# Effect of Covishield

**Sandip D Pagare[1], Andhale A.K[2], Kamble H.V.[3]**
[1, 2, 3]Loknete Shree Dadapatil Pharate College Of Pharmacy Mandavgaon Pharata

***Abstract***- *Covishield (ChAdOx1-nCOV or AZD1222) is a recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 S glycoprotein vaccine currently being developed by the Serum Institute of India (SII), Pune, based on the AstraZeneca-Oxford model [15, 16]. The AZD1222 COVID-19 vaccine was licensed by the UK on December 30, 2020, and India on January 2, 2021 [11]. This contains nonreplicating SARS-CoV-2 and adenovirus strains (causative of the common cold) that have been genetically engineered and weakened. According to the interim research, AZD1222 is 70.4% effective against COVID-19 prevention with no significant side [09]. A number of 5 × 1010 ChAdOx1-S (recombinant) virus particles are contained in one dose (0.5 ml). This vaccine also comprises the recipients' magnesium chloride hexahydrate, L-histidine, L-histidine hydrochloride monohydrate, disodium edetate dihydrate, sodium chloride, ethanol, sucrose, polysorbate 80, and water for injection, in addition to ChAdOx1-S (recombinant) [13]. Both vaccines are stored and transferred at 2–8 °C [14, 1]. The immunization regimen of Covaxin and Covishield consists of two doses; in the case of Covaxin, 28 days apart; intramuscular injections are advised, and Covishield (0.5 ml in each dose) should be given 4–6 weeks apart [11].*

***Keywords***- Covishield, Vaccine effectiveness, Test-negative design

## I. INTRODUCTION

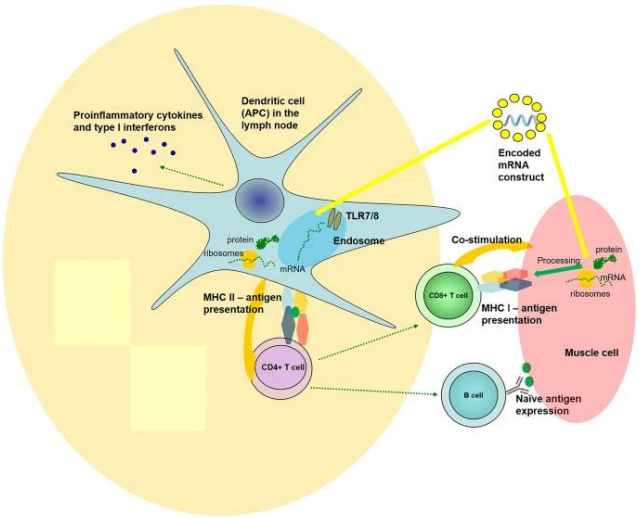
Ever since the Corona Virus Disease (COVID-19) pandemic, India has recorded more than 10.5 million cases and 150000 deaths.1 India began its vaccine roll out against COVID-19 on16 January 2021 to Healthcare Workers (HCWs), almost a year after the index case was detected in the sub-continent. The country has approved two vaccines so far. Covaxin, a whole-Virion Inactivated VeroCell vaccine developed by Bharat Biotech in collaboration with Indian Council of Medical Research (ICMR) andCovishield (ChAdOx1nCoV-19), recombinant vaccine manufactured by SerumInstitute of India in partnership with Oxford-AstraZeneca.2 The Government of India (GOI) has procured 11 and 5.5 million doses of Covisheild and ChAdOx1nCoV-19, respectively for the initial rollout. 3 Though the country has experienced the pandemic's fury, many rumours were associated with the vaccine, even among the Health Care workers (HCWs). Hence vaccine was welcomed with the paradox of urgency and hesitancy. Though vaccine trials and data are available, people, including HCWs, need more real-life data from their contexts to get over the vaccine hesitancy. We aimed to determine the incidence of Adverse Event Following Immunisation (AEFI) among HCWs after their first dose of ChAdOx1nCoV-19 vaccine.

