Cardiothoracic Transplant Patient Group

Submission on Draft Guidance to NICE Appraisal 6136 (Tix-cil)

General Comments

The Cardiothoracic Transplant Patient Group appreciates that the clinical evidence suggests that tix-cil is unlikely to be effective against the current relevant Covid 19 variants.

The Cardiothoracic Transplant Patient Group believe that the extreme length of the assessment process has directly led to a missed opportunity of tix-cil's window of effectiveness. The Medicines and Healthcare products Regulatory Agency approved tix-cil on 17 March 2022. At this time Omicron BA.2 was the dominant UK variant and remained so until approximately June 2022. Omicron BA.5 then succeeded in becoming the dominant variant until approximately Nov 2022.

The In Vitro Advisory Group report demonstrated tix-cil had neutralising activity against Omicron BA.2 and to a lesser extent Omicron BA.5 which were the dominant strains for the 8 months preceding the drug's authorisation. Additionally, the observational study Young-Xu et al was conducted when Omicron BA.2 was one of the dominant variants.

If approval and delivery of tix-cil had been given as close as possible to 17 March 2022, then the Cardiothoracic Transplant Patient Group believe that some of its patient population could have gained a material benefit.

As a direct consequence of the length of assessment process some patients who have received a heart and / or lung transplant will have experienced avoidable morbidity and mortality.

Whilst the preliminary recommendations have not been discriminatory, the speed at which they have been produced has discriminated against people whose life is sustained by either a donated heart or lung.

The Cardiothoracic Transplant Patient Group appreciate further organisations in addition to NICE were involved during the whole decision process for tix-cil. These include commissioners and the Medicines and Healthcare products Regulatory Agency.

The Cardiothoracic Transplant Patient Group would encourage all relevant bodies to work collaboratively in the future to ensure appraisals and approvals of any treatments to prevent Covid 19 in high-risk groups are conducted rapidly.

The Cardiothoracic Transplant Patient Group is concerned that the committee may have not received all relevant evidence related to cardiothoracic transplant recipients due to the lack of professional inclusion and engagement from the cardiothoracic transplant clinical community. The Cardiothoracic Transplant Patient Group are extremely concerned that the list of professional groups does not include The British Transplantation Society, or any cardiac related group such as The British Society for Heart Failure.

The Cardiothoracic Transplant Patient Group is further concerned by the relative lack of stakeholder engagement from cardiac related patient / carer groups. Other relevant groups could include, British Heart Foundation, Somerville Heart Foundation, Pumping Marvellous and Pulmonary Hypertension Association UK.

The Cardiothoracic Transplant Patient Group consider that the NICE appraisal process should place patients at the centre of their decision making. To achieve this patient engagement could be enhanced. Representative patients from NHS formally appointed bodies should be considered preferential to those from other organisations. The Cardiothoracic Transplant Patient Group (part of NHSBT) would be a good example of such a body. The Group has formal processes to ensure that the views it gives are representative of a whole patient population rather than that of an individual patient.

Comments on Specific Sections

3.17

The Cardiothoracic Transplant Patient Group recognise the challenges the NICE Appraisal Committee have with estimating Covid-19 hospitalisation risk. The Group, however, considers that the Appraisal Committee need to improve engagement with stakeholder groups to facilitate this process.

Whilst NICE acknowledge that the benefit gain will vary within the selected eligible population the only defined sub patient group which has a hospitalisation rate tested by NICE is that within Shield et al. (2022). More proactive engagement with stakeholder groups on this specific matter may yield further useful information.

The Cardiothoracic Transplant Patient Group wish to highlight several pieces of additional information, all of which indicate that NICE may have underestimated hospitalisation risk in certain high-risk patient groups, with some specific references to risk within solid organ transplant recipients and cardiothoracic transplant recipients.

1) Callaghan et al (2023) (Vaccine Effectiveness Against the SARS-CoV-2 B.1.1.529 Omicr... : Transplantation (lww.com)) measured vaccine effectiveness against the Covid 19 Omicron B.1.1.529 variant in solid organ or islet transplant recipients. This revealed an overall hospitalisation or death risk of 5.8% in this patient population. Further interrogation of the information provided, showed a Covid 19 mortality rate of 6.2% and 12.0% for heart and lung recipients respectively in the whole study period (Dec 20 – March 22 - which is post UK vaccine deployment). Every solid organ transplant study demonstrates heart and particularly lungs transplant recipients to be at higher risk of severe Covid 19 than the whole transplant population. It is thus reasonable to assume that the risk of hospitalisation or death risk to heart and lung transplant recipients was much higher than 5.8% in the Covid 19 Omicron B.1.1.529 variant era.

