ANNEX I

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

BIMERVAX emulsion for injection
COVID-19 Vaccine (recombinant, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial which contains 10 doses of 0.5 mL

One dose (0.5 mL) contains 40 micrograms of selvacovatein adjuvanted with SQBA.

Selvacovatein is a SARS-CoV-2 virus recombinant spike (S) protein receptor binding domain (RBD) fusion heterodimer (B.1.351 and B.1.1.7 strains) produced by recombinant DNA technology using a plasmid expression vector in a CHO cell line.

SQBA adjuvant containing per 0.5 mL dose: squalene (9.75 mg), polysorbate 80 (1.18 mg), sorbitan trioleate (1.18 mg), sodium citrate (0.66 mg), citric acid (0.04 mg) and water for injections.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Emulsion for injection (injection)
White homogeneous emulsion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BIMERVAX is indicated as a booster for active immunisation to prevent COVID-19 in individuals 16 years of age and older who have previously received a mRNA COVID-19 vaccine (see sections 4.2 and 5.1).

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

4.2 Posology and method of administration

Posology

Individuals 16 years of age and older
A single intramuscular dose (0.5 mL) of BIMERVAX should be administered. There should be an interval of at least 6 months between prior receipt of a mRNA vaccine and administration of BIMERVAX (see section 5.1).

Elderly population
No dose adjustment is required in elderly individuals ≥ 65 years of age.

Paediatric population

The safety and efficacy of BIMERVAX in children and adolescents less than 16 years of age have not been established yet. No data are available.

Method of administration

BIMERVAX is for intramuscular administration only, preferably into the deltoid muscle of the upper arm.

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

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 regarding handling and disposal of the vaccine, 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 medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Events of anaphylaxis have been reported with COVID-19 vaccines. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination.

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 acute severe febrile illness or acute infection. 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 an intramuscular administration in these individuals.

Immunocompromised individuals

The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of BIMERVAX may be lower in immunocompromised individuals.

Duration of protection

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

Limitations of vaccine effectiveness

As with any vaccine, vaccination with BIMERVAX may not protect all vaccine recipients.

Excipients

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

Sodium
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 of BIMERVAX with other vaccines has not been studied.

4.6 Fertility, pregnancy, and lactation

Pregnancy

There is no experience with the use of BIMERVAX in pregnant women. 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 BIMERVAX during pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

It is unknown whether BIMERVAX is excreted in human milk.

No effects on the breast-fed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to BIMERVAX is negligible.

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

BIMERVAX has no or negligible influence on the ability to drive and use machines. However, some of the effects 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 most common adverse reactions reported were injection site pain (82.2%), headache (30.2%), fatigue (30.9%) and myalgia (20.2%). The median duration of local and systemic adverse reactions was 1 to 3 days. Most adverse reactions occurred within 3 days following vaccination and were mild to moderate in severity.

Tabulated list of adverse reactions

The safety profile presented below is based on interim pooled safety data generated in two phase 2b and phase 3 clinical trials with a total of 3 192 individuals 16 years of age and older, that received one booster dose of BIMERVAX at least 3 months after a previous COVID-19 vaccine. The median duration of the safety follow-up was 5 months for a 84% of the individuals, and 7.5 months for a 16% of the individuals.

Adverse reactions observed during clinical trials are listed below according to the following frequency categories: 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 (< 1/10 000) and not known (cannot be estimated from the available data).

Table 1: Adverse reactions

System organ class	Very common	Common	Uncommon	Rare	Not known
Blood and lymphatic system disorders		Lymphadenopathy[a]			
Psychiatric disorders			Insomnia		
Nervous system disorders	Headache		Dizziness Somnolence	Paraesthesia Hypoaesthesia	
Cardiac disorders					Pericarditis[c]
Gastrointestinal disorders		Diarrhoea Vomiting Nausea	Odynophagia Abdominal pain[b]		
Skin and subcutaneous tissue disorders			Pruritus	Urticaria Cold sweats Rash Erythema	
Musculoskeletal and connective tissue disorders	Myalgia		Arthralgia	Back pain	
General disorders and administration site conditions	Injection site pain Fatigue	Injection site swelling Injection site erythema Injection site induration Pyrexia Axillary pain	Asthenia Chills Malaise Injection site pruritus Injection site hypersensitivity	Injection site bruising	