### History of Covishield

AZD1222 by Astra Zeneca and University of oxford On December 30, 2020, UK and on January 2, 2021, India approved AZD1222 COVID-19 vaccine developed by AstraZeneca and the Oxford Vaccine Group at the University of Oxford. It was previously called as ChAdOx1, a chimpanzee adenovirus vaccine. This group has previously developed a MERS vaccine. In India, this vaccine is jointly developed by Serum Institute of India and AstraZeneca and is branded as Covishield. Oxford University and AstraZeneca, a pharmaceutical company both are engage in developing Covishield vaccine. Its Indian partner ―Serum institute‖ Pune, is enduring for production of viral vector vaccine as brand name AZD1222. This contains weakened, genetically modified, nonreplicating strains of SARS-CoV-2 and adenovirus (causative of common cold). From the interim analysis, AZD1222 is found 70.4% efficacious against prevention of COVID-19 with no prominent adverse effects.[2]

### Mechanism of action covishield

Mechanism of action AZD1222 vaccine is a monovalent vaccine composed of a single recombinant, replication deficient chimpanzee adenovirus vector encoding the S glycoprotein of SARS-CoV-2 (ChAdOx1-S (recombinant). The SARS-CoV-2 S immunogen in the vaccine is expressed in the trimeric prefusion conformation. The coding sequence has not been modified, in order to stabilize the expressed S-protein in the prefusion conformation. Adenoviruses are nonencapsulated, icosahedral particles (virions), and contain a single copy of the double-stranded DNA genome. The expression cassette for the SARS-CoV-2 spike protein fused to the tissue plasminogen activator leader sequence uses a modified human cytomegalovirus promoter and a bovine growth hormone polyadenylation sequence.[3]




**Composition of Covishield**

Composition One dose (0.5ml) contains 5 x 1010 ChAdOx1-S (recombinant) viral particles. The vaccine is produced in genetically modified human embryonic kidney (HEK) 293 cells. In addition to ChAdOx1-S (recombinant), this product also contains the excipients L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80, ethanol, sucrose, sodium chloride, disodium edetate dihydrate and water for injection. None of the excipients are of animal or human origin. The excipients are well established for pharmaceutical products.[3]

**Administration**

The vaccination course consists of two doses (each 0.5 ml) and should be administered within 4–6 weeks apart.[2]

**Adverse events for covishield**

Adverse events Very common (≥10% of subjects): headache, nausea, myalgia, arthralgia, injection site tenderness, injection site pain, injection site warmth, injection site pruritus, fatigue, malaise, feverishness, chills. Common (1–10% of subjects): injection site swelling, injection site erythema, fever ≥ 38 °C.[3]

**Storage for covishield**

A shelf-life of 6 months is proposed. Chemical and physical in-use stability from the time of vial opening (first needle puncture) to administration is up to 48 hours in a refrigerator (2–8 ºC). Within this period, the product may be kept and used at temperatures up to 30 ºC for a single period of up to 6 hours, after which it must be discarded. It should not be returned to the refrigerator.[3]

**Immune response of Covishield**

The adenovirus vector ChAdOx1 nCoV-19 adenoviral vector-based vaccine (AZD1222) carries the entire structural surface glycoprotein (S protein) of the SARS-CoV-2. The S protein encoded by ChAdOx1 nCoV-19 has a codon-optimized coding sequence [26]. Human adenovirus, often known as the common cold virus, is the most prevalent nonreplicating viral vector used in the COVID-19 vaccine, i.e., Covishield [24]. ChAdOx1 nCoV-19 generates a widespread and robust T cell response in the host. There was a considerable increase in B cell activation and proliferation, as well as anti-IgA and anti-IgG antibodies, to the SARS-CoV-2 virus after immunization. S proteins were easily recognized in vaccinated people's serum [21]. CD4 + T cells mainly produced Th1 cytokines (IFN-$\gamma$, IL-2, and TNF-$\alpha$/$\beta$) instead of Th2 cytokines (IL-5 and IL-13). Importantly, it is shown, using a number of approaches, that immunization with ChAdOx1 nCoV-19 induces mostly a Th1 response [16]. ChAdOx1 nCoV-19 was found to be safe, tolerable, and immunogenic, with paracetamol being found to reduce reactogenicity andtolerability. A single dose of this vaccine can develop both humoral and cellular responses, and a booster dose generates neutralizing antibody titers [21].

