# SUMMARY OF PRODUCT CHARACTERISTICS

▼ This vaccine is subject to additional monitoring. This triangle will enable the rapid identification of a new safety information. Health professionals are expected to report suspected adverse reactions to the TÜFAM. See Section 4.8 Reporting of suspected adverse reactions?

## 1. NAME OF THE MEDICINAL PRODUCT

TURKOVAC 3 mcg/ 0,5 mL suspension for IM injection
Inactive SARS-CoV-2 virus (hCoV-19/Turkey/ERAGEM 001/2020 strain) antigen
Sterile

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Active substance:**
One dose of vaccine (0.5 mL):
contains 3 mcg/0.5 mL of antigen from the SARS-CoV-2 virus[1] (inactive).
It is produced in [1](VERO CCL-81) cell culture.

**Excipients:**
In one dose of vaccine (0.5 mL):

| | |
|---|---|
| Sodium chloride: …… | 8.77 g/L |
| Potassium chloride: …… | 0.2 g/L |
| Potassium dihydrogen phosphate: ……..... | 0.24 g/L |
| Disodium hydrogen phosphate heptahydrate: …… | 2.73 g/L |

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Suspension for IM injection
Opalescent suspension, layer sediments can be removed by shaking, there should be no sediment or aggregation after shaking.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

TURKOVAC is indicated for active immunization against the SARS-CoV-2 virus and booster dose for the prevention of diseases caused by the SARS-CoV-2 virus (see section 4.2).
TURKOVAC can be administered from people over 18 years of age (see section 5.1).
TURKOVAC must be administered according to official recommendations.

### 4.2. Posology and method of administration

**Posology/ Administration frequency and duration:**

Persons over 18 years of age
TURKOVAC is administered to people over 18 years of age as a total of two doses, one dose four weeks apart in primary immunization.
In any case, if the second dose of TURKOVAC is administered earlier than four weeks, the early administered dose should not be evaluated as the current dose and a repeat dose four weeks after the early dose is recommended.
The rappel dose is administered as a single dose.

18 years and younger

There are no efficacy and safety data on the use of TURKOVAC in people aged 18 and under.
With the help of the available information, TURKOVAC is not recommended for active COVID-19 patients, people who have had COVID-19 disease within 180 days (confirmed by PCR test) and who have been in contact with a confirmed case of COVID-19 within 10 days before the vaccine is administered.

**Route of administration:**

The vaccine should be injected intramuscularly (IM). The preferred injection site is the deltoid region. The vaccine should be administered while the person is sitting.

**It is not injected intravenously.**

The vaccine should not be administered subcutaneously (SC) or intradermally (ID).
See sections 4.4 and 6.6 for precautions to be taken before the use or administration of the medicinal product and instructions for the preparation of the medicinal product before its administration.

**Additional information on special populations:**

**Renal/ Hepatic impairment:**

TURKOVAC does not have a study on patients with renal/hepatic impairment. It does not require dose adjustment.

**Pediatric population:**

The safety and efficacy of TURKOVAC in people aged 18 years and under have not been determined.

**Geriatric population:**

The safety and efficacy of TURKOVAC in people aged 65 years and older have not been determined.

**4.3. Contraindications**

The second dose is not administered in the presence of a history of life-threatening allergy/anaphylaxis to any substance contained in the vaccine and in the presence of a history of anaphylaxis after the first dose of the vaccine.
It is not preferable to administer the vaccine in acute periods of fever, acute illness and chronic diseases.
Situations in which vaccination should be postponed (temporary contraindication):

- People with a fever of 38ºC and above,
- Acute diseases for which a definitive diagnosis has not yet been made,
- During acute attacks of chronic diseases should be postponed.

**4.4. Special warnings and precautions for use**

As a psychogenic response to injection with a needle, syncope (fainting) can be observed after vaccination or even before vaccination. This may be accompanied by many neurological symptoms such as temporary visual impairment, paresthesia and tonic-clonic movements during

recovery. It is important that the necessary procedures are ready to prevent injuries that may occur due to fainting.
As with all injectable vaccines, appropriate medical treatment should always be available in case of rare anaphylactic reactions after the vaccine has been administered.
People with a history of allergies may be potentially at higher risk for anaphylaxis or anaphylactoid reactions. After vaccination, close monitoring is recommended for early signs of such reactions.
In the presence of a history of acute allergic reactions to any substance contained in the vaccine or non-anaphylaxis following the first dose of the vaccine; an allergist/immunologist should be consulted before administering the next dose of the vaccine.
After the vaccine administration, the person should be informed about possible allergic reactions and the person should not leave the health facility for 15 minutes. People with a history of allergies should not leave the health facility for 30 minutes. In the later period, it should be said to apply to the nearest health institution in case of any side effects.
It should be administered carefully to people with thrombocytopenia or bleeding disorders as bleeding may occur after intramuscular administration.
Those with uncontrolled epilepsy and neurological diseases such as Guillain-Barre Syndrome, transverse myelitis that can be exacerbated by infection and vaccination are decided to be vaccinated depending on the evaluation to be made by the following clinician.
Vaccination decision is made based on the evaluation to be made by the clinician following the patients with a diagnosis of primary immunodeficiency.

