SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1 NAME OF THE MEDICINAL PRODUCT

SKYCovion suspension and emulsion for emulsion for injection.

COVID-19 vaccine (recombinant, adjuvanted).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

These are two multidose vials (antigen vial and adjuvant vial) that must be mixed before use.

The volume after mixing one vial of antigen suspension (2.5 mL) with one vial of AS03 adjuvant emulsion (2.5 mL) corresponds to 10 doses of 0.5 mL vaccine. See section 6.5 for the number of doses per vial.

One dose (0. 5 mL) contains 25 µg of recombinant COVID-19 subunit nanoparticle produced in *Escherichia coli* and Chinese Hamster Ovary (CHO) by recombinant DNA technology.

AS03 adjuvant is composed of squalene (10.69 milligrams), DL-α-tocopherol (11.86 milligrams) and polysorbate 80 (4.86 milligrams).

For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Suspension and emulsion for emulsion for injection.

The suspension (antigen) is clear or slightly opalescent liquid.

The emulsion (adjuvant) is whitish to yellowish homogeneous milky liquid.

The emulsion (antigen mixed with adjuvant) is a whitish to yellowish homogeneous milky liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

SKYCovion is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 18 years of age and older

The vaccination course consists of two separate doses of 0.5 mL each. It is recommended to administer the second dose 4 weeks (28 days) after the first dose (see section 5.1).

There are no data available on the interchangeability of this vaccine with other COVID-19 vaccines to complete the vaccination course. Individuals who have received the first dose of SKYCovion should receive a second dose of SKYCovion to complete the primary vaccination course.

Elderly population

No dose adjustment is required for individuals ≥65 years of age.

Paediatric population

The safety and immunogenicity of SKYCovion in children and adolescents less than 18 years of age have not yet been established. No data are available.

Method of administration

The vaccine should be administered after mixing with accompanied adjuvant vial.

The vaccine is for intramuscular injection only, preferably in the deltoid muscle of the upper arm.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions on handling, administration and disposal, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medical products, the name and batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of SKYCovion.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation, or stress related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from an acute severe febrile illness or acute infection (see section 4.3). However, the presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any

coagulation disorder (such as haemophilia) because bleeding or bruising may occur following administration in these individuals.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical trials.

Immunocompromised individuals

The efficacy, safety and immunogenicity of the vaccine have not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy.

Limitations of vaccine effectiveness

Based on immunogenicity data in SARS-CoV-2 naïve subjects, no protection is anticipated after the first vaccine dose and individuals may not be fully protected until 14 days after their second dose. As with all other vaccines, SKYCovion may not protect all vaccine recipients. Efficacy was not evaluated as part of the clinical trial programme.

Excipients

This vaccine contains less than 1 mmol potassium (39 mg) per dose, that is to say essentially ‘potassium-free’.

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Concomitant administration with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no experience with the use of SKYCovion in pregnant women from clinical trials.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo-foetal development, parturition or post-natal development. (see section 5.3).

Administration of SKYCovion during pregnancy should only be considered where the potential benefits outweigh any potential risks (including those described in sections 4.4 and 4.8) for the mother and foetus.

Breastfeeding

It is unknown whether SKYCovion is excreted in human milk.

No direct and indirect adverse effects of the vaccine were observed on breastfeeding dams in a reproductive and developmental toxicity study conducted in rats (see section 5.3).

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

This vaccine is expected to have no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of SKYCovion was assessed in two clinical trials. A total of 3,133 subjects 18 years of age or older received at least 1 dose of vaccine, 2,963 subjects (94.6%) aged between 18 and 65 years and 170 subjects (5.4%) 65 years of age and older. A total of 3,002 subjects received 2 doses.

The most frequent adverse reactions were injection site pain (57%), fatigue (33%), myalgia (32%), and headache (31%). Most reactions were mild to moderate in severity and resolved within a few days after vaccination. Most reactions were

reported at a similar frequency after the two vaccine doses, except for injection site pain and myalgia (less frequent after the second injection) and pyrexia and chills (more frequent after the second injection).

Tabulated list of adverse reactions

Adverse reactions are listed by MedDRA System Organ Class (SOC) according to the following frequency categories: Very common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), Not known (cannot be estimated from the available data).