In the vaccine, the adenovirus of chimpanzees is used. Some genes (E1 and E3) of this adenovirus are removed by a biotechnological method that makes adenovirus replication incompetent [24]. The gene of RNA of SARS-CoV-2, which synthesizes S protein through the process of reverse transcription from double-stranded DNA, S protein. Then, the DNA gene is inserted into the adenovirus, and the adenovirus is converted into the vector-based DNA vaccine and, after entering into the cell, activates the immune response. Then, adenovirus enters into the host cell and forms an endocytotic vesicle. Extrachromosomal DNA is converted into SARS CoV's S protein mRNA, and it comes out of the nucleus. Next, the mRNA of S protein is translated by using the cellular translation machinery into the S protein [25]. Then, the S protein is processed, and some fragment of S protein (epitope) is displayed by MHC-I on the surface of this host cell. Next, the cytotoxic T cell (CD8 + lymphocyte) interacts with the MHC-I receptor and becomes active. Some S protein particles are picked up by B lymphocytes. APC engulfs the S protein particle and the viral DNA transcribed and translated by the cell machinery and produces S proteins. Some of these S proteins break into small pieces and are represented by the MHC-II on the surface of this cell to the CD4 + T cell. Through these interactions, some chemokines and interleukins are released and activate the growth and proliferation of CD8+ T cells and B cells. When the cytotoxic T cells become active, some of them destroy the vaccine-

infected host cell by releasing granzyme and perforin, and some convert them to memory T cells. Then, the B cells are converted into plasma cells and memory B cells. The plasma cell produces antibodies against the S protein. This vaccine is based on highly immunogenic technology and stimulates a strong antibody and cell-mediated immune response, which provides long-term protection [27].

## II. CONCLUSION

Covishield vaccine protected significantly against Covid-19, with a higher protection rate against severe forms of disease.

## REFERENCES


[1] https://dmerharyana.org/covaxin-vs-covishield

[2] Cima Hamieh, M. D., M. D. Mahmoud El Hussein, M. D. Yara SkJim Abi aff, M. D. Frem, and M. D. Elie Zaghrini. "COVID-19 Vaccines, What do we know so Far? A Narrative Review.

[3] MISRA, SHASHI KIRAN, KAMLA PATHAK, DEVENDER PATHAK, and RAMAKANT YADAV. "CURRENT UPDATES ON COVID-19 VACCINES." Asian Journal of Pharmaceutical and Clinical Research, 2021; 17-23.

[4] World Health Organization. Background document on the AZD1222 vaccine against COVID-19 developed by Oxford University and AstraZeneca: background document to the WHO Interim recommendations for use of the AZD1222 (ChAdOx1-S [recombinant]) vaccine against COVID19 developed by Oxford University and AstraZeneca, 1 March 2021. No. WHO/2019-nCoV/vaccines/SAGE_recommendation/AZD1222/background/20

[5] Thiagarajan, Kamala. "What do we know about India's Covaxin vaccine?." Bmj, 2021; 373

[6] Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomized, controlled, phase 2/3 trial.Lancet. 2021;396(10267):1979-1993.

[7] Glover RE, Urquhart R, Lukawska J, Blumenthal KG. Vaccinating against covid-19 in people who report allergies. BMJ. 2021 Jan 18;372:n120

[8] 130.Gharate JS, Daitkar SA, Aher KA. Approved COVID 19 vaccines: a review. World J Pharm Res. 2021;10(10):523–42.

[9] Vogel FR. Improving vaccine performance with adjuvants. Clin Infect Dis. 2000; 30(Supplement_3):S266–70.

[10] Liang Z, Zhu H, Wang X, Jing B, Li Z, Xia X, Sun H, Yang Y, Zhang W, Shi L, Zeng H. Adjuvants for coronavirus vaccines Front Immunol. 2020;11:

[11] Singh AK, Phatak SR, Singh R, Bhattacharjee K, Singh NK, Gupta A, Sharma A. Antibody response after first and second-dose of ChAdOx1-nCOV (CovishieldTM®) and BBV-152 (CovaxinTM®) among health care workers in India: the final results of cross-sectional coronavirus vaccine-induced antibody titre (COVAT) study. Vaccine. 2021;39(44)

[12] Malabadi RB, Meti NT, Chalannavar RK. Applications of nanotechnology in vaccine development for coronavirus (SARS-CoV-2) disease (Covid-19). Int J Res Sci Inno. 2021;8(2):191–8.

[13] Voysey M, Clemens SA, Madhi SA, Weckx LY, Folegatti PM, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. Lancet. 2021;397(10277):881–91.

[14] Thiagarajan K. What do we know about India's Covaxin vaccine. bmj. 2021;373:n997.

[15] Misra SK, Pathak K, Pathak D, Yadav R. Current updates on COVID-19 vaccines. Asian J Pharm Clin Res. 2021;7:17–2

[16] World Health Organization. Interim recommendations for use of the Bharat Biotech BBV152 COVAXIN® vaccine against COVID-19: interim guidance, 3 November 2021.

