Initiation of antiretroviral treatment (ART) during the coronavirus pandemic

This interim guidance is intended for use during the COVID-19 pandemic and is temporary. The need to utilise the guidance will depend on local circumstances, which may vary over time. We advise that where any service has the capacity to operate as they would usually, they continue to do so, but where circumstances limit access to investigations or appointments, the appropriate parts of this guidance are followed accordingly.

Due to these unprecedented circumstances of COVID-19, to produce pragmatic advice about HIV treatment in a timely manner, our usual rigorous guideline development process has not been undertaken.

HIV services have a key role to play in the NHS response to coronavirus and this must be planned. In response to pressures on the NHS, the elective component of our work may be altered. However patients will continue to need care & we should seek the best local solutions to continue their proper management while protecting resources for the response to coronavirus. In addition, we also need to consider the possibility that services may be compromised due to a combination of factors including staff sickness and decreased laboratory capacity.

All BHIVA statements related to COVID-19 are available on the website: https://www.bhiva.org/Coronavirus-COVID-19

High risk patient groups

In general, government advice regarding social distancing and shielding should be followed (https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people/guidance-on-social-distancing-for-everyone-in-the-uk-and-protecting-older-people-and-vulnerable-adults).

There is emerging evidence that people with HIV may be at a higher risk of COVID-19 mortality but whether this is due to other co-morbidities or socio-demographic factors is not clear. The latest evidence is available in the regularly updated joint British HIV Association (BHIVA) statements with the Terrence Higgins Trust (THT) and European AIDS Clinical Society (EACS).

BHIVA and EACS advise that people who do not have controlled HIV on treatment or who have an impaired immune system (CD4 <200) may be at increased risk of severe disease. Government advice for this group is to be particularly stringent in following social distancing measures (see link above).

Additionally BHIVA and the Terrence Higgins Trust suggest:

- People with low nadir CD4 and/or other risk factors for severe COVID-19 (age >50, co-morbidities) may be at higher risk and should follow advice for higher risk groups as and when it emerges.
- People with significant immune suppression (CD4 <50 or recent opportunistic illness) may be extremely vulnerable. Please ensure people who meet these criteria receive the appropriate advice and can access the support they are entitled to: https://www.bhiva.org/COVID-19-and-shielding-advice-for-HIV-clinicians-GPs-and-people-living-with-HIV

Maintaining antiretroviral (ART) supply and provision

ART should not be interrupted. NHS England and NHS Improvement and HIV providers will continue to work together to maintain both the continuous provision and effective use of ART, thereby preventing avoidable harm, including:

- complications of immune suppression, including opportunistic infections
- non-HIV related complications associated with treatment interruption
- onward transmission of HIV
- development of drug resistance and limitation of active drug options.

Antiretroviral supply

NHS England and NHS Improvement are monitoring the supply and demand of HIV medicines at a national level, working closely with suppliers and putting in place necessary processes to ensure supply is maintained.

HIV providers will need to ensure they continue with current prescribing and dispensing arrangements to minimise the impact on any supply shortages.

If providers experience any issues with supply, they must in the first instance contact their local pharmacy procurement team, who will if necessary contact the regional pharmacy procurement specialist to resolve an issue.

Leadership

- Existing HIV regional networks should develop simple mechanisms to flag, in real time, any issues related to ART prescribing/provision or basic HIV care.
- The HIV Clinical Reference Group (CRG) will oversee treatment policies and respond to issues not been resolved at regional level. Issues can be raised with the CRG by emailing: ENGLAND.npoc-bloodandinfection@nhs.net

Categories of people receiving ART: prescribing and monitoring

Treatment of COVID-19

- The HIV CRG **recommends against using any antiretrovirals in the treatment of patients with COVID-19 infection** except within registered clinical trials.
- A randomised trial reported in March 2020 showed lopinavir/ritonavir had no benefit over standard of care alone in hospitalised adults with severe COVID-19 and the large UK RECOVERY Trial has confirmed those findings.[1,2]
- Evidence for activity against SARS-CoV-2 is conflicting. A Spanish cohort analysis suggested a protective effect for tenofovir-DF although it could not fully adjust for potential confounders. Updates regarding evidence for antiretrovirals & COVID-19 can be found here: https://www.bhiva.org/updated-BHIVA-DAIG-EACS-GESIDA-Polish-Scientific-AIDS-Society-statement-on-risk-of-COVID-19-for-PLWH
- The Intensive Care Society and BHIVA have produced guidance to support the NICE COVID-19 rapid guideline for critical care in adults (https://www.nice.org.uk/guidance/NG159), acknowledging the need to consider co-morbidities and underlying health conditions in all cases. The recommendations aim to support appropriate decision-making around escalation of care for people with HIV and safe maintenance of HIV therapy, including common issues. https://www.bhiva.org/Coronavirus-COVID-19

Antiretroviral maintenance

- Most people receiving ART are virally suppressed.

