

HEADQUARTERS

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THALASSAEMIA INTERNATIONAL FEDERATION POSITION STATEMENT

COVID-19 VACCINES & HAEMOGLOBIN DISORDERS

Introduction

The Thalassaemia International Federation (TIF)¹ in the context of its mission to safeguard the rights of patients with Haemoglobin Disorders (transfusion and non-transfusion thalassaemia and Sickle Cell Disease) globally for access to quality medical, social and other care, and in view of the COVID-19 pandemic has developed a series of educational resources, guidance and recommendations². These seek to support healthcare professionals, decision making authorities and healthcare systems in every country to build on and develop their own national recommendations or guiding documents where patients with haemoglobin disorders are concerned.

Patients with thalassaemia and sickle cell disease (SCD) are likely to be at increased risk of complications from COVID-19. There is a broad spectrum of severity of these syndromes due to the various mutations and combinations of mutations which cause them. In addition, each patient has a different expression of the disorder on account of the vast heterogeneity of the quality of medical care provided worldwide (particularly in developing countries) but also on account of challenges related to adherence to treatment, socio-economic status and migration conditions / aspects and which are met both in the Western world and across the globe.

An effort has been made by the Federation to classify the **level of potential risk** affecting these patients, based on an amalgamation of practices and recommendations that have been either published in peer-reviewed journals, and/or national government or medical professional society websites and/or national patient NGOs (See [Thalassaemia & Sickle Cell Disease: Classification of Risk Groups & Other Considerations – Guidance for Patients, Parents & Healthcare Professionals](#)³).

¹ The Thalassaemia International Federation (TIF) is a patient-oriented non-profit, non-governmental umbrella federation, established in 1986 with Headquarters in Nicosia, Cyprus. TIF's mission is to help ensure equal access to quality health and other care for every patient with thalassaemia and other haemoglobin disorders around the world. To-date membership boasts 232 members from 64 countries across the globe. TIF works in official relations with the World Health Organization (WHO) since 1996 and enjoys active consultative status with the United Nations Economic and Social Council (ECOSOC) since 2017. Moreover, it is a strategic partner of the European Commission under the Third Health Programme since 2018 and a member of the Patients and Consumers Working Party (PCWP) of the European Medicines Agency (EMA) since 2010. In 2019, TIF obtained a participatory status at the Council of Europe, as a Member of the Conference of International NGOs. Moreover, TIF was awarded, in the context of the 68th World Health Assembly in May 2015, the 'Dr Lee Jong-wook Memorial Prize' for its outstanding contribution to public health.

² TIF Haemoglobin Disorders & COVID-19 Publication series (2020) <https://thalassaemia.org.cy/covid-19-pandemic/tif-material-on-covid-19/>

³ Thalassaemia & Sickle Cell Disease: Classification of Risk Groups & Other Considerations – Guidance for Patients, Parents & Healthcare Professionals – A TIF Publication (2020) <https://thalassaemia.org.cy/publications/tif-publications/covid-19-haemoglobin-disorders-a-classification-of-risk-groups-other-considerations-2020/>

This risk classification is intended to be used as a guidance only, considering that every single patient with a haemoglobin disorder, on account of the disorders' nature, genetic background, complicated pathophysiology and consequently its vastly heterogeneous clinical outcome, requires personalized, tailored to the individual management needs, for which the key responsibility lies with the long-term treating specialist.

In view of the plans made by national health authorities in every country across the world for the widespread vaccination of individuals against the SARS-CoV-2 virus, the Thalassaemia International Federation herein presents the latest information concerning the to-date authorized vaccinations (information about other vaccines in the pipeline are available in TIF's relevant publication⁴) as well as the Federation's position about the vaccination of patients with haemoglobin disorders against SARS-CoV-2.

“Immunization is a key component of primary health care and an indisputable human right. It's also one of the best health investments money can buy. Vaccines are thus critical to the prevention and control of infectious-disease outbreaks. They underpin global health security and will be a vital tool in the battle against antimicrobial resistance”⁵. – World Health Organization

Vaccines for SARS-CoV-2

A total of **56** vaccines for the SARS-CoV-2 virus are in clinical development, of which **11** are in phase 3 trials and another **166** in pre-clinical development (information correct as of 22 December 2020)⁶. One vaccine that has completed the phase 3 of the clinical trial (Pfizer BioNTech COVID-19) has already received Emergency Use Authorization by the Food & Drug Agency (FDA) in the USA⁷, approval by the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK⁸ and authorization by the European Medicines Agency (EMA)⁹ – the responsible regulatory body for the 27 EU Member States¹⁰. This vaccine has received the trademark name Comirnaty in the EU¹¹. In addition, another vaccine (Moderna Mrna-1273) has received Emergency Use Authorization by the FDA in the USA¹² and is pending authorization by the EMA in Europe. Further approvals / authorizations of other vaccines (including the vaccine developed by AstraZeneca & Oxford University) are expected in the coming weeks. Moreover, another vaccine is provided to people in Russia albeit with no related published literature or authorization certification from the EU or FDA.

