NHS Wales National Antiviral Service Pathway

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1.0	16 Aug 2022	Alana Adams	Development of Pathway	Final

Major Version Approvals

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Contents

1. Introduction

1.1 The National Antiviral Service (NAVS) is hosted within the Welsh Medicines Advice Service of Cardiff and Vale University Health Board (CAVUHB) and is commissioned by Welsh Government, to provide antiviral treatment or referral for antibody treatment for extremely high-risk individuals with COVID-19 symptoms in the community. More information about NAVS and eligibility can be found on at this link National Antiviral Service (NAVS) - Healthcare Professionals site - Welsh Medicines Information Centre (wales.nhs.uk)

2. Background

2.1 Since December 2021, the NHS in Wales has been providing antiviral and antibody treatments for eligible individuals who are at highest risk of severe COVID-19 and the extremely vulnerable with **symptomatic** COVID-19 in the community, even if the symptoms are mild.

2.2 When individuals in Wales test positive for COVID-19 following a PCR test or after reporting a Lateral Flow Device test online, the Digital Health and Care Wales (DHCW) system, identifies eligible individuals from their medical history (see Appendix 1) and prescribed medications, generating a report which is used by the NAVS team to contact those identified individuals.

2.3 Telephone assessment is offered to all identified eligible individuals via text*. If assessment is accepted by the individual, a member of the NAVS team, will contact them within 24-48 hours, to assess and decide which treatment pathway is appropriate.

2.4 Those who are meet the eligibility criteria will be offered treatment within **five days (discretion up to 7 days)** of symptom onset.

2.5 It is recognised there are individuals who are eligible for treatment but who are not identified correctly by the DHCW system, when they test positive for COVID-19 (newly diagnosed, inaccurate or delayed clinical coding). These individuals can access NAVS via NHS 111 or by another health care professional.

* When the service is operating at low levels of COVID-19 transmission, all individuals identified, may be contacted by telephone rather than by initial text message

3. Pathway Purpose

3.1 The purpose of the NAVS Pathway is to provide a consistent way of triaging and assessment of individuals for either an oral antiviral preparation or referral to the local health board within which they reside, for an infusion of a monoclonal antibody (MAB).

4. Referral process to NAVS

4.1 DHCW issues a daily report to the NAVS team which contains a list of eligible individuals who have tested positive for COVID-19 in the last 24 hours, identified primarily by hospital coding. The list is sent to the NAVS email address.

Inclusions: Symptomatic high-risk individuals who have tested positive for COVID-19 with no previous positive test within the last 30 days.
Exclusions: Asymptomatic high-risk individuals who have tested positive for COVID-19 or have been treated within the last 30 days.

4.2 A member of the NAVS admin team will prepare the list for onward sharing to health boards across Wales (a separate document exists outlining the process for this). Individuals not suitable for oral antiviral Paxlovid® ▼are identified in grey, for triage by local health boards for neutralising monoclonal antibody (nMAB) treatment.

4.3 The *NAVS team prioritise the remaining calls by date of positive test* and will ONLY call those, who have requested a call back. Two attempts are then made to contact the individual. Unfortunately, during times of extreme demand on the service, only one attempt may be possible. If the call is not answered, a message will be left identifying the NAVS caller as NHS, with a message that the service will try again later. The NAVS team will try on one other separate occasion, on this occasion, they will leave a message informing individual to contact NHS 111 if antivirals are required.

4.4 Individual are triaged for Paxlovid®▼ as first line therapy. Those with contraindications to Paxlovid®▼ or with significant drug-drug interactions rendering Paxlovid®▼ unsuitable for use, are offered referral to their Local Health Board (LHB) for nMAB treatment (an internal checklist is used for this). Should they decline nMAB treatment, or where nMAB treatment capacity is not available, a third option, molnupiravir is offered. Molnupiravir has a lower efficacy (relative risk reduction of hospitalisation and death) compared to nMAB and Paxlovid®▼treatments. Individuals will be made aware of this before they make their decision. The outcome and decision for outcome is recorded on the shared list for each individual.

4.5 At 12pm and 2pm daily (11.30am Saturday and Sunday) individuals requiring Paxlovid®▼ or Molnupiravir are referred to UHL (University Hospital Llandough) pharmacy for dispensing and delivery by Royal Mail next day delivery. Urgent deliveries identified will be delivered by taxi. Royal Mail offer a Monday to Saturday collection and delivery service (excluding Sunday)

4.6 Individuals triaged after 2pm are identified for delivery 48 hours later, if they are identified as urgent then delivery by taxi will be used. Individuals who decline nMAB treatment after being offered it by their local health board, may be offered oral molnupiravir by NAVS OR by the local health board to avoid treatment delay in agreement with NAVS for the supply by NAVS. Supply of all the treatments are made via Patient Group Direction (PGD). Current PGDs can be viewed on the NAVS website.