[1] Cao B et al.A trial of lopinavir-ritonavir in adults hospitalized with severe COVID-19. N Engl J Med 2020 Mar 18.
[2] https://www.recoverytrial.net/news/no-clinical-benefit-from-use-of-lopinavir-ritonavir-in-hospitalised-covid-19-patients-studied-in-recovery; accessed 07/08/2020

- Usual efficacy and safety monitoring is six-monthly for people who are virologically stable on ART. In the extenuating circumstances of COVID-19 this can reasonably be deferred until next planned follow-up for most in the context of good adherence, no new tolerability/toxicity concerns and no drug–drug interaction issues.
- No ART switch should be undertaken unless absolutely necessary, e.g. pregnancy, virological failure, significant tolerability/toxicity or major drug–drug interactions. ART should not be stopped or switched without discussing with the patient's HIV specialist.
- Monitoring should only be undertaken if it will change short-term management. All other non-essential monitoring should be deferred.
- If laboratory capacity is limited, viral resistance testing should be limited to:
    - baseline testing of new diagnoses
    - people with **confirmed** (two consecutive tests) viraemia >200 copies/mL on a low genetic barrier regimen (pre-emptive switch to a high barrier regimen can be undertaken before results are available if clinically appropriate to do so)
    - people reporting good adherence with new viraemia >1000 copies/mL on a high genetic barrier regimen.
- To protect medication supplies continue with usual duration prescriptions (typically six months) unless otherwise directed:
    - do not recall patients early: where patients are concerned about running out of medication or being unable to access the clinic, a prescription for deferred dispensing can be provided – but medicines should not be dispensed more than 1 month before their scheduled appointment
    - do not prescribe for longer than the current prescribing protocol
    - if a patient **must** receive their medication earlier than usual, it should be for an appropriately shorter duration.

Where homecare companies do not have capacity for new sign-ups individual trusts will manage non-homecare prescriptions according to their own arrangements, including collection from pharmacy, Royal Mail and courier services.

First-line antiretroviral initiation

- First-line ART decisions are usually based on several factors, including viral characteristics, patient characteristics, preferences and cost.

- If the capacity for clinic visit and/or monitoring requirements is limited, we include pragmatic 1st line prescribing recommendations which can be followed until more usual capacity resumes.
- This advice **does not override** existing national policies and regional algorithms but we suggest you interpret this 1st line prescribing advice, and how your modified MDT arrangements meet current requirements, in the patient-focused, pragmatic manner you already do.

Potential limiting factors

- **Access to baseline resistance testing:** where laboratory capacity is limited due to COVID19 activity, it is highly likely that capacity to process HIV resistance tests will be limited. This means that there may be increased turnaround times, restricted or even suspended testing because of staffing and reagent shortages and need to divert testing platforms to COVID-19. It is possible that HIV viral load testing will be similarly restricted. **This necessitates use of a regimen with a high barrier to resistance,** ie based on a protease inhibitor or second-generation integrase inhibitor.
- **Appointments:** we need to minimise patient visits for medications and tests. **This necessitates use of a well-tolerated regimen with high efficacy, a high barrier to resistance and low risk of toxicity.** Protease inhibitors are associated with a higher risk of short-term toxicity (eg rash, hepatotoxicity), long-term toxicity (eg renal impairment, cardiovascular disease) and tolerability issues (eg gastrointestinal adverse events) so second-generation integrase inhibitors are preferred.
- **Tests:** where the capacity for viral load and safety monitoring is limited, high barrier regimens and non-tenofovir-DF (TDF) regimens are most suitable for lower frequency monitoring (TDF requires baseline and regular renal monitoring at initiation). **This necessitates use of a well-tolerated, non-TDF regimen with high efficacy, a high barrier to resistance and low risk of toxicity.**
- **Advice:** where capacity for counselling is limited (pharmacists may not have the capacity to provide usual detailed counselling about drug–drug interactions, eg cations, CYP-metabolised drugs; HIV teams may not have the capacity to offer usual adherence counselling and support). **This necessitates use of a regimen with few major drug–drug interactions (thus excluding protease inhibitors which, as boosted agents, are associated with numerous interactions some of which can cause serious harm) and ideally a single tablet regimen without food requirements.**

Suggested first-line ART algorithm if investigations/follow-up restricted

- ART options should still be discussed and, where necessary, tailored according to patient needs and requirements.
    - **Recommended:** bictegravir/tenofovir–alafenamide/emtricitabine (Biktarvy) unless contra-indicated due to:
        - drug-drug interactions.
        - new diagnosis in a pregnant woman (follow BHIVA guidelines).
    - **Alternative:** whichever alternative regimen is clinically appropriate and acceptable to the patient can be used if bictegravir/tenofovir–alafenamide/emtricitabine are unsuitable or not tolerated, based on individual patient characteristics and the capacity of a service to provide advice and monitoring.
- **Prescribing and monitoring:**
    - Two-month initial supply with recommended (not mandatory) viral load at one month
    - additional testing based on patient characteristics and regimen choice
    - one-month phone check, additional four-month supply.

MDT review

- ART initiated during COVID-19, based on modified MDT arrangements, should be reviewed at full MDT as soon as this is practical.

Authorship & review

V1 1st May 2020: authored by David Asboe & Laura Waters as chairs of HIV CRG & BHIVA; reviewed by HIV CRG sub-group, BHIVA Officers, BHIVA executive committee community representative & BHIVA guidelines sub-committee chair

V2 7th August 2020: updated by Laura Waters, BHIVA Chair; reviewed by BHIVA Officers, BHIVA executive committee community representative, BHIVA guidelines sub-committee chair & vice-chair