Both of the above authorized vaccines use **mRNA technology**, which triggers an immune response, not by the insertion of a weakened or inactivate virus (as is common with other vaccines) but, by making a protein that produces antibodies which offers immunity against the SARS-CoV-2 virus¹³.

More information is available in TIF's 'Vaccinations & Therapeutic Drugs' publication¹⁴.

⁴ Vaccinations & Therapeutic Drugs – A TIF Publication (2020) <https://thalassaemia.org.cy/publications/weekly-update-developing-vaccinations-therapeutic-drugs-for-covid-19/>

⁵ Vaccines & Immunization, World Health Organization <https://www.who.int/health-topics/vaccines-and-immunization>

⁶ Landscape of COVID-19 candidate vaccines, World Health Organization <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines> (Last Updated: 17 Dec 2020)

⁷ Pfizer / BioNTech Vaccine, FDA <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>

⁸ Pfizer / BioNTech Vaccine, MHRA <https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19/information-for-healthcare-professionals-on-pfizer-biontech-covid-19-vaccine>

⁹ Comirnaty, European Medicines Agency <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/comirnaty>

¹⁰ Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain and Sweden.

¹¹ Comirnaty, European Medicines Agency <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/comirnaty>

¹² Moderna, FDA <https://www.fda.gov/media/144434/download>

¹³ CDC, <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html>

¹⁴ Vaccinations & Therapeutic Drugs <https://thalassaemia.org.cy/publications/weekly-update-developing-vaccinations-therapeutic-drugs-for-covid-19/>

Indications, Administration & Immunity

Pfizer BioNTech^{15 16 17}:

- Authorized for persons aged 16 and above.
- Intra-muscular administration in 2 doses (21 days apart).
- Immunity from infection occurs 1 week after the second dose.

Moderna Mrna-1273¹⁸:

- Authorized for persons aged 18 and above.
- Intra-muscular administration in 2 doses (28 days apart) subcutaneously.
- Immunity from infection occurs 1 week after the second dose.

Safety & Efficacy

Evidence collected to-date have shown that the efficacy of the two vaccines for preventing infection from the SARS-CoV-2 virus range from 94% – 95%.

The Pfizer BioNTech / Comirnaty vaccine was evaluated for safety and efficacy in a Phase 3 Clinical Trial with 44,000 participants. The trial demonstrated a 95% efficacy in people over 16 years of age (including people over 75 years of age). Furthermore, a 95% reduction was demonstrated for persons at risk of developing severe COVID-19, including those with asthma, chronic lung disease, diabetes, high blood pressure or high body mass index. The most common side effects with Comirnaty in the trial were usually mild or moderate and got better within a few days after vaccination. These included pain and swelling at the injection site, tiredness, headache, muscle and joint pain, chills and fever. They affected more than 1 in 10 people. Redness at the injection site and nausea occurred in less than 1 in 10 people. Itching at the injection site, pain in the limb, enlarged lymph nodes, difficulty sleeping and feeling unwell were uncommon side effects (affecting less than 1 in 100 people).¹⁹.

The safety and efficacy of Moderna's Mrna-1273 vaccine was demonstrated in a Phase 3 Clinical Trial with 30,000 participants. The trial showed a 94% efficacy in people between 18 – 65 years of age and 86% in those over 65. The most commonly reported side effects, which typically lasted several days, were pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, swollen lymph nodes in the same arm as the injection, nausea and vomiting, and fever. Of note, more people experienced these side effects after the second dose than after the first dose²⁰.

Additional data for both vaccines is required to assess effectiveness in paediatric population, immunocompromised people, pregnant and breast-feeding women^{21 22}.

¹⁵ CDC, Pfizer / BioNTech Vaccine <https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/index.html>

¹⁶ Pfizer / BioNTech Vaccine, MHRA <https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19/information-for-healthcare-professionals-on-pfizerbiontech-covid-19-vaccine>

¹⁷ Comirnaty, European Medicines Agency https://www.ema.europa.eu/en/documents/product-information/comirnaty-product-information-approved-chmp-21-december-2020-pending-endorsement-european-commission_en.pdf

¹⁸ CDC, Moderna Vaccine <https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/index.html>

¹⁹ Comirnaty, European Medicines Agency <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/comirnaty>

²⁰ Moderna, FDA <https://www.fda.gov/media/144434/download>

²¹ Comirnaty, European Medicines Agency <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/comirnaty>

²² Moderna, FDA <https://www.fda.gov/media/144434/download>

Should patients with haemoglobin disorders be vaccinated? TIF's Position

The Thalassemia International Federation (TIF) has firmly declared, in conjunction with the opinion and recommendations of leading international experts in the field as well as national professional associations in the UK²³ and the USA²⁴ that all patients with haemoglobin disorders, wherever they may live, should be included amongst the 'vulnerable' groups of every country's population²⁵.