[a] This term also included events reported as lymphadenitis
[b] This term also included events reported as upper and lower abdominal pain
[c] Based on a single event during clinical trials

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 the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, Covid-19 vaccines, ATC code: J07BN

Mechanism of action

BIMERVAX is a recombinant protein vaccine whose active substance (antigen) is SARS-CoV-2 virus recombinant spike (S) protein receptor binding domain (RBD) fusion heterodimer – B.1.351-B.1.1.7 strains. Following administration, an immune response is generated, both at a humoral and cellular level, against the SARS-Co-V-2 RBD antigen. Neutralising antibodies against the RBD domain of SARS-CoV-2 prevent RBD binding to its cellular target ACE2, thus blocking membrane fusion and viral infection. Moreover, BIMERVAX induces antigen-specific T-cell immune response, which may contribute to protection to COVID-19.

Efficacy

Efficacy of BIMERVAX has been inferred by immunobridging of immune responses to an authorised COVID-19 vaccine, for which vaccine efficacy has been established.

Immunogenicity

The immunogenicity of BIMERVAX was evaluated in one pivotal phase 2b multi-centre clinical trial (Study HIPRA-HH-2) and in one phase 3 multi-centre clinical trial (Study HIPRA-HH-5).

Study HIPRA-HH-2
Study HIPRA-HH-2 is an ongoing phase 2b, double-blind, randomised, active-controlled, multi-centre, non-inferiority clinical trial to assess immunogenicity and safety of a booster vaccination with BIMERVAX compared to tozinameran/COVID-19 mRNA Vaccine, in adults fully vaccinated against COVID-19 with a mRNA vaccine at least 6 months before enrolment. This phase 2b clinical trial excluded individuals who were pregnant, individuals who were immunocompromised or had received immunosuppressants within 12 weeks, as well as individuals with previous COVID-19 infection. Individuals were also required a minimum interval of 3 months after receipt of any immunotherapy (monoclonal antibodies, plasma) prior to the study.

A total of 765 subjects were vaccinated; 513 subjects received BIMERVAX, and 252 subjects received the COVID-19 mRNA vaccine (tozinameran). A total of 751 subjects were analysed (504 BIMERVAX subjects and 247 COVID-19 mRNA vaccine subjects) excluding those who tested positive for COVID-19 within 14 days of the booster. Randomisation was stratified by age group (18-64 versus ≥ 65 years). The median age was 42 years (range: 19 to 76 years), with similar age ranges in both vaccine arms, including 7.4% and 7.1% of subjects 65 years of age and older in the BIMERVAX and COVID-19 mRNA vaccine groups, respectively.
Immunogenicity of a booster dose of BIMERVAX was based on an assessment of geometric mean titres (GMT) of neutralising antibodies, measured by a pseudovirion-based neutralisation assay (PBNA) against SARS-CoV-2 (D614G) strain, Beta, Delta and Omicron BA.1 variants. GMT ratio is the result of the GMT values (ID_{50}) of COVID-19 mRNA vaccine (tozinameran)/BIMERVAX. Non-inferiority of BIMERVAX to COVID-19 mRNA vaccine (tozinameran) is concluded if the upper limit of the 2 sided 95% Confidence Interval (CI) of the GMT ratio is < 1.4. Superiority of BIMERVAX to COVID-19 mRNA vaccine (tozinameran) is concluded if the upper limit of the 2-sided 95% Confidence Interval of the GMT ratio is < 1.0 (see Table 2, GMT ratio column).

