is the stock we think we can secure if we move quickly (in green), and the stock we have requested speculatively (black). We are working with PHE to purchase the stock in green. However we know that Abbvie (for example) are working with WHO on global stock allocation so there is no guarantee that we can secure black stock in timeframes consistent with the RWC scenario.

Supplier	Max possible quantity
Abbvie – Kaletra	10,000 packs (speculative request)
Mylan – Kaletra generic equivalent	5,000 packs (2900 redirected from foreign markets, 2100 in Q4 2020)
Accord – Kaletra generic equivalent	10,000 packs (442 decommissioned sample packs requiring quality release – MHRA considering, 1710 packs Romanian stock currently in Malta, rest speculative request)
Alliance – chloroquine tablets	59,723 packs in stock, and 54,152 individual tablets
Wallace – chloroquine liquid	9000 packs (MHRA approved expiry date extension)

We wanted to alert you to this position, and ask for a steer on:

- Target volumes
- Treatment dosing regimen and duration – can we split packs to support multiple patients?
- Eligibility guidelines
- Whether we should explore additional supply of other HIV drugs or other possible treatments? If so what
- Reviewing prescribing policy – HIV patients are currently prescribed 6 months at a time, could this be reviewed to free up some stock
- Is hydroxychloroquine a possible alternative? it's more widely used so stock should (hopefully?) be easier to source.

Thanks

Kathryn

Department of Health & Social Care

Kathryn Glover
Deputy director – EU exit, medicines supply
(job share with Helen Lovell – please copy all emails to helen.lovell@dhsc.gov.uk)

South Wing, Floor 3, 39 Victoria St, London SW1H 0EU
E: kathryn.glover@dhsc.gov.uk T I&S Personal Data

Please note I work Monday to Wednesday.

From: Van Tam, Jonathan
Sent: 14 February 2020 17:22
To: Lovell, Helen <helen.lovell@dhsc.gov.uk>; Whitty, Chris <Chris.Whitty@dhsc.gov.uk>
Cc: Personal Data @dhsc.gov.uk>; david simmons Personal Data @officeforlifesciences.gov.uk>; Personal Data Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk> Personal Data Personal Data @nhs.net> PD (NHS ENGLAND & NHS IMPROVEMENT - X PD nhs.net>; Covid-I&S @dhsc.gov.uk>; Glover, Kathryn <kathryn.glover@dhsc.gov.uk> PD PD @dhsc.gov.uk>; I&S , England (NHS ENGLAND & NHS IMPROVEMENT - X24) I&S @nhs.net>
Subject: RE: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

Dear Helen,

Please can you link up with PD and PD s next week.

We are right now in a meeting trying to work out treatment numbers. But essentially the numbers are astronomical and the working rule for now, until Keith comes back with better ball park figures, is that over 1M treatment courses could be required of KL and CQ in the hope that one or the other works. This is based very crudely on RWC scenario of 33M infected with symptoms and 4% requiring hospital care. And a rather simplistic picture that all requiring hospital care (even if they can't get into hospital) may sensibly need treatment.

We are picking up more and more signals internationally that everyone is trying Kaletra. The supply situation does not sound good and the lead in times are not in our favour. Deliveries in 6 months may not be relevant. Can we begin to scour the international markets please for stock Steve? even if it is not UK licenced; MHRA can sort that with exemptions. It feels urgent.

Darunavir + separate low dose ritonavir is definitely an alternate say HCID physicians. I don't know about other protease inhibitors

JVT

From: Lovell, Helen
Sent: 14 February 2020 13:07
To: Van Tam, Jonathan <Jonathan.VanTam@dhsc.gov.uk>
Cc: Personal Data @dhsc.gov.uk>; Personal Data @officeforlifesciences.gov.uk>; Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk> Personal Data Personal Data @nhs.net> PD (NHS ENGLAND & NHS IMPROVEMENT - X24 PD @nhs.net>; Covid-I&S @dhsc.gov.uk>; Personal Data @dhsc.gov.uk> Personal Data @dhsc.gov.uk>
Subject: FW: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