Others
People with immunosuppression should be vaccinated based on the evaluation of the attending clinician to determine the time frame in which the vaccine response may be best. It should be administered as a total of two doses, one dose four weeks apart. If necessary, an additional dose may be administered by the decision of the clinician.
As with other vaccines, not all people vaccinated with TURKOVAC will receive full protection.
To interact with laboratory tests: See section 4.5.
In order to better track biotechnological medicinal products, the brand name and batch number of the administered product should be clearly recorded (or indicated) in the patient file.
TURKOVAC contains less than 1 mmol (23 mg) sodium in a 0.5 mL single dose; that is, the sodium content is negligible.
TURKOVAC contains less than 1 mmol (39 mg) potassium in a 0.5 mL single dose; that is, the potassium content is negligible.

**4.5. Interaction with other medicinal products and other forms of interaction**
**Use with immunosuppressive therapy**
Immune inhibitor monoclonal antibodies, chemotherapy drugs, corticosteroids, etc. may affect the body's immune response to this vaccine.

**Use with immunoglobulin therapy**
Although TURKOVAC is an inactivated vaccine, simultaneous administration of immunoglobulin (IG) is not preferred. If necessary, the vaccine response is not expected to be affected if it is given simultaneously.

**Use with other vaccines**
There are insufficient clinical trial data on the concomitant (before, after, or concurrent) administration of other vaccines.
However, experience with these vaccines can be taken into account, as it has been shown to have a similar safety and immunogenicity profile as the formulation of other inactivated SARS-CoV-2 vaccines. According to this;

- TURKOVAC and inactivated seasonal influenza vaccines can be administered simultaneously. If these vaccines are to be administered at the same visit, they must be administered from different extremities.
- TURKOVAC and pneumococcal, meningococcal and other inactivated routine vaccines can be administered simultaneously. If these vaccines are to be administered at the same visit, they must be administered from different extremities.
- Live vaccines can be administered simultaneously with TURKOVAC. There is no need to leave time between (before and after) vaccinations. However, if possible, it is preferable to leave it for four weeks.
- It can be administered without leaving a time interval with vaccines that must be administered after exposure, such as rabies and tetanus vaccines. If these vaccines are to be administered at the same visit, they must be administered from different extremities.

Compatibility of primary batch with other COVID-19 vaccines
There is no data on the completion of the primary batch by administering TURKOVAC with other COVID-19 vaccines in COVID-19 vaccination.

Interaction of TURKOVAC with laboratory tests is not expected.

**Additional information on special populations:**
**Pediatric population:**
There are no pediatric population studies.

**4.6. Pregnancy and lactation**
**General advice**
Pregnancy category: C

**Women of childbearing potential / contraception**
No data is available.

**Pregnancy**
There are no data on the administration of TURKOVAC in clinical studies, as pregnant women were excluded from the study.
There are insufficient data on the administration of TURKOVAC during pregnancy. It is recommended by the World Health Organization that pandemic SARS-CoV-2 vaccines can be administered to pregnant women who are at high risk of severe transmission of COVID-19 disease, at their own request.

**Lactation**
There are no data on the administration of TURKOVAC in clinical studies, as breastfeeding women were excluded from the study.

There are insufficient data on the administration of TURKOVAC during the lactation period. It is recommended by the World Health Organization that pandemic SARS-CoV-2 vaccines can be administered to pregnant women who are at high risk of severe transmission of COVID-19 disease, if they wish.

**Reproductive ability / Fertility**
There is no fertility data for TURKOVAC.

**4.7. Effects on ability to drive and use machines**
No studies have been conducted on the effects of TURKOVAC on the ability to drive and use machines. TURKOVAC is expected to have no or negligible effect on the ability to drive and use machines.

**4.8. Undesirable effects**
Safety Profile Summary

**A Randomized, Observer-Blinded Phase III Clinical Trial Evaluating Efficacy, Immunogenicity, and Safety of Two-Dose CoronaVac (Sinovac) Vaccine Against Two Doses of Inactive COVID-19 Vaccine (TURKOVAC) in Healthy Volunteers**