Table 2: Post-booster GMT ratio for BIMERVAX versus COVID-19 mRNA vaccine (tozinameran) with neutralisation titres (PBNA) against SARS-CoV-2 (D614G strain), Beta, Delta and Omicron BA.1 at days 14, 28, 98 and 182 post-booster dose (per protocol population)

	BIMERVAX N=504		COVID-19 mRNA vaccine (tozinameran) N=247		COVID-19 mRNA vaccine (tozinameran) / BIMERVAX
	GMT	95% CI	GMT	95% CI	GMT Ratio; (95% CI)
Day 14 post-booster					
D614G strain	1953.89	1667.17; 2289.93	3336.54	2778.56; 4006.57	1.71 (1.45; 2.02)
Beta	4278.92	3673.99; 4983.46	2659.02	2213.05; 3194.86	0.62 (0.52; 0.75)
Delta	1466.65	1250.52; 1720.14	1490.42	1238.77; 1793.19	1.02 (0.86; 1.21)
Omicron BA.1	2042.36	1775.91; 2348.79	1217.90	1023.84; 1448.75	0.60 (0.50; 0.72)
Day 28 post-booster					
D614G strain	2230.95	1903.29; 2615.01	2958.40	2465.00; 3550.55	1.33 (1.12; 1.56)
Beta	3774.87	3240.63; 4397.18	2467.06	2054.58; 2962.35	0.65 (0.54; 0.79)
Delta	1711.24	1458.85; 2007.29	1515.79	1260.56; 1822.71	0.89 (0.75; 1.05)
Omicron BA.1	1515.40	1317.43; 1743.13	996.73	838.49; 1184.83	0.66 (0.55; 0.79)
Day 98 post-booster (N: BIMERVAX: 78; N: tozinameran: 42 as per protocol subset)					
D614G strain	1193.35	921.24; 1545.85	1048.32	750.90; 1463.54	0.88 (0.60; 1.29)
Beta	2051.21	1571.51; 2677.34	1179.68	831.77; 1673.11	0.58 (0.38; 087)
Delta	2089.64	1609.52; 2712.99	1093.64	780.28; 1532.87	0.52 (0.35; 0.77)
Omicron BA.1	658.87	506.16; 857.66	395.69	279.04; 561.10	0.60 (0.40; 0.91)
Day 182 post-booster					
D614G strain	1205.49	1028.22; 1413.33	751.64	626.02; 902.46	0.62 (0.53; 0.74)
Beta	2569.17	2204.98; 2993.52	1786.38	1487.00; 2146.03	0.70 (0.58; 0.84)
Delta	2303.74	1963.44; 2703.03	1257.77	1045.54; 1513.07	0.55 (0.46; 0.65)
Omicron BA.1	882.92	767.34; 1015.91	668.32	561.92; 794.85	0.76 (0.63; 0.91)

N: number of participants in the population per-protocol.
Abbreviations: GMT = Geometric Mean Titre; CI: Confidence intervals; PBNA = pseudovirion-based neutralisation assay
Non-inferiority of BIMERVAX to COVID-19 mRNA vaccine (tozinameran) is concluded if the upper limit of the 2-sided 95% Confidence Interval (CI) of the GMT ratio COVID-19 mRNA vaccine (tozinameran)/BIMERVAX is < 1.4.
Superiority of BIMERVAX to COVID-19 mRNA vaccine (tozinameran) is concluded if the upper limit of the 2-sided 95% Confidence Interval of the GMT ratio COVID-19 mRNA vaccine (tozinameran)/BIMERVAX is < 1.0.

HIPRA-HH-5

This study is an ongoing open label, single arm, multicentre, phase 3 clinical trial to assess the safety and immunogenicity of a booster vaccination with BIMERVAX for the prevention of COVID-19 in subjects vaccinated with several primary vaccine schedules, with or without previous non-severe COVID-19 infections. BIMERVAX was administered at least 91 days after the last dose or at least 30 days after the COVID-19 infection. This phase 3 clinical trial excluded individuals who were pregnant as well as individuals who were immunocompromised or had received immunosuppressants within 12

weeks. Individuals were also required a minimum interval of 3 months after receipt of any immunotherapy (monoclonal antibodies, plasma) prior to the study.