[17] Ella R, Reddy S, Jogdand H, Sarangi V, Ganneru B, Prasad S, Das D, Raju D, Praturi U, Sapkal G, Yadav P, Reddy P, Verma S, Singh C, Redkar SV, Gillurkar CS, Kushwaha JS, Mohapatra S, Bhate A, Rai S, Panda S, Abraham P, Gupta N, Ella K, Bhargava B, Vadrevu KM. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: interim results from a double-blind, randomised, multicentre, phase 2 trial, and 3-month follow-up of a double-blind, randomised phase 1 trial. Lancet Infect Dis. 2021;21(7):950–61.

[18] Ella R, Vadrevu KM, Jogdand H, Prasad S, Reddy S, Sarangi V, Ganneru B, Sapkal G, Yadav P, Abraham P, Panda S, Gupta N, Reddy P, Verma S, Kumar Rai S, Singh C, Redkar SV, Gillurkar CS, Kushwaha JS, Mohapatra S, Rao V, Guleria R, Ella K, Bhargava B. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a doubleblind, randomised, phase 1 trial. Lancet Infect Dis. 2021;21(5):637–46.

[19] Ganneru B, Jogdand H, Daram VK, Das D, Molugu NR, Prasad SD, Kannappa SV, Ella KM, Ravikrishnan R, Awasthi A, Jose J. Th1 skewed immune response of whole virion inactivated SARS CoV 2 vaccine and its safety evaluation. Iscience. 2021;24(4):102298.

[20] García LF. Immune response, inflammation, and the clinical spectrum of COVID-19. Front Immunol. 2020;11:1441.
[21] Steinman RM, Hawiger D, Nussenzweig MC. Tolerogenic dendritic cells. Annu rev immunol.
[22] Kaiko GE, Horvat JC, Beagley KW, Hansbro PM. Immunological decision-making: how does the immune system decide to mount a helper T-cell response? Immunology. 2008;123(3):326–38
[23] Abbas AK, Burstein HJ, Bogen SA. Determinants of helper T cell-dependent antibody production. Semin Immunol. 1993;5
[24] Pennock ND, White JT, Cross EW, Cheney EE, Tamburini BA, Kedl RM. T cell responses: naive to memory and everything in between. Adv Physiol Educ. 2013;37(4):273–83. .
[25] Dörner T, Radbruch A. Antibodies and B cell memory in viral immunity. Immunity. 2007;21 27(3):3849
[26] Folegatti PM, Ewer KJ, Aley PK, Angus B, Becker S, Belij-Rammerstorfer S, Bellamy D, Bibi S, Bittaye M, Clutterbuck EA, Dold C. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet. 2020;396:467–78.
[27] Flanagan KL, Best E, Crawford NW, Giles M, Koirala A, Macartney K, Russell F, Teh BW, Wen SC. Progress and pitfalls in the quest for effective SARS-CoV-2 (COVID-19) vaccines. Front Immunol. 2020;11:2410.
[28] Goyal K, Goel H, Baranwal P, Tewary A, Dixit A, Pandey AK, Benjamin M, Tanwar P, Dey A, Khan F, Pandey P. Immunological mechanisms of vaccine-induced protection against SARS-CoV-2 in humans.
[29] Kovesdi I, Hedley SJ. Adenoviral producer cells. Vaccine. 2010;2:1681–703.
[30] Doerfler W. Adenoviral vector DNA-and SARS-CoV-2 mRNA-based COVID-19 vaccines: possible integration into the human genome-are adenoviral genes expressed in vector-based vaccines? Virus Res. 2021;302:198466.
[31] Dong Y, Dai T, Wei Y, Zhang L, Zheng M, Zhou F. A systematic review of SARS-CoV-2 vaccine candidates. Signal Transduct Target Ther. 2020;5(1)
[32] hateeb J, Li Y, Zhang H. Emerging SARS-CoV-2 variants of concern and potential intervention approaches. Crit Care. 2021;25(1):1–8.
[33] Garcia-Beltran WF, Lam EC, Denis KS, Nitido AD, Garcia ZH, Hauser BM, Feldman J, Pavlovic MN, Gregory DJ, Poznansky MC, Sigal A. Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity. Cell. 2021;184(9):2372–83.
[34] Cherian S, Potdar V, Jadhav S, Yadav P, Gupta N, Das M, Rakshit P, Singh S, Abraham P, Panda S, Team NI. SARS-CoV-2 spike mutations, L452R, T478K, E484Q and P681R, in the second wave of COVID-19 in Maharashtra, India. Microorganisms. 2021;9(7):1542.