1290 volunteers were included in the study and 2508 doses of vaccine were administered.
No severe allergic reaction was observed in the first 24 hours in the volunteers who received the study vaccines.
Safety analyzes of vaccines include data from 1290 volunteers. According to these data, a total of 2399 adverse events were observed in 710 volunteers. The most common and reported systemic adverse effects after the first dose were fatigue (168 events) and headache (163 events). After the second dose, the most common and reported systemic adverse effects were headache (130 events), sore throat (107 events). The most common and reported systemic adverse effects in the CoronaVac arm were headache (151 events) and fatigue (133 events). The most common and reported systemic adverse effects in the TURKOVAC arm were headache (142 events) and fatigue (140 events).
All of the adverse effects observed were Stage 1 (Mild) (89.49%), Stage 2 (Moderate) (10.47%) and Stage 3 (Severe) (0.04%). The frequency of the most common and reported systemic adverse effects were headache 12.2%, fatigue 11.4%, and sore throat 8.1%, respectively.
683 of the reported systemic adverse events (28.5%) were “not vaccine-related” (no relationship), 249 (10.4%) were “not likely vaccine-related” (unlikely), and 900 (37.5%) were “vaccine-related” (probable, possible, definite). The most common and reported systemic adverse events were headache 7.3%, fatigue 7.3%, sore throat 3.2%, respectively.

**Two-Arm, Open-Label, Multicenter, Phase IIb Clinical Trial to Determine the Effectiveness, Safety and Immunogenicity of Booster Vaccination (TURKOVAC) to SARS-CoV-2**

In this study, undesirable effects after TURKOVAC vaccine administered to volunteers who had at least 90 days and maximum 240 days after the 2nd dose of Comirnaty (Code name: BNT162b2) vaccine were evaluated. The analyses were based on data from 19 August 2022, by which time 65 volunteers had been included in the study.
In volunteers who received the study vaccine, no severe allergic reaction was observed within the first 24 hours.

A total of 36 adverse events were observed in 17 volunteers.
It was observed that the most common and reported local adverse effect after the study vaccine was given was pain in the vaccine arm (3 events) and the most common and reported systemic adverse effect was sore throat (5 events) and headache (4 events).

**Open-Label, Multicenter, Phase III Clinical Trial to Determine the Effectiveness, Safety and Immunogenicity of Booster Vaccination Against SARS-CoV-2**

Below is presented information on adverse effects after booster doses of inactivated COVID-19 vaccines given to those who have passed at least 90 days and up to 270 days after the 2nd dose of the CoronaVac vaccine in the Phase III vaccine study. The analyses were made according to the data dated August 22, 2022 A total of 4.340 volunteers were included in the Inactivated Booster Phase III study, including 488 with the vaccine arm CoronaVac and 3.852 with TURKOVAC.
The safety analyses of the administered vaccine included 4.340 volunteers who were included in the study. A total of 4.035 adverse events were observed in 1.689 volunteers.
After CoronaVac vaccination, the most common and reported local adverse effect was pain at the vaccination site (47 cases, 46 volunteers, 9.4%), and the most common and reported systemic adverse effect was headache (47 cases, 39 volunteers, 8.0%) and fatigue (41 cases, 30 volunteers, 6.1%).
After TURKOVAC vaccination, the most common and reported local adverse effect was pain at the vaccination site (846 cases, 827 volunteers, 21.5%), and the most common and reported systemic adverse effect was headache (326 cases, 292 volunteers, 7.6%) and fatigue (320 cases, 270 volunteers, 7.0%).

Adverse reactions are listed according to the MedDRA System Organ Class. Within each frequency grouping, adverse events are graded according to their decreasing severity. The frequency is defined as follows:
Very common (≥ 1/ 10), Common (≥ 1/ 100 to < 1/ 10), Uncommon (≥ 1/1000 to < 1/ 100), Rare (≥ 1/ 10,000 to < 1/ 1000) Very rare (< 1/10,00), Unknown (cannot be estimated from the available data.

**Nervous system diseases**
Common: Headache
Uncommon: Dizziness, loss of odor

**Eye diseases**
Uncommon: Eye pain, blurred vision

**Respiratory, chest disorders and mediastinal diseases**
Common: Sore throat, runny nose, cough, nasal congestion
Uncommon: Chest pain, sneezing, itching in the throat

**Cardiovascular diseases**
Uncommon: Hypotension, tachycardia

**Gastrointestinal diseases**
Common: Diarrhea
Uncommon: Vomiting, nausea, constipation, abdominal pain, difficulty swallowing

**Skin and subcutaneous tissue diseases**
Uncommon: Itching on the body

**Musculoskeletal, connective tissue and bone disorders**
Common: Muscle pain
Uncommon: Low back pain, joint pain

**General disorders and administration site conditions**
Very Common: Pain at the injection site
Common: Hardening or swelling at the injection site, fatigue
Uncommon: Arm pain at the injection site, redness at the injection site, sensitivity at the injection site, fever, chills, sweating

Reporting of suspected adverse reactions

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

**4.9. Overdose and treatment**

In studies performed on experimental animals, no histopathological findings were detected in applications up to 50 times the normal dose. Studies are still continuing. It will be updated as data becomes available.