As such, vaccination programmes should treat **patients with haemoglobin disorders as a priority**, on a par with other vulnerable groups. From the available published information and practices of international medical experts in Reference Centres across Europe, there is no indication that patients with haemoglobin disorders will be left out of SARS-CoV-2 vaccination programmes. Indeed, **haemoglobin disorders should be given prioritization within a national vaccination programme as part of the vulnerable groups.**

The SARS-CoV-2 infection presents particular challenges and great risks to patients with haemoglobin disorders and, if their appropriate clinical management as described in international Guidelines²⁶ is not safeguarded in the context of national policies developed for fighting COVID-19, their health and quality of life will be tragically impacted. In addition, and considering their worldwide occurrence, an immense strain will be imposed on the healthcare system, and in particular public health programmes of every country across the globe.

TIF's 'Thalassaemia & Sickle Cell Disease Classification of Risk Groups Guidance'²⁷ as previously mentioned offers a gross but hopefully useful stratification of risk levels for patients with haemoglobin disorders. This can offer significant guidance on which patients need to be vaccinated in the first phases, followed by others in second and third phases of the vaccination programmes offered to vulnerable populations.

Having described this proposed sequence of the vaccination process, the treating physician has the responsibility of acknowledging any **allergies** the patient is known to have, and/or levels of **immunosuppression** related to drug treatment that the patient is currently undergoing or has recently undergone. The comprehensive knowledge of the clinical status of each patient is borne by each patients' treating physician.

In addition, it should be noted that the patients meeting the following criteria, should be offered the vaccine as soon as possible, as suggested by the UK Haemoglobinopathy Panel²⁸:

1. All adults with SCD
2. Thalassaemia patients with severe iron overload
3. Splenectomized patients
4. Patients with 1 or more underlying co-morbidities including diabetes, pulmonary hypertension, endocrine, cardiac, respiratory disease

Moreover, acknowledging that each disorders' nature, genetic background, and pathophysiology is complex and heterogenous, a personalized decision for each patient separately is required to be taken by the treating physician concerning a possible vaccination against SARS-CoV-2.

²³ National Haemoglobinopathy Panel, UK <https://www.nationalhaempanel-nhs.net/>

²⁴ American Society of Hematology, USA <https://www.hematology.org/covid-19/covid-19-and-thalassemia>

²⁵ TIF POSITION STATEMENT "COVID-19: Inclusion of thalassaemia and Sickle Cell Disease patients in the high risk population" https://thalassaemia.org.cy/wp-content/uploads/2020/04/TIF-Position-Statement_Thal-SCD-High-Risk-Group-1.pdf

²⁶ Guidelines for the Management of Transfusion Dependent Thalassaemia, 3rd Edition, Issued by Thalassaemia International Federation <https://thalassaemia.org.cy/publications/tif-publications/guidelines-for-the-management-of-transfusion-dependent-thalassaemia-3rd-edition-2014/>

²⁷ Thalassaemia & Sickle Cell Disease: Classification of Risk Groups & Other Considerations – Guidance for Patients, Parents & Healthcare Professionals – A TIF Publication (2020) <https://thalassaemia.org.cy/publications/tif-publications/covid-19-haemoglobin-disorders-a-classification-of-risk-groups-other-considerations-2020/>

²⁸ National Haemoglobinopathy Panel, UK <https://ukts.org/wp-content/uploads/2020/11/HBOCOVID-19vaccinationstatementDecember2020.pdf>

In addition, evidence for specific groups of people (e.g. those with thalassaemia, sickle cell disease, splenectomy / asplenia etc) to evaluate any attenuated or reduced response to vaccination should be gathered.

For haemoglobin disorders, doctors at treating centres should strictly adhere to providing detailed information to the **post-authorization safety monitoring processes** in place by marketing authorization holders to support the accumulation of long-term efficacy and safety data collection. In this context, patient organizations and treating physicians together should **reliably inform patients** on all available details, including possible side effects, about the vaccines. Collectively they should encourage those who receive the vaccine to **report every adverse event** (side effect) they exhibit by facilitating access to the relevant channels (i.e. pharmacovigilance websites).