Table 1: Adverse reactions from clinical trials with SKYCovion

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)
Blood and lymphatic system disorders				Lymphadenopathy
Nervous system disorders	Headache		Dizziness Paraesthesia	Hypoaesthesia Somnolence
Gastrointestinal disorders		Nausea, vomiting Diarrhoea		Abdominal pain
Musculoskeletal and connective tissue disorders	Arthralgia Myalgia		Pain in extremity	
General disorders and administration site conditions	Injection site pain Fatigue Pyrexia, chills[a]	Injection site redness, swelling	Injection site warmth, pruritus Chest pain	Injection site bruising Asthenia
Skin and Subcutaneous Tissue Disorders			Rash	Pruritus Urticaria Hyperhidrosis
Respiratory, thoracic and mediastinal disorders				
Cardiac disorders			Palpitations	
Metabolism and nutrition disorders				Decreased appetite

a. Pyrexia and chills were observed more frequently after the second dose than after the first dose.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via a Yellow card. Reporting forms and information can be found at

https://coronavirus-yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store and include batch/Lot number if available.

4.9 Overdose

In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccine, other viral vaccines, ATC code: J07BX03

Mechanism of Action

SKYCovion contains nanoparticles of recombinant Receptor Binding Domain (RBD) of SARS-CoV-2 Spike (S) protein from the parental D614G strain and an adjuvant system (AS03). The vaccine elicits neutralising antibodies as well as cellular immune responses (Th1), which may contribute to protection against COVID-19.

Immunogenicity

The efficacy of SKYCovion has been inferred by immunobridging of immune responses to an authorised COVID-19 vector vaccine (ChAdOx1-S) encoding the SARS-CoV-2 S protein, for which vaccine efficacy has been established.

The main objective of the clinical phase III study was to assess the immunogenicity and safety of SKYCovion compared to the control vaccine (ChAdOx1-S). This was a multicentre, observer-blind, randomised clinical trial in adults over the age of 18 years conducted in the Republic of Korea, the Philippines, Thailand, Vietnam, Ukraine, and New Zealand. The primary immunogenicity analysis set (Per Protocol Set) included 1,318 subjects. This population was mostly Asian (95%), included 59% of male participants and had a mean age of 42 years (range 18 to 79 years), with 5% of participants being 65 years or older.

Co-primary endpoints were superiority of neutralising antibody geometric mean titre (GMT) and non-inferiority of neutralising antibody seroconversion rate (SCR; percentage of subjects with $\geq$ 4-fold rise from baseline) determined in baseline seronegative subjects 2 weeks after the second vaccine dose, administered 4 weeks after the first vaccine dose, of either SKYCovion or ChAdOx1-S. A live virus neutralisation assay was used (focus reduction neutralisation test; FRNT50). The trial met its primary endpoints and results are shown in Table 2.

Table 2: Neutralising antibody response against SARS-CoV-2 (ancestral strain) by FRNT*

		SKYCovion (N=877)	**ChAdOx1-S (N=441)**
Geometric mean titre (GMT)	GMT[a] (95% CI[b])	272.12 (240.40, 308.02)	92.75 (80.79, 106.48)
	GMT Ratio (GBP510/ChAdOx1-S) (95% CI)	2.93 (2.63, 3.27)	
Seroconversion Rate (SCR)	Participants with ≥ 4-fold rise (%; n/N) (95% CI)	98.06 (860/877) (96.91, 98.87)	87.30 (385/441) (83.83, 90.26)
	Difference in SCR (GBP510 - ChAdOx1-S) (95% CI)	10.76 (7.68, 14.32)	

*FRNT was converted to IU/mL using WHO International Standard.

a. GMT adjusted for age and baseline antibody level
b. CI = Confidence Interval

A similar analysis of neutralising antibodies determined 4 weeks after the first vaccine dose in a subset of participants (195 in the GBP150 arm and 96 in the ChAdOx1-S arm) showed a GMT ratio of 0.27 (95%CI: 0.21, 0.34) and a SCR difference of -50.61 (95%CI: -60.89, -39.62). However, in participants seropositive at baseline, the GMT ratio was 0.97 (95%CI: 0.34, 2.80).

The trend for neutralising antibodies was the same in the two age groups: 18 - 65 years and ≥ 65 years.

Similar to the neutralising antibodies, a higher GMT of anti-RBD binding antibodies (IgG ELISA) was observed 2 weeks after the second vaccine dose in the GBP150 arm (2,850 [95%CI: 2,587, 3,142]) compared to the ChAdOx1-S arm (GMT 216 [95%CI: 194, 240], with a GMT ratio of 13.22 (95%CI: 12.13, 14.40). In contrast to the neutralising antibodies, the GMT of anti-RBD binding antibodies after the first vaccine dose was already higher in the GBP150 arm (131 [95%CI: 118, 146]) compared to the ChAdOx1-S arm (GMT 92 [95%CI: 82, 104], with a GMT ratio of 1.43 (95%CI: 1.30, 1.57).