## 5. PHARMACOLOGICAL PROPERTIES

**5.1. Pharmacodynamic properties**

Pharmacotherapeutic Group: Viral vaccines, Covid-19 vaccines
ATC Code: J07BN03

Clinical Efficacy Assessments with Phase I and Phase II study data, titled "Randomized, Observer-Blind Phase III Clinical Study Evaluating Efficacy, Immunogenicity, and Safety of Two-Dose CoronaVac (Sinovac) Vaccine Against Two-Dose Inactive COVID-19 Vaccine (TURKOVAC) in Healthy Volunteers" Within the scope of the study, it was obtained after administering at least 1 dose to a total of **1.251*** people and 2 doses to **1.041** people. A total of **2.292** doses were administered. 2 doses were administered on the 0th day and 28th day.
In addition, a total of 2875 volunteers were evaluated in the Inactivated Booster Phase III study, including 258 with CoronaVac and 2617 with TURKOVAC.

Immunogenicity and Clinical Efficacy Assessment

Phase I: A total of 44 volunteers were enrolled in the in phase 1 study and in final analysis; 31 volunteer results were evaluated in order to investigate the safety of TURKOVAC vaccine by side effect monitoring. 13 volunteers drop out from final analysis for various reasons (independent of the study product). A total of 25 side effects event were observed in the first 43 days of the study. 6 of them were headaches, 10 of them were pain and sensitivity at the vaccination site. While the other observed side effects were observed in the vaccine groups one for each, no side effects were

observed in any volunteers who received a placebo. No differences were identified between the vital signs (pulse, blood pressure and fever) and laboratory blood results checked throughout the study, as well as the EKGs taken at the beginning and end of the study. In general, there was no difference in safety between doses of vaccine. IgG antibody formation was observed in all volunteers (100%) who received both doses of ERUCOV-VAC vaccine on 43rd day of the study. Quantitatively , there was no significant difference between IgG rates between both vaccines. IgG antibody formation was not observed in volunteers receiving placebo. There were neutralizing antibody in any of the placebo group. Neutralizing antibodies could not be measured in only 5 of the volunteers who received the vaccine. A titre higher than 2 was measured 35 days after the 1st dose in 27 out of a total of 32 volunteers who received the vaccine. These results showed that there was no statistically significant difference between doses of vaccine. Safety, which is the main purpose of the study, has been shown by this study.

Phase II: To demonstrate the effectiveness and immunogenicity of the newly developed inactive COVID-19 vaccine, 250 volunteers were included in the study, a low-dose vaccine was administered to 100 of them, a high-dose vaccine to 100 of them and a placebo of 2 doses to 50 of them for comparison purposes. Volunteers were called to the center at certain time intervals and were observed for a total of 12 months.

With a subsequent addition to the study, from volunteers who received a low dose of vaccine, the accepting volunteers were given the 3rd vaccine at the 4th month of the study with the same dose. IgG antibody formation was observed in all volunteers (100%) who received both doses of ERUCOV-VAC vaccine on the 43rd day of study. Quantitively, there was no significant difference between IgG rates between both vaccines. IgG antibody formation was not observed in volunteers receiving placebo.

Neutralizing antibodies could not be measured in only 6 of the volunteers who received the vaccine and none of the volunteers who received a placebo. A titre higher than 8 was measured 43rd day after the dose in 182 of a total of 188 volunteers who received 2 vaccines. These results showed that there was no statistically significant difference between the vaccine doses, but it significantly caused the production of antibodies compared to placebo.

Applied to volunteers who accept 3. after 3µg/0.5 mL vaccine, statistically significant increases in both IgG and neutralizing antibody were observed in the vaccinated group compared to the control group on 4th month. In the later stages of the study, especially in volunteers who received only 2 doses, the antibody rates showed a rapid decrease for both IgG and neutralizing antibodies. 244 side effects have been observed until 14th days after 1st and 2nd vaccination. Of these side effects, 84 of them were evaluated as mild (stage 1), 159 of them were evaluated as moderate (stage 2) and 1 of them was evaluated as severe (stage 3). In addition, 32 more side effects were observed till 43rd day. 9 of them were evaluated as mild severe and 23 of them were evaluated as moderate severe.

3 serious side effects were observed till 43rd day of the study. These have been falls while skiing, death as a result of a heart attack 20 days after the first investigational vaccine was administered, and hospitalization due to COVID-19 disease. After the 43rd day of the study, 2 more serious adverse events (kidney stones and ankle fracture due to falling from a height) were observed. Vaccines have not been suspected as the primary cause in these side effects.

The most important side effect seen was pain in the vaccination side after the 1st and 2nd vaccination. No problems were observed in the vital signs (pulse, blood pressure and fever) and laboratory blood results checked throughout the study. In general, there was no difference in safety between doses of vaccines.

A total of 16 side effects were observed in volunteers receiving the booster vaccine until 2 months after the 3rd dose of the vaccine.