Hi JVT,

Further to your note last night re **Kaletra**:

There are 3 suppliers – one brand originator (Abbvie) and 2 generics companies (Accord and Mylan). We will have further catch up with them all next week but the position at this point:

Initial calls with these suppliers have shown supply is limited in terms of supporting additional demand and all suppliers are want to ensure that HIV patients already stabilised on treatment are not affected by extra requests for stock, so will be carefully managing orders. In summary:

- **Abbvie** has normal usage of <1000 packs a month in the UK across all presentations. Around 1-2 months' excess supply in excess at present in the UK due to EU exit stockpiling and are not sure lead times for further stock but will follow up. UK are trying to keep the stock in this country. All requests for additional stock coming in worldwide are being channelled through the Chicago office, with prioritisation of their HIV patients. They will communicate our interest. Not aware that any sales to other countries have yet been agreed. We will follow up next week.
- **Accord** manufactures in India through a third party manufacturer. Lead in time of 6 months for additional stock. Currently have 272 packs (pack size 100) available now and a further 155 potentially for release but some issues over testing. Now planning to alert their manufacturing site and explore lead in times further.
- **Mylan** also manufactures in India with a 6 month lead in time. May have some excess stock (potentially 600 packs), and will also explore with their manufacturer about potential for additional stock.

Issues

- The requirement will need to be refined in the light of the supply situation: What would be the eligible patient population, and treatment regime to ensure best clinical benefit from limited supply – and from that can we model the volumes required?
- We will then need to explore the most appropriate procurement model – for example if usage will be limited to the treatment centres, or to ICU, that will be a different approach to more widespread use.
- Are there alternative HIV medicines that could be considered?

- **Please can you (and copyees) advise who can take forward the clinical and modelling work required? While we will continue discussions with suppliers and explore procurement models this has to be done in parallel with the further clinical assessment.**

We have opened dialogue with chloroquine suppliers and will revert when we have more information.

Department of Health & Social Care

Dr Helen Lovell
Deputy Director, EU Exit: Medicines supply (Jobshare with Kathryn Glover)
South Wing, Floor 3, 39 Victoria St, London SW1H 0EU |
E: PD @dhsc.gov.uk
T: I&S
M: Personal Data
I jobshare with Kathryn Glover. Please copy all emails to Kathryn.Glover@dhsc.gov.uk

****DHSC Emails have changed. My email address is now helen.lovell@dhsc.gov.uk.*****

From: Van Tam, Jonathan
Sent: 13 February 2020 18:07
To: Personal Data @dhsc.gov.uk>; Personal Data @officeforlifesciences.gov.uk>
Personal Data Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk>; Personal Data

Personal Data @nhs.net>; Personal Data (NHS ENGLAND & NHS IMPROVEMENT - X Personal Data @nhs.net>; I&S Personal Data @dhsc.gov.uk>
Subject: RE: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

That's simple. Sort of.

Kaletra will need to be in treatment quantities for hospitalised patients*. I suggest modelled, but for 50% of hospitalised patients during times when we can operate a normal threshold for hospital admissions. But per RWC scenario when likely only severe patients will get hospital care for close to 100% in those weeks of max surge. Personal Data Personal Data's NHS clinical group may well be able to opine on a model and PD d the two PD may have initial thoughts. I can't make a stab at quantities here and now.

*I think it's a clinical question not even discussed yet about whether we'd ever want to look at specific treatment modalities in primary care; my hunch is not…

I suggest a quantity of QC equivalent to Kaletra in patient-dose-days.