The evaluation of T-cell responses showed a Th1 response to the Spike RBD protein after the second vaccine dose, which was more pronounced after GBP150 than after ChAdOx1-S, while no Th2 response was apparent with any vaccine.

Paediatric population

The licensing authority has deferred the obligation to submit the results of clinical studies in the paediatric population (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and reproductive and developmental toxicity.

Genotoxicity/carcinogenicity

Neither genotoxicity nor carcinogenicity studies were performed. The components of the vaccine are not expected to have genotoxic potential.

Reproductive toxicity

Reproductive and developmental toxicity study was conducted to evaluate the effect of SKYCovion on pregnant or lactating female Sprague-Dawley rats including maternal toxicity, fertility and embryo-foetal and peri- and post-natal development following intramuscular administration of 12 μg recombinant SARS-CoV-2 surface antigen protein with AS03 adjuvant. For the caesarean sectioning subgroup, female rats were intramuscularly injected at four weeks and two weeks before pairing (Days 1 and 15), and on gestation days (GD) 8 and 15 (total four times) to assess the embryo-foetal developmental toxicity. For the natural delivery subgroups, female rats were intramuscularly injected at four weeks and two weeks before pairing (Days 1 and 15), on GD 8 and 15, and on lactation day (LD) 7 (total 5 times) to assess the pre- and post- natural development toxicity until weaning.

SARS-CoV-2 RBD antibodies were increased in female rats and offspring. There were no vaccine related effects on female fertility, maternal function, survival, growth, and development of offspring through post-natal 21 days. No SKYCovion data are available on vaccine placental transfer or excretion in milk.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Antigen vial

Sodium chloride

Tromethamine

Arginine

Sucrose

Water for injections

Adjuvant vial

Sodium chloride

Disodium hydrogen phosphate

Potassium dihydrogen phosphate

Potassium chloride

Water for injections

For adjuvant, see also section 2.

6.2 Incompatibilities

This vaccine must not be mixed with other medicinal products.

6.3 Shelf life

Unopened vial

12 months when stored in a refrigerator (2°C - 8°C).

Punctured vial

After mixing, the product should be used within 6 hours and protected from light. If it has not been used within 6 hours, it should not be refrigerated again and should be discarded.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Store in the outer package in order to protect from light.

For storage conditions after mixing of the medicinal product, see section 6.3.

6.5 Nature and contents of container

One pack contains:

- Antigen: 2.5 mL of suspension in a 10 multidose vial (type I glass) with a stopper (chlorobutyl) with an aluminium overseal and a plastic flip-off cap.
- Adjuvant: 2.5 mL adjuvant emulsion in a 10 multidose vial (type 1 glass) with a stopper (chlorobutyl) and an aluminium seal with a plastic flip-off cap.

6.6 Special precautions for disposal

Handling and administration instructions

This vaccine should be handled by a healthcare professional using aseptic technique to ensure the sterility of each dose.

Preparation for use

Before mixing the two components, the suspension (antigen) and emulsion (adjuvant) should be allowed to reach room temperature for a minimum of 15 minutes, protecting them from light.

Prior to administration, the two components, adjuvant and antigen, must be mixed.

The vaccine is mixed by withdrawing the entire contents of the vial containing the adjuvant by means of a 5 mL syringe and by adding it to the vial containing the antigen. It is recommended to equip the syringe with a 23-G needle (or narrower).

Record the date of time of mixing on the antigen vial label. Use within 6 hours after mixing.

Inspect the vial

Gently mix the multidose vial by inverting the vial 10 times before and in between each dose withdrawal so that the antigen and the adjuvant are completely mixed.

After mixing, each multidose vial contains a whitish to yellowish homogeneous milky liquid emulsion.

Visually inspect the contents of the vial for visible foreign particulate matter and/or abnormal physical appearance prior to administration. Do not administer the vaccine if either are present.

Administer the vaccine

After mixing, the vial contains 5.0 mL corresponding to 10 doses of 0.5 mL.

Each 0.5 mL dose is withdrawn into a 1 mL syringe for injection and administered intramuscularly, preferably in the deltoid muscle of the upper arm. It is recommended to equip the syringe with a 23-G needle or narrower.

The vaccine should be administered in accordance with the recommended posology (see section 4.2).

The vaccine taken by the syringe should be used immediately.

Storage after mixing

After mixing, store the vaccine between 2°C to 8°C for up to 6 hours, see section 6.3

Discard

Discard this vaccine if not used within 6 hours after mixing, see section 6.3.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

SK Chemicals GmbH,

Mergenthalerallee 77,

65760 Eschborn,

Germany.

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 33611/0029

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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