Till the end of the study, 425 adverse events had been recorded in 149 out of a total of 250 volunteers.

All the advers event spontenously resolved except two (bone fracture due to fall during ski and the other was MI which is stated as unrelated) In addition, 2 volunteers did not return to the clinic for repeat PCR tests after COVID-19 infection. Therefore, it is not known whether the PCR tests returned negative.
Both doses of the TURKOVAC vaccine were well tolerated in healthy volunteers and it was observed that it generated sufficient immunogenicity in the 18 – 62 age range. The rate of adverse events observed with both doses was found to be similar. There was no statistically significant difference between the humoral immune responses that occurred after both doses of the vaccine.

Phase III: According to the first interim results obtained on the efficacy, immunogenicity and safety of two doses of TURKOVAC and CoronaVac vaccines, in a randomized, observer-blind, non-inferiority study; volunteers were randomized between the ages of 18-55 and in a ratio of 1:1. either TURKOVAC or CoronaVac were both administered 3 g/0.5 mL aluminum adsorbed inactive vaccine on the 0th day and on the 28th day. The primary efficacy result was the prevention of cases with polymerase chain reaction (PCR) positivity. Confirmed symptomatic cases of coronavirus disease 2019 (COVID-19) at least 14 days after the second dose were evaluated in both vaccine groups per protocol (mPP). 1290 participants were randomized to the study between the 22 June 2021 to 7 January 2022. During an average follow-up period of 90 days (IQR 86–90), the relative risk reduction with TURKOVAC compared to CoronaVac in preventing PCR-confirmed symptomatic cases was 41.03% (95% CI 12.95–60.06). Generally, the incidence of adverse events (AE) was 58.8% in TURKOVAC and 49.7% in CoronaVac. No deaths or serious fourth-degree adverse events were detected in the study. In terms of effectiveness, TURKOVAC was not inferior to CoronaVac and showed a good safety and tolerability profile.

Clinical Studies of the SARS-CoV-2 Vaccine in Healthy Adults:

**Table 1: Phase I Results**

| Phase | Different Antibody Responses | Time | Group 3 mcg | Group 6 mcg | Placebo | P1 value | P2 value |
|---|---|---|---|---|---|---|---|
| Phase I | 0.day (Reference). The 14th and 28th day after vaccination. | | | | | | |
| | Neutralizing antibody (MN) | Reference GM (95% CI) | 2.0 (2.4-1.5) | 1.8 (2.0-1.6) | 1.6 (2.0-1.3) | 0.4410 | 0.3988 |
| | | $14^{th}$ day GM (95% CI) | 9.3 (11.2-7.5) | 9.1 (11.0-7.9) | 1.8 (2.0-1.5) | 0.9999 | 0.0001 |
| | | $28^{th}$ day GM (95% CI) | 10.4 (14.2-6.6) | 10.8 (13.5-9.5) | 1.8 (2.0-1.6) | 0.7021 | 0.0001 |
| | Neutralizing antibody (FRNT) | Reference GM (95% CI) | 1.8 (1.8-1.6) | 1.7 (1.7-1.4) | 1.4 (1.4-1.1) | 0.5560 | 0.1688 |
| | | $14^{th}$ day GM (95% CI) | 9.3 (11.-7.4) | 9.2 (11.0-7.5) | 1.8 (2.0-1.5) | 0.7322 | 0.0001 |
| | | $28^{th}$ day GM (95% CI) | 11.6 (15.4-7.8) | 11.8 (13.8-9.9) | 2.0 (2.4-1.5) | 0.3986 | 0.0001 |
| | | Reference | 47.2 (49.8-43.6) | 46.4 | 45.4 | 0.6701 | 0.4533 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | GM (95% CI) | | (49.2-43.6) | (48.4-42.6) | | |
| | Antibody response to S1-RBD | 14th day GM (95% CI) | 437.2 (568.9-305.4) | 461.5 (501.8-421.1) | 48.0 (50.4-45.6) | 0.5840 | 0.0001 |
| | | 28th day GM (95% CI) | 488.8 (630.2-347.3) | 504.2 (539.7-468.6) | 47.0 (49.8-44.2) | 0.5404 | 0.0001 |
| | Antibody response to complete antigen | Reference GM (95% CI) | 47.2 (49.8-44.7) | 46.4 (49.2-43.6) | 44.7 (47.6-41.7) | 0.6254 | 0.7065 |
| | | 14th day GM (95% CI) | 375.9 (428.8-208.4) | 395.6 (471.7-319.4) | 48.9 (50.7-47.2) | 0.5206 | 0.0001 |
| | | 28th day GM (95% CI) | 414.5 (525.3-303.2) | 442.0 (522.1-361.8) | 47.0 (49.8-44.2) | 0.6860 | 0.0001 |