4.7 In times of extremely high demand, NAVS will implement the business continuity plan. This involves requesting the local health boards to triage individuals identified to their organisation as per the shared list. This will be done collaboratively with the NAVS team centrally.

5. Referral process via NHS 111 Wales

The Welsh Government COVID-19 treatment website will advise high-risk individuals who test positive for COVID-19 who have not been contacted by NAVS/LHB within 48 hours of receiving a positive test result, to contact NHS 111 Wales for NAVS assessment/referral for treatment if appropriate. The information will clearly specify that antiviral treatment is only available for individuals who are **symptomatic** and who meet the eligibility criteria.

5.1 When individuals call NHS 111 Wales, they will be offered a clinical assessment first. Those with minor symptoms not requiring clinical assessment will be sent directly to the Health Information Team of NHS 111 Wales for NAVS eligibility assessment/referral.

5.2 Health Information Advisers will contact the caller to undertake a NAVS eligibility assessment using the NAVS portal.

5.3 Callers who meet the referral criteria will be asked for permission to share their details with NAVS. They will be advised that they will be contacted by a health professional from NAVS within 24 hours, for a telephone consultation to assess their eligibility for antiviral treatment. Callers who contact the NHS 111 Wales service during the weekend who do not require urgent intervention will be advised that they will be contacted by NAVS on the Monday morning.

5.4 NHS 111 Wales are able to view the NAVS daily list so they can be aware of the call volumes and they can check the status of an individual on the list before referral.

6. Referral process via Health Professionals

6.1 Eligible individuals who have not been identified by DHCW may present at their GP, A&E or other specialist services.

6.2 General practitioners, other specialists and their teams may refer eligible individuals using the NAVS portal. The individuals must meet the eligibility criteria (Appendix 1) or they will be declined after speaking with the NAVS team. N.B. Individuals should only be referred in this direct way if they have *not* been identified automatically usually 24-48 hours after registering their positive test.

6.3 A webinar outlining the National Antiviral Service and eligibility assessment by the specialist team can be viewed at https://gpcpddev.heiw.net/cpdon-demand/covid-19/.

7. Out of Hours

7.1 NAVS is available between 8.30am & 5.00pm Monday to Friday. From 30th July 2022, NAVS will provide a skeleton service for urgent referrals between 9-1pm on Saturdays. Health care professionals can refer individuals using the NAVS portal.

7.2 Health Care Professionals (HCPs) attempting to contact the service outside of these hours should be informed that they will be contacted on the next working day, antiviral supply is not urgent and can be made up to 7 days from symptom onset and positive test.

After 4pm Monday to Thursday
Referrals will be processed from 8.30 am the following day.

After 4pm Friday
Urgent referrals will be processed on Saturday morning and/or occasionally on a Sunday morning.

After 12pm Saturday
Referrals will be processed from 8.30am on Monday morning (unless it is a bank holiday).

8. Panoramic Study

8.1 Individuals aged between 18 – 49 and over 50's who are not eligible for antiviral treatment as part of their standard care but have a medical condition that means they are clinically vulnerable, may be considered for inclusion in the Panoramic Study, details of which should be offered by NAVS team or by NHS 111 Wales if appropriate.

9. Concerns

9.1 General concerns relating to the NAVS pathway should be referred to Concerns and complaints - Cardiff and Vale University Health Board (nhs.wales)