The interim report includes data from a total of 2 646 subjects who were vaccinated with BIMERVAX as a booster dose in healthy individuals (at least 16 years old) previously vaccinated with different COVID-19 vaccines (mRNA COVID-19 vaccines: tozinameran and elasomeran, and adenovirus-vector vaccines (COVID-19 Vaccine (ChAdOx1-S [recombinant]) and COVID-19 vaccine (Ad26.COV2-S [recombinant]). Of these, 230 (8%) subjects were included in the immunogenicity population. In the immunogenicity analysis, the population of the Comirnaty/Comirnaty vaccine group were all subjects between 16-17 years old.

Overall, the median age was 34.4 years (range: 16 to 85 years of age). Subjects were balanced between genders, 52.49% male and 47.47% female.

Immunogenicity was measured by Pseudovirion-based neutralisation assay (PBNA) against SARS-CoV-2 (D614G) strain and against Beta, Delta and Omicron BA.1. Data on GMT (geometric mean titre: ID_{50}) at baseline (prior to the administration of the booster dose) and at Day 14 (2 weeks after the administration of the booster dose) are provided in the following table.

Table 3: Neutralising antibody Geometric Mean Titres (GMT) at 14 days post-booster with BIMERVAX in individuals 16 years of age and older-per protocol analysis

	mRNA primed (tozinameran) 16-17 years old N=11		**Ad-vector primed (ChAd=x1-S recombinant) ≥ 18 years old N=40**		**mRNA primed (elasomeran) ≥ 18 years old N=171**	
	Pre-booster					
	GMT	95% CI	GMT	95% CI	GMT	95% CI
D614G strain	720.10	356.96; 1452.64	288.58	194.56; 428.02	657.49	499.52; 865.43
Beta	471.68	208.39; 1067.60	539.49	345.97; 841.26	497.77	376.98; 657.26
Delta	803.84	376.27; 1717.26	283.75	182.43; 441.35	914.68	657.97; 1271.55
Omicron BA.1	257.99	99.98; 665.71	159.34	94.02; 270.05	221.62	155.51; 315.84
	Day 14 post-booster					
D614G strain	4753.65	2356.45; 9589.48	2298.81	1549.89; 3409.63	4437.27	3371.158; 5840.55
Beta	8820.74	3897.14; 19964.72	5009.47	3212.53; 7811.54	6857.95	5193.76; 9055.38
Delta	7564.79	3541.05; 16160.76	2600.31	1671.78; 4044.56	5811.47	4180.44; 8078.87
Omicron BA.1	5757.43	2231.25; 14856.19	1847.41	1090.05; 3131.00	4379.81	3073.24; 6241.85

N: Number of participants with available data for the relevant endpoint
Abbreviations: GMT = Geometric Mean Titre; CI: Confidence intervals

Elderly population

The immunogenicity of BIMERVAX has been shown in the elderly population (≥ 65 years old) including 38 (7.4%) of individuals receiving BIMERVAX.

Paediatric population

The European medicines Agency has deferred the obligation to submit the results of studies with BIMERVAX in one or more subsets of the paediatric population in the prevention of COVID-19 (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.

Genotoxicity and carcinogenicity

BIMERVAX has not been evaluated for its genotoxic or carcinogenic potential. The components of the vaccine are not expected to have genotoxic or carcinogenic potential.

Reproductive toxicity

A developmental and reproductive toxicity study was performed in female and male rats prior to mating and during gestation. BIMERVAX was administered intramuscularly (equivalent to a full human dose) to female rats in four occasions, 21 and 14 days prior to mating and on gestation days 9 and 19. Males received three administrations, 35, 28 and 6 days prior to mating. No vaccine-related adverse effects on fertility, pregnancy/lactation, or development of the embryo/foetus and offspring were observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate dodecahydrate
Potassium dihydrogen phosphate
Sodium chloride
Potassium chloride
Water for injections

For adjuvant, see section 2

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened vial

21 months at 2 ºC – 8 ºC.