**Table 2: Antibody responses on day 14th day 28th day and 3rd month; after the second vaccination**

| | Phase II Clinical trial | | | | Phase II Clinical trial | | | |
|---|---|---|---|---|---|---|---|---|
| | Group 3 mcg | Group 6 mcg | Placebo | P value* | Group 3 mcg | Group 6 mcg | Placebo | P value* |
| Neutralizing antibodies against live SARS-CoV-2 virus (MN assay) | | | | | Neutralizing antibodies against live SARS-CoV-2 virus (FRNT assay) | | | |
| 14th day Geometric average titer, 95% CI | 30.0 (37.9-22.0) | 34.9 (47.6-22.1) | 1.96 (2.11-1.88) | 0.0666 | 28.9 (37.7-20.0) | 30.1 (41.6-18.5) | 2 (2.19-2.1.90) | 0.3366 |
| 28th day Geometric average titer, 95% CI | 36.5 (49.9-23.0) | 43.5 (60.3-26.6) | 2 (2.12-1.92) | 0.2149 | 34.2 (44.5-23.8) | 40.4 (58.0-20.7) | 1.96 (2.23-1.86) | 0.0854 |
| 3rd month Geometric average titer, 95% CI | 14.7 (18.5-10.88) | 14.8 (17.3-12.2) | 1.93 (2.09-1.85) | 0.8303 | 11.8 (14.4-9.1) | 11.4 (12.9-9.8) | 1.90 (2.19-1.80) | 0.8853 |
| IgG response endpoint to SI-RBD | | | | | IgG response endpoint to complete SARS-CoV-2 antigen | | | |
| 14th day Geometric average titer, 95% CI | 2561.5 (2969.8-2153.1) | 2549.6 (3349.4-1749.7) | 49.2 (50.07-48.53) | 0.2301 | 1586.3 (1773.73) | 1964.2 (2139.6-1788.7) | 48.4 (49.6-47.5) | 0.0226 |
| 28th day Geometric average | 2710.7 (3143.5-2277.8) | 2688.0 (3531.4-1844.5) | 49.4 (50.17-48.89) | 0.3181 | 1738.7 (1954.3-1538.6) | 2056.5 (2264.1-1848.8) | 48.2 (49.4-47.2) | 0.0233 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| titer, 95% CI | | | | | | | | |
| 3rd month Geometric average titer, 95% CI | 865.0 (1065.5-664.4) | 770 (897.3-642.6) | 49.7 (50.22-49.31) | 0.1154 | 493.8 (604.5-383.0) | 565.4 (627.8-502.9) | 48.8 (50.3-47.7) | 0.1319 |

Abbreviations CI- Confidence Interval, MN- Microneutralization, FRNT- Focus Reduction Neutralization Titer, S1-RBD- Spike S1 Receptor Binding Domain. All participants in Phase II were randomly selected for vaccination and samples were collected for antibody responses. The geometric average titer of antibody responses was calculated at 14, 28, and 3 months after the 2nd vaccination. Unpaired t-test is used to compare between groups. *p value shows comparison between 3 μg and 6 μg groups. The geometric average titer is shown with the upper and lower limits of the 95% confidence interval.

**Table 3: Seroconversion rates at day 14th day 28th day and 3th month after second vaccination (%)**

| | Phase II Clinical trial | | | Phase II Clinical trial | | |
|---|---|---|---|---|---|---|
| | Group 3 mcg | Group 6 mcg | Placebo | Group 3 mcg | Group 6 mcg | Placebo |
| Neutralizing antibodies against live SARS-CoV-2 virus (MN assay) | | | | Neutralizing antibodies against live SARS-CoV-2 virus (FRNT assay) | | |
| 14th day Seroconversion rate % | 95.6% (88 out of 92 people) | 98.9% (95 out of 96 people) | 0.0% | 95.6% (88 out of 92 people) | 98.9% (95 out of 96 people) | 0.0% |
| p value (Fisher's exact test) | 0.000965 | 0.000338 | | 0.002994 | 0.001649 | |
| 28th day, Seroconversion rate % | %96.6 (85 out of 88 people) | 98.9% (89 out of 90 people) | 0.0% | %96.6 (85 out of 88 people) | 98.9% (89 out of 90 people) | 0.0% |
| p value (Fisher's exact test) | 0.000316 | 0.000204 | | 0.002238 | 0.000759 | |
| 3rd month, seroconversion rate % | 79.6% (70 out of 88 people) | 81.1% (73 out of 90 people) | 0.0% | 79.6% (70 out of 88 people) | 84.4% (76 out of 90 people) | 0.0% |
| p value (Fisher's exact test) | 0.003757 | 0.009739 | | 0.042399 | 0.007436 | |
| IgG response endpoint to SI-RBD | | | | IgG response endpoint to complete SARS-CoV-2 antigen | | |
| 14th day Seroconversion rate % | 100% (92 out of 92 people) | 100% (96 out of 96 people) | 0.0% | 100% (92 out of 92 people) | 100% (96 out of 96 people) | 0.0% |
| p value (Fisher's exact test) | 0.000217 | 0.007179 | | 0.001036 | 0.001188 | |
| 28th day, Seroconversion rate % | 100% (88 out of 88 people) | 100% (90 out of 90 people) | 0.0% | 100% (88 out of 88 people) | 100% (90 out of 90 people) | 0.0% |