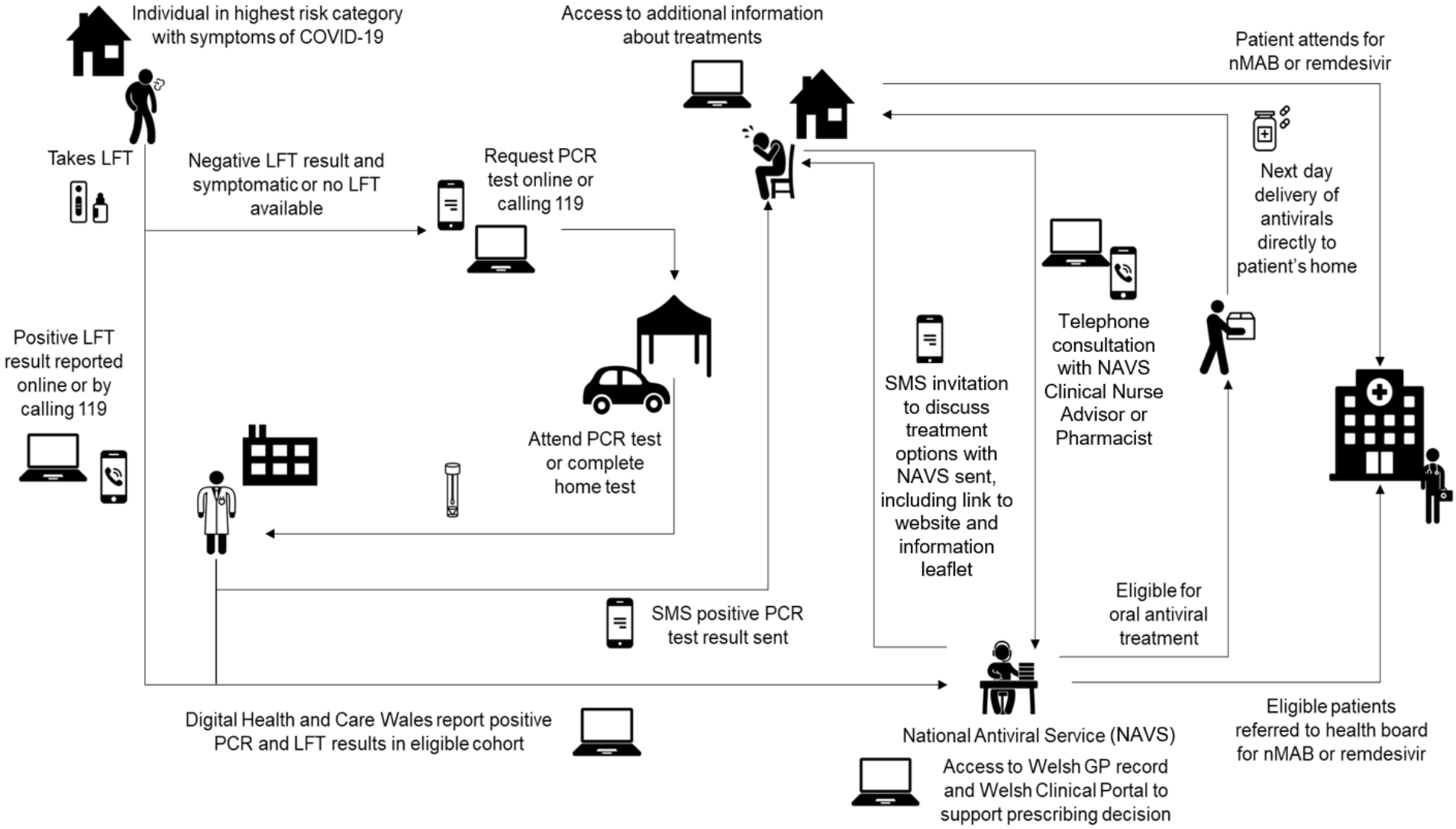
10. Reporting

10.1 Weekly reports are available.

11. Referral Outcomes

11.1 General Practitioners will be informed of the antiviral supply to their patients either electronically or by letter.

12. Appendix 1 - Flowchart



13. Appendix 2 - Eligible individuals

The following patient cohorts below were determined by an independent advisory group commissioned by the Department of Health and Social Care (DHSC). Please refer to the most recent Interim Commissioning Policy for an up to date list of the patient cohorts. They are considered to be at the highest risk from COVID-19 to develop severe illness. The Interim Commissioning Policy focuses on prioritising these patients for treatment.

Cohort	Description
Down's syndrome and other genetic disorders	• All patients with Down's syndrome • Patients with chromosomal disorders known to affect immune competence[1]
Patients with a solid cancer	• Active metastatic cancer and active solid cancers (at any stage) • Locally advanced inoperable cancer • Lung cancer (at any stage) • All patients receiving **any** chemotherapy within the last 12 months (including antibody-drug conjugates and PI3K inhibitors) • Patients receiving radiotherapy within the last 12 months • Cancer resection within the previous 12 months, who received no adjuvant chemotherapy or radiotherapy