Punctured vial

Chemical and physical in-use stability has been demonstrated for 6 hours at 2 ºC – 8 ºC from the time of first needle puncture.

From a microbiological point of view, after first opening (first needle puncture), the vaccine should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.

Keep the vials in the outer carton in order to protect from light.

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

6.5 Nature and contents of container

5 mL of emulsion in a multidose vial (type I glass) closed with a type I elastomeric stopper and an aluminium seal fitted with a plastic flip-off cap.

Each vial contains: 10 doses of 0.5 mL

Pack size: 10 multidose vials.

6.6 Special precautions for disposal and other handling

Handling instructions and administration

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

Preparation for use

- The vaccine comes ready to use.
- Unopened vaccine should be stored at 2 ºC to 8 ºC and kept within the outer carton to protect from light.
- Immediately prior to use, remove the vaccine vial from the outer carton.
- After first puncture of the vial, record the discard date and time (6 hours after first puncture) on the designated area of the vial label.

Inspect the vial

- Gently swirl the multidose vial before and in between each dose withdrawal. Do not shake.
- Each multidose vial contains a white and homogeneous emulsion.
- Visually inspect the vaccine for particulate matter and/or discolouration prior to administration. Do not administer the vaccine if any of these are present.

Administer the vaccine

- An overfill is included in each vial to ensure that a maximum of 10 doses of 0.5 mL each can be extracted. Discard any remaining vaccine in the vial after 10 doses have been extracted.
- Each 0.5 mL dose is withdrawn into a sterile needle and sterile syringe to be administered by intramuscular injection, preferably in the deltoid muscle of the upper arm.
- Once the vaccine is loaded in the syringe, it is stable up to at least 6 hours either under refrigerated conditions or at room temperature (< 25 ºC).
- Do not mix the vaccine in the same syringe with any other vaccines or medicinal products.
- Do not pool excess vaccine from multiple vials.

Storage after first needle puncture

- After first puncture, store the opened vial at 2 °C to 8 °C for up to 6 hours.

Discard
Discard this vaccine if not used within 6 hours after first puncture of the vial, 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

Hipra Human Health, S.L.U.
Avda. la Selva, 135
17170 Amer (Girona)
SPAIN

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1709/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30 March 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance(s)

Laboratorios Hipra, S.A.
Ctra. C-63, Km 48,300. Polígono
Industrial El Rieral,
17170 Amer (Girona)
Spain

Name and address of the manufacturer(s) responsible for batch release

Laboratorios Hipra, S.A.
Avda La Selva nº135
17170 Amer (Girona)
Spain

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON LABEL

1. NAME OF THE MEDICINAL PRODUCT

BIMERVAX emulsion for injection
COVID-19 Vaccine (recombinant, adjuvanted)
selvacovatein

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose (0.5 mL) contains 40 micrograms of selvacovatein adjuvanted with SQBA.

SQBA adjuvant contains squalene, polysorbate 80, sorbitan trioleate, sodium citrate, citric acid and water for injections.

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dodecahydrate, potassium dihydrogen phosphate, sodium chloride, potassium chloride and water for injections
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Emulsion for injection
10 multidose vials
Each vial contains 10 doses of 0.5 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Read the package leaflet before use

QR code to be included
For more information, scan or visit www.hipracovidvaccine.com

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze.
Keep the vials in the outer carton in order to protect from light.
After first puncture, store at 2 ºC – 8º C, use within 6 hours.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Hipra Human Health, S.L.U.
Avda. la Selva, 135
17170 Amer (Girona)
SPAIN

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1709/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC

SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

BIMERVAX emulsion for injection
COVID-19 Vaccine (recombinant, adjuvanted)
selvacovatein
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

QR code to be included
For more information, scan or visit www.hipracovidvaccine.com

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses of 0.5 mL

6. OTHER

Discard Date/Time:

B. PACKAGE LEAFLET

Package leaflet: Information for the user

BIMERVAX
COVID-19 vaccine (recombinant, adjuvanted)
selvacovatein

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effect you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you recieve this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What BIMERVAX is and what it is used for

BIMERVAX is a vaccine used to prevent COVID-19 caused by the SARS-CoV-2 virus.