2) The first results of the MELODY study have been published, Pearce et al (2023)

(Antibody prevalence after 3 or more COVID-19 vaccine doses in 23,000 immunosuppressed individuals: a cross-sectional study from MELODY | medRxiv).

This investigated the prevalence of spike-protein antibodies following at least 3 Covid 19 vaccinations in immunocompromised individuals. Three patient groups were included, solid organ transplants, rare autoimmune rheumatic diseases, and lymphoid malignancies. The headline results revealed that solid organ transplant recipients had the highest levels (23.3%) of no detectable IgG spike protein antibodies in the three patient cohorts.

Further interrogation of the data reveals that heart (25.7%) and lung (35.4%) have the highest percentage of undetectable antibodies of the solid organ transplant cohort.

3) Evans et al (2023) (Real-world effectiveness of molnupiravir, nirmatrelvir-ritonavir, and sotrovimab on preventing hospital admission among higher-risk patients with COVID-19 in Wales: a retrospective cohort study | medRxiv) undertook a retrospective study on high risk patients in Wales eligible for out of hospital Covid 19 therapies. This study revealed an all-cause hospitalisation or death risk within 28 days of 10.9% of those who had not received any treatment.

4) Radcliffe et al (2022) (Real-world experience with available, outpatient COVID-19 therapies in solid organ transplant recipients during the omicron surge - American Journal of Transplantation (amjtransplant.org)) conducted a single centre retrospective study on the effectiveness of out of hospital Covid therapies on reducing the risk of hospitalisation. This showed that of the patient cohort which did not receive any treatment, 27% were hospitalised within 30 days of Covid 19 diagnosis. It should be noted that the study group did not contain any lung transplant recipients and 18% were heart transplant recipients.

5) The latest Covid 19 mortality figures published by NHS Blood and Transplant (monthly-report-on-covid-19-nhsbt-16-march-2022.pdf (windows.net)), reveals mortality rates of 15.5% and 7.5% for lung and heart transplant recipients respectively.

In summary The Cardiothoracic Transplant Patient Group believe that future NICE appraisals must, where information is available, analyse benefit at a defined patient cohort level. This is especially relevant where the patient cohort is congruent with a single identifiable protected characteristic such as individuals with donated heart or lungs.

The Cardiothoracic Transplant Patient Group is concerned that the focus on hospitalisation risk underestimates the risk of severe Covid 19. Data provided by Callaghan et al (2023) revealed that in solid organ or islet transplant recipients 0.71% of patients died within 28 days of a positive Covid 19 test who were not admitted to hospital for a noninjury. As such The Cardiothoracic Transplant Patient Group believe that in future calculations of severe Covid 19 NICE should utilise hospitalisation and mortality statistics. Alternatively, a multiplier on hospitalisation

risk could be used to estimate the additional patient cohort – based on Callaghan et all, for solid organ or islet transplants this would be 1.14.

3.23

The Cardiothoracic Transplant Patient Group commend the NICE Evaluation Committee for recognising the urgent need for an effective prophylactic treatment for people who do not have an adequate response to vaccination. The Cardiothoracic Transplant Patient Group believe that the NHS need to commit to all members of the public receiving an equitable opportunity for protection from Covid 19 regardless of their disability.

4.1

The Cardiothoracic Transplant Patient Group welcome the NICE Evaluation Committee acknowledging the need for tix-cil to be evaluated quickly against all new variants.

The Cardiothoracic Transplant Patient Group would also encourage the company to enter tix-cil into the suggested ongoing platform trials.

4.2

The Cardiothoracic Transplant Patient Group supports the recommendation outlined in 4.2.

In the stakeholder meeting of 15 February 2023, a potential quicker assessment timeframe of 90 days was suggested. The Cardiothoracic Transplant Patient Group does not consider this aim to be sufficiently ambitious. Covid variant evolution is rapid and variant domination can easily pass within such a time duration.

As such the Cardiothoracic Transplant Patient Group would recommend a pre-emptive approval and delivery model. Such a model could establish pre agreed in vitro efficacy achievement levels at which the required cost effectiveness estimates are delivered. This could grant automatic (or very rapid authorisation) and trigger pre planned delivery methods. The model and delivery could be tailored at patient group levels, with different authorisation points depending on benefit gained by each group.

The Cardiothoracic Transplant Patient Group, post-transplant patients, would be an excellent example of a known defined, very high-risk patient group.