| | | | | | | |
|---|---|---|---|---|---|---|
| p value (Fisher's exact test) | 0.000211 | 0.006991 | | 0.001118 | 0.001252 | |
| 3rd month, seroconversion rate % | 100% (88 out of 88 people) | 100% (90 out of 90 people) | 0.0% | 96,5% (85 out of 88 people) | 100% (90 out of 90 people) | 0.0% |
| p value (Fisher's exact test) | 0.000927 | 0.049847 | | 0.012157 | 0.006082 | |

The seroconversion rate (%) is determined by a four-fold increase in the neutralizing antibody or ELISA titer from the baseline value for each subject. In this case, the percentage of seroconversion is calculated. Parenthesis '()' indicates the number of seroconversions from the total number of subjects in each group. Fisher's exact test p-value shows significant differences between seroconverted and non-seroconverted volunteers.

## A Randomized, Observer-Blinded Phase III Clinical Trial Evaluating Efficacy, Immunogenicity, and Safety of Two-Dose CoronaVac (Sinovac) Vaccine Against Two Doses of Inactive COVID-19 Vaccine (TURKOVAC) in Healthy Volunteers

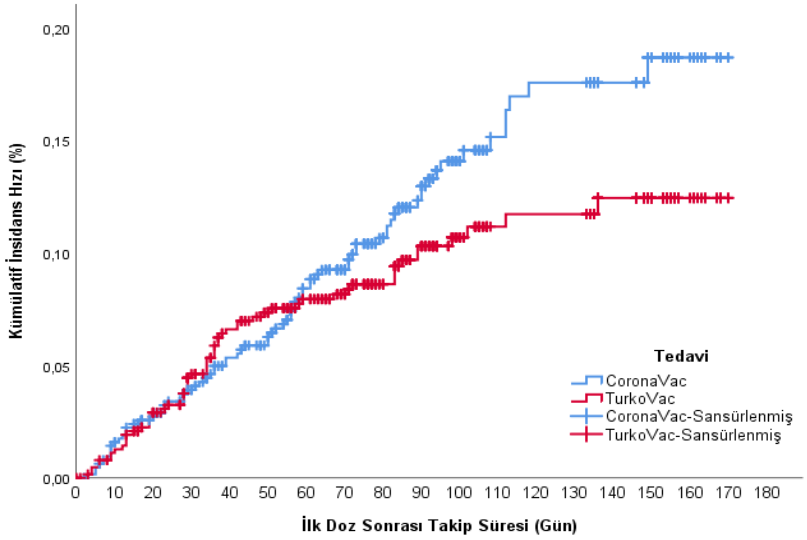
**Table 4: Preventing Symptomatic Disease**

| **Treatment Arm** | **Number of Covid-19 Cases*** | **Total Number of Volunteers**** | **%** | **Person-Day Exposure***** | **Incidence Rate (/1000 person-years)** | **Incidence Rate (/100 person-days)** |
|---|---|---|---|---|---|---|
| CoronaVac | 40 | 519 | 7.71 | 30.030 | 486.51 | 0.133 |
| TURKOVAC | 20 | 527 | 3.80 | 30.993 | 235.70 | 0.065 |
| Total | 60 | 1046 | | | | |

* Based on symptomatic and PCR positive COVID-19 cases 14 days after 2nd dose
** Number of volunteers 14 days after 2nd dose and beyond
***As per 09.12.2021

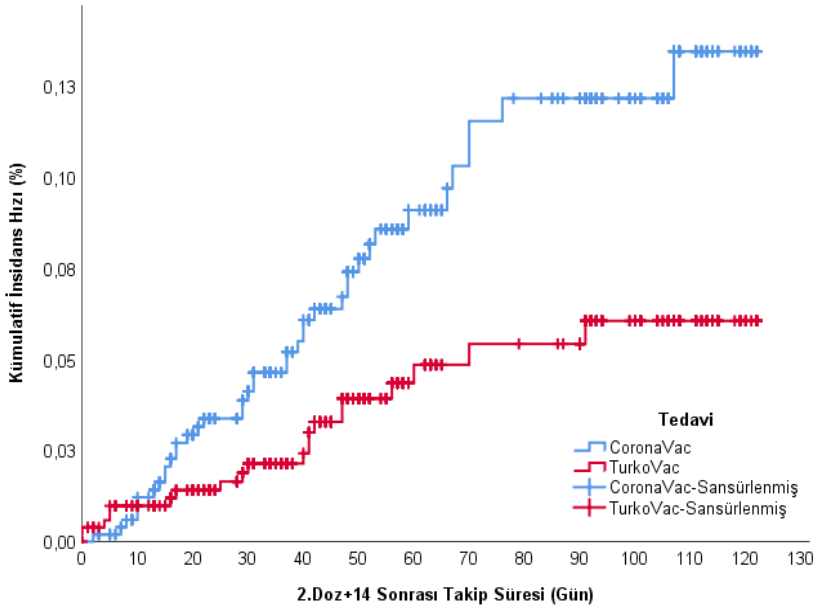
| | | $CI_{95}$ |
|---|---|---|
| RRR (Relative Risk Reduction) | 50.76% | (16.94-70.81) |
| ARR (Absolute Risk Reduction) | 3.51% | (1.09-6.85) |
| OR (Odds Ratio) | 2.12 | (1.22-3.67) |