BIMERVAX is given to individuals 16 years of age and older who have previously received a mRNA COVID-19 vaccine.

The vaccine stimulates the immune system (the body's natural defences) to produce specific antibodies that work against the virus, giving protection against COVID-19. None of the ingredients in this vaccine can cause COVID-19.

2. What you need to know before you receive BIMERVAX

BIMERVAX should not be given
- if you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before receiving BIMERVAX if:
- you have ever had a severe or life-threatening allergic reaction after receiving any other vaccine injection;
- you have ever fainted following any needle injection;
- you have a high temperature (over 38 °C) or severe infection. However, you can have your vaccination if you have a mild fever or upper airway infection like a cold;
- you have bleeding problems, you bruise easily or you use a medicine to prevent blood clots (anticoagulant medicine);

- your immune system does not work properly (immunodeficiency) or you are taking medicines that weaken the immune system (such as high-dose corticosteroids, immunosuppressants, or cancer medicines).

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist, or nurse before you are given BIMERVAX.

As with any vaccine, BIMERVAX may not fully protect all those who receive it, and it is not known how long you will be protected.

Children and adolescents
BIMERVAX is not recommended for children aged below 16 years. Currently, there is no information available on the use of BIMERVAX in children younger than 16 years of age.

Other medicines and BIMERVAX
Tell your doctor, pharmacist, or nurse if you are taking, have recently taken, or might take any other medicines or vaccines.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, ask your doctor, pharmacist, or nurse for advice before you receive this vaccine.

Driving and using machines
Some of the side effects of BIMERVAX listed in section 4 (Possible side effects) may temporarily reduce your ability to drive and use machines. Wait until any effects of the vaccine have worn off before you drive or use machines.

BIMERVAX contains sodium and potassium
This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

This vaccine contains less than 1 mmol potassium (39 milligrams) per 0.5 mL dose, that is to say, essentially 'potassium-free'.

3. How BIMERVAX is given

BIMERVAX will be given to you as 0.5 mL injection into a muscle of your upper arm.

It is recommended that you receive BIMERVAX as a single dose at least 6 months after a previous vaccination series with mRNA COVID-19 vaccine.

After the injection, your doctor, pharmacist or nurse will watch over you for around 15 minutes to monitor for signs of an allergic reaction.

If you have any further questions on the use of BIMERVAX, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Most of the side effects occur within 3 days of getting the vaccine and go away within a few days of appearing. If symptoms persist, contact your doctor, pharmacist or nurse.

Get urgent medical attention if you get symptoms of a severe allergic reaction shortly after vaccination. Such symptoms may include:

- feeling faint or light-headed
- changes in your heartbeat
- shortness of breath
- wheezing
- swelling of your lips, face, or throat
- itchy swelling under the skin (hives) or rash
- feeling sick (nausea) or vomiting
- stomach pain.

The following side effects may occur with BIMERVAX:

Very common (may affect more than 1 in 10 people)
- headache
- pain where the injection is given
- feeling very tired (fatigue)
- muscle pain

Common (may affect up to 1 in 10 people)
- redness, swelling or tenderness where the injection is given
- feeling sick (nausea) or getting sick (vomiting)
- diarrhoea
- fever
- enlarged lymph nodes
- axillary pain

Uncommon (may affect up to 1 in 100 people):
- chills or feeling feverish
- insomnia
- dizziness
- itching where the injection is given
- hipersensitivity where the injection is given
- joint pain
- feeling weak or lack of energy
- feeling sleepy
- abdominal pain
- itchy skin
- pain when swallowing
- generally feeling unwell

Rare (may affect up to 1 in 1 000 people):
- Cold sweating
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)
- decreased feeling of sensitivity, especially in the skin (hypoaesthesia)
- allergic reactions such as hives, rash or itching
- Back pain
- Bruise where the injection is given

Not known (cannot be estimated from available data, based on a single case during clinical trials):
- Inflammation of the lining outside the heart (pericarditis), which can result in breathless, palpitations or chest pain

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V and include batch/Lot number if available. By reporting side effects, you can help provide more information on the safety of this vaccine.