Corticosteroids and IFN will be specially labelled stock for a clinical trial prepared by a CTU pharmacy unit. I do not suggest extra ordering (some inhalational IFN is unlicensed anyway) for either, but corticosteroids were already on your shopping list for supportive meds

JVT

From: Personal Data
Sent: 13 February 2020 17:41
To: Van Tam, Jonathan <Jonathan.VanTam@dhsc.gov.uk>; Personal Data Personal Data @officeforlifesciences.gov.uk>
Cc: Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk>; Personal Data Personal Data @nhs.net>; Personal Data (NHS ENGLAND & NHS IMPROVEMENT - X Personal Data nhs.net>; Covid-I&S @dhsc.gov.uk>
Subject: Re: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

Thanks JVT!
Initial reaction: we already have remdesivir and Kaletra on the go, so for the corticosteroid, the CQ and the interferon, would need to have an indication of the likely quantum you believe we need to potentially acquire , either in a trial setti;g or for empirical treatment in case of an epidemic.

I leave the team to assess how they work this up with you.
Thanks
Personal Data

From: Van Tam, Jonathan <Jonathan.VanTam@dhsc.gov.uk>
Sent: Thursday, February 13, 2020 5:17:26 PM
To: Personal Data @officeforlifesciences.gov.uk>; Personal Data @dhsc.gov.uk>
Cc: Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk Personal Data Personal Data @nhs.net Personal Data (NHS ENGLAND & NHS IMPROVEMENT - X Personal Data @nhs.net> I&S Personal Data @dhsc.gov.uk>
Subject: FW: Drugs for specific coronavirus treatment OFFICIAL SENSITIVE (COMMERCIAL)

OFFSEN/COMMSEN

Hi Personal Data

I have made what I hope is a measured deliberation on this matter, and CMO has agreed per below.

Hopefully you and the appropriate teams can now do something with this on the grounds that if we don't have stock we can't later do anything, even if we want to.

To note the CQ dose is likely to be at the RA end not the malarial end.

On further procurement thoughts, I know you are active in the FFP3 space. But if this proves thorny I would go to FFP2 which are N95 and the US standard for many many things and still better than SFMs.

JVT

From: Whitty, Chris
Sent: 13 February 2020 16:58
To: Van Tam, Jonathan <Jonathan.VanTam@dhsc.gov.uk>
Cc: Personal Data @dhsc.gov.uk>; Harries, Jenny <Jenny.Harries@dhsc.gov.uk>; Personal Data
Personal Data dhsc.gov.uk>; Personal Data @dhsc.gov.uk>
Subject: RE: Drugs for specific coronavirus treatment

I agree on both kaletra and CQ, and agree on factorial design ideally.

It's a pretty no-regrets policy, as kaletra has a lot of possible uses and CQ is cheap (and also widely used). I think for CQ we should be going for rheumatological doses.

C

From: Van Tam, Jonathan
Sent: 13 February 2020 15:36
To: Whitty, Chris <Chris.Whitty@dhsc.gov.uk>
Personal Data @dhsc.gov.uk>; Harries, Jenny <Jenny.Harries@dhsc.gov.uk>; Personal Data
Personal Data @dhsc.gov.uk>; Personal Data @dhsc.gov.uk>
Subject: Drugs for specific coronavirus treatment

Dear Chris,

Scenario:

1. As you know I have been tasked with looking at whether there are certain drugs, which are potentially useful for the specific treatment of novel coronavirus infections, based on the possible scenario that if Covid-19 affects the UK significantly, we may wish to treat a large number of UK citizens, either with drugs we hope will be effective; or with drugs we know are effective.

2. Any such drugs are likely to be in significant worldwide demand, particularly once known to be effective; therefore one scenario is that UK will be unable to acquire the supplies it needs, in whole or in part if it waits for theoretically the ideal time to make a final decision.
3. One option to mitigate that risk is to acquire supplies of drugs now which look, in principle (use for SARS/MERS, in vitro or animal data), like they might be effective.
4. A further factor in considering early acquisition is the likely safety of any target drugs and physician familiarity; older, commonly used and re-purposed drugs are more likely to meet these criteria and more likely to be available from multiple manufacturers
5. Making a decision to acquire now runs a clear risk that what is acquired will not ultimately prove to be useful, meaning that resources will have been wasted
6. Making a decision to acquire later, based on more certain evidence, runs the risk of being unable to secure supplies in time or in sufficient quantity
7. Putting in place contracts to acquire and being able to trigger these at very short notice (next day) should evidence in favour of use emerge is another potential approach, but may be tricky to implement.
8. If the UK were to acquire drugs for use, it would be a separate issue (for later discussion) to decide if we wished to deploy these products in the UK under clinical trial arrangements (potentially an adaptive 2 x 2 factorial design) or based on-unlicensed use (physician-patient discussion) on a 'give-it-a-go' treatment (with some observational data collection); or a combination of either/or in parallel.