Cumulative Covid-19 Case Incidence After First Dose Vaccination




*Based on symptomatic COVID-19 PCR positive cases.

Incidence of COVID-19 Cases 14 Days or More After Second Dose Vaccine




*Based on symptomatic COVID-19 PCR positive cases.

### 5.2. Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

### 5.3. Preclinical safety data

No toxic effects were reported in mice and ferrets in single, repeated, and high-dose acute toxicity tests. No irritation was observed in local tolerance studies.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Aluminum hydroxide
Sodium chloride
Potassium chloride
Potassium dihydrogen phosphate
Disodium hydrogen phosphate heptahydrate
Water for injection

### 6.2. Incompatibilities

Due to the lack of compatibility studies, this vaccine must not be mixed with other medicinal products.

### 6.3. Shelf Life

15 months.

### 6.4. Special precautions for storage

Store in the refrigerator between 2 - 8 °C.
It is sensitive to frost and sunlight; care should be taken not to freeze the vaccine. Frozen products should not be thawed and administered.
It can be stored on any shelf of the vaccine cabinet.
In no-frost refrigerators that do not have a vaccine cabinet (if there is no vaccine cabinet, only no-frost refrigerators should be used), it should be stored preferably on the second shelf from the top and on the side of the shelf close to the door, so that it does not touch the inner wall of the cabinet and is not in front of the blowing channels.
There should preferably be a freezing indicator in the cabinet.
It has been shown that TURKOVAC, which is offered for use as 5 doses, can be used within 8 hours after opening, provided that it is stored under storage conditions.
Cold chain should be provided in accordance with the Extended Immunization Program Circular.

### 6.5. Nature and contents of container

It is presented in packages with flip-off cap, bromo buthyl stopper, containing 1 vial (type I transparent) with 5 doses in 1 package.
Packing size: 10 pcs vials

### 6.6. Special precautions for disposal and other handling

It is important to use a separate sterile syringe and needle for each patient to ensure injection safety.

Vaccine Preparation Instructions:
TURKOVAC is supplied in a 5-dose pre-filled vial without an injector. Administration should be done with a standard vaccine injector.
1 dose is 0.5 mL.
It is administered intramuscularly to people over 18 years of age as 0.5 mL at a 90º angle.
It should be shaken well before use.

TURKOVAC is in the form of an opalescent suspension. Layered precipitates can be removed by agitation, after agitation there should be no residue or agglomeration.
It is not administered if foreign particles are noticed in the vial and if there is crack or defect in the vaccine package.
If particulate matter is observed in the vaccine vial or its appearance differs from that described above, the vaccine should not be used.
TURKOVAC should not be administered after the expiry date on the package.
After the first opening of TURKOVAC 3 mcg/ 0.5 mL suspension for IM injection can be kept for a maximum of 8 hours at a storage temperature between +2 and +8 °C. Planning should be done so that the vial will be used within 8 hours at the latest. The opening time should be recorded on the vial. If there is any vaccine left in the vial after 8 hours, it should not be used and the remaining vaccine should be disposed of properly.
In accordance with the rules of asepsis, the **stopper of the vial should be wiped with an antiseptic** and administered without waiting by withdrawing 0.5 mL to the vaccine injector distributed by the Ministry of Health in accordance with this vaccine. No other injector should be used.
If there is any vaccine left in the vial after 5 doses of vaccine withdrawal, the remaining amount in the vial should not be used as a new vaccine dose and should be disposed of appropriately.
Unused products or waste materials must be disposed of in accordance with the "Regulation on the Control of Medical Waste" and the "Regulation on the Control of Packaging and Packaging Waste".

## 7. MARKETING AUTHORISATION HOLDER

SBT Sağlık Bilim ve Teknolojileri A.Ş.
Üniversiteler Mah. Şehit Mehmet Bayraktar Cad. No:3
Çankaya/ANKARA

## 8. MARKETING AUTHORISATION NUMBER

2023/169

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first approval: 10.05.2023
Date of renewal of the approval:

## 10. DATE OF REVISION OF THE TEXT