5. How to store BIMERVAX

Keep this medicine out of the sight and reach of children.

Your doctor, pharmacist, or nurse is responsible for storing this vaccine and disposing of any unused product correctly. The following information about storage, expiry, use and handling as well as disposal is intended for healthcare professionals.

Do not use this vaccine after the expiry date which is stated on the label after EXP.

Store in a refrigerator (2 °C – 8 °C). Do not freeze. Keep vials in outer carton in order to protect from light.
After first puncture, store at 2 °C – 8 °C, use within 6 hours.

Information on handling are described in the section intended for healthcare professionals at the end of the package leaflet.

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

6. Contents of the pack and other information

What BIMERVAX contains

- One dose (0.5 mL) contains 40 micrograms of selvacovatein adjuvanted with SQBA.
- Selvacovatein is SARS-CoV-2 virus recombinant spike (S) protein RBD fusion heterodimer B.1.351 and B.1.1.7 strains) produced by recombinant DNA technology.
- SQBA is included in this vaccine as an adjuvant to accelerate and improve the protective effects of the vaccine. SQBA contains per 0.5 mL dose: squalene (9.75 mg), polysorbate 80 (1.18 mg), sorbitan trioleate (1.18 mg), sodium citrate (0.66 mg), citric acid (0.04 mg) and water for injections.
- The other ingredients (excipients) are: disodium phosphate dodecahydrate, potassium dihydrogen phosphate, sodium chloride, potassium chloride and water for injections. BIMERVAX contains potassium and sodium (see section 2).

What BIMERVAX looks like and contents of the pack

The vaccine is a white homogeneous emulsion for injection.

5 mL of emulsion is provided in a vial with a rubber stopper and a plastic flip-off top.

Each vial contains 10 doses of 0.5 mL.

Pack size: 10 multidose vials.

Marketing Authorisation Holder

Hipra Human Health, S.L.U.
Avda. la Selva, 135
17170 Amer (Girona)
SPAIN

Manufacturer

Laboratorios Hipra, S.A.
Avda. la Selva, 135
17170 Amer (Girona)
SPAIN

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Scan the code with a mobile device to get the package leaflet in different languages.

QR code to be included

Or visit the URL: www.hipracovidvaccine.com

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Administer BIMERVAX intramuscularly, preferably into the deltoid muscle of the upper arm.

Traceability

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

Handling instructions and administration

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

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

Preparation for use

- The vaccine comes ready to use.

- Unopened vaccine should be stored at 2 °C to 8 °C and kept within the outer carton to protect from light.
- Immediately prior to use, remove the vaccine vial from the outer carton.
- After first puncture of the vial, record the discard date and time (6 hours after first puncture) on the designated area of the vial label.

Inspect the vial
- Gently swirl the multidose vial before and in between each dose withdrawal. Do not shake.
- Each multidose vial contains a white and homogeneous emulsion.
- Visually inspect the contents of the vaccine particulate matter and/or discolouration prior to administration. Do not administer the vaccine if either are present.

Administer the vaccine:
- An overfill is included per multidose vial to ensure that a maximum of ten (10) doses of 0.5 mL each can be extracted. Discard any remaining vaccine in the vial after 10 doses have been extracted.
- Each 0.5 mL dose is withdrawn into a sterile needle and sterile syringe to be administered by intramuscular injection, preferably in the deltoid muscle of the upper arm.
- Once the vaccine is loaded in the syringe, it is stable up to at least 6 hours either under refrigerated conditions or at room temperature (< 25 ºC).
- Do not mix the vaccine in the same syringe with any other vaccines or medicinal products.
- Do not pool excess vaccine from multiple vials.

Discard
- Discard this vaccine if not used within 6 hours after first puncture of the vial.

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