Patients with a haematological disease and stem cell transplant recipients
 	
(continued over page)
	• Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases)
	• Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
	• Individuals with haematological malignancies who have
	  ○ received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or
	  ○ radiotherapy in the last 12 months
	• Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months
	• All patients who do not fit the criteria above, who are diagnosed with:
	  ○ myeloma (excluding MGUS)
	  ○ AL amyloidosis
	  ○ chronic B-cell lymphoproliferative disorders (e.g. chronic lymphocytic leukaemia, follicular lymphoma)
	  ○ myelodysplastic syndrome (MDS)
	  ○ chronic myelomonocytic leukaemia (CMML)
	  ○ myelofibrosis
	• All patients with sickle cell disease
	• Thalassaemia or rare inherited anaemia with any of the following:
	  ○ Severe cardiac iron overload (T2* < 10ms)[2]
	  ○ Severe to moderate iron overload (T2* ≥ 10ms) PLUS an additional co-morbidity of concern (e.g. diabetes, chronic liver disease or severe hepatic iron load on MRI)

Cohort	Description
Patients with a haematological disease and stem cell transplant recipients (continued)	• Individuals with non-malignant haematological disorder (e.g. aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (e.g. anti-CD20, anti-thymocyte globulin [ATG] and alemtuzumab) within the last 12 months

Patients with renal disease	• All renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who:
	  ○ Received B-cell depleting therapy within the past 12 months (including alemtuzumab, rituximab, ocrelizumab, ofatumab, obinutuzumab [anti-CD20], anti-thymocyte globulin)
	  ○ Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals
	  ○ Not been vaccinated prior to transplantation
	• Non-transplant patients who have received a comparable level of immunosuppression
	• Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 mL/min/1.73m^2) without immunosuppression

Patients with liver disease	• Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease) • All liver transplant recipients • Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) • Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Solid organ transplant recipients	• All recipients of solid organ transplants not otherwise specified above

Patients with immune-mediated inflammatory disorders (IMID)	• IMID treated with rituximab or other B-cell depleting therapy[3] in the last 12 months
	• Currently treated with/have been treated within the past 6 months with:
	  ○ Cyclophosphamide (IV or oral)
	  ○ Biologics or small molecule JAK-inhibitors[4]
	• Current treatment with mycophenolate mofetil, oral tacrolimus, azathioprine/mercaptopurine (for major organ involvement such as kidney, liver and/or interstitial lung disease), methotrexate (for interstitial lung disease only) and/or ciclosporin
	• Taking equivalent or greater than prednisolone 10mg per day (including budesonide) for at least 28 days prior to positive test
	• IMID patients with active/unstable[5] disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate

Cohort	Description
Immune deficiencies	• Common variable immunodeficiency (CVID) • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) • Hyper-IgM syndromes • Good's syndrome (thymoma plus B-cell deficiency) • Severe Combined Immunodeficiency (SCID) • Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) • Primary immunodeficiency associated with impaired type I interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
HIV/AIDS	• Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • On treatment for HIV with CD4 <350 cells/mm^3 and stable on HIV treatment or CD4>350 cells/mm^3 and additional risk factors (e.g. age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, those with alcohol-dependence)
Rare neurological conditions	• Multiple sclerosis • Motor neurone disease • Myasthenia gravis • Huntington's disease

[1] Examples of chromosomal disorders know to affect immune competence: DiGeorge syndrome (22q11.2 deletion), CHARGE syndrome (CHD7 mutation), Corneal de Lange syndrome, Chromosome 8 or 18 abnormalities, Primary immunodeficiency syndromes, including: X-linked agammaglobinaemia, X-linked lymphoproliferative syndrome

[2] T2* is referring to the MRI T2 weighted image to make the diagnosis. If this information is not available, the patient may be asked questions such as whether they have haemochromatosis (a disease of increased iron storage) or any condition requiring recurrent blood or iron transfusions

[3] Local additional information: B-cell depleting therapies used in the treatment of immune-mediated inflammatory disorders include: alemtuzumab, belimumab, natalizumab, ocrelizumab, ofatumumab, rituximab, obinutuzumab
See MiDatabank Enq. No:353373

[4] Examples of small molecule JAK-inhibitors may include: abrocitinib, baricitinib, fedratinib, filgotinib, peficitinib, ruxolitinib, tofacitinib, upadacitinib.

[5] Definition of active/uncontrolled IMID: people who exhibit at least one of: (a) uncontrolled or clinically active disease (that is required recent increase in dose or initiation of new immunosuppressive drug or IM steroid injection or course of oral steroids within the 3 months prior to positive PCR); and/or (b) major organ involvement such as significant kidney, liver or lung inflammation or significantly impaired renal, liver and/or lung function)