Drugs:

9. In trying to come to a recommendation for you to consider, I have drawn on: a) NERVTAG advice; b) advice from **Personal Data** on behalf of the HCID network; c) a discussion with the ID physicians treating the UK's first two case of Covid-19; d) informal discussions with the EMA Head of Anti-Infective medicines; e) the WHO Covid-19 Blueprint; f) informal conversations with you; g) the WHO literature review. My advice is as follows:
10. Remdesivir: there is broad agreement that the in-vitro signal is that this unlicensed drug (intravenous route) from Gilead shows potent anti-coronavirus activity; a clinical trial is underway in China but there are concerns whether the timing of treatment in that study was optimal; there are unresolved questions about the adequacy of tissue levels. Gilead have been very clear that stock is only available worldwide as part of an international clinical trial. UK participation is possible but realistically will be in hospitalised patients only.
11. Kaletra® (lopinavir/ritonavir). There are supportive data from SARS treatment of human cases, in vitro data, and animal models. There is a rumour that the current Chinese trial shows no difference but also that the study is underpowered. Other rumours from China suggest it is effective. Treatment timing and dosage used may be factors. The drug is safe, has some known-side-effects, but is familiar to many physicians and orally administered making it suitable in theory for use in both primary and secondary care.
12. Chloroquine. The EC50 looks very impressive for Covid-19. Against this, the drug looks effective against several other virus pathogens in vitro but has failed to demonstrate clinical effectiveness. Likely, high doses are required. The drug is very safe, orally administered, and comparatively very cheap. Many physicians have prescribed it during their careers. Chinese physicians remarked to WHO this week (without supporting data) that chloroquine 'is working' in Covid-19 cases.
13. Corticosteroids. There is clinical equipoise about corticosteroids, which has been confirmed in the recent WHO discussions in Geneva this week. A clinical trial of corticosteroids was trailed by WHO as a research priority. The UK has an NIHR pandemic sleeping contract for an RCT of corticosteroids in severe pandemic influenza. This can be reassigned to Covid-19 and I respectfully suggest we give consideration to activating this trial relatively soon.
14. Other possible therapies include interferon-β1a (parenteral and inhaled) and convalescent plasma, both possibly deployable as part of a clinical trial. NERVTAG and HCID have both expressed caution about the

safety of interferon therapy; convalescent plasma would not offer any kind of scalable solution for widespread treatment.

Conclusion:

15. The only practical options for consideration for rapid stock acquisition, consistent with a degree of evidence in favour and ability to operationalise in a widespread way in NHS service are Kaletra® and Chloroquine.
16. As neither product carries any assurance of effectiveness, acquisition would be a calculated risk, to which we cannot attach meaningful mathematical odds at the present time, given a) the uncertainties about drug effectiveness; b) the uncertainty about whether Covid-19 can be contained in China or SE Asia.
17. One option would be to use both in a 2 x 2 factorial design, whilst offering unlicensed use on a give-it-a-go alongside, since both are products with relatively assured safety profiles.

Your thoughts would be appreciated as we need to feedback to Personal Data in the near future. Subject to your views we could put a consolidated view to NERVTAG but my overriding view is that this is a policy and possibly a ministerial decision once we have a consolidated CMO Office view.

I hope this is helpful,

Regards

JVT

Department of Health & Social Care

Professor Jonathan Van-Tam MBE (mil)
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