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

VidPrevtyn Beta solution 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. After mixing, the vaccine vial contains 10 doses of 0.5 mL.

One dose (0.5 mL) contains 5 micrograms of SARS-CoV-2 spike protein (B.1.351 strain) produced by recombinant DNA technology using a baculovirus expression system in an insect cell line that is derived from Sf9 cells of the fall armyworm, *Spodoptera frugiperda.*

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

VidPrevtyn Beta may contain traces of octylphenol ethoxylate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution and emulsion for emulsion for injection.

The antigen solution is a colourless, clear liquid.
The adjuvant emulsion is a whitish to yellowish homogeneous milky liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

VidPrevtyn Beta is indicated as a booster for active immunisation to prevent COVID-19 in adults who have previously received an mRNA or adenoviral vector 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 18 years of age and older
VidPrevtyn Beta is administered intramuscularly as a single dose of 0.5 mL at least 4 months after a previous COVID-19 vaccine. VidPrevtyn Beta may be given once as a booster to adults that have

received prior vaccination series with either mRNA or adenoviral vector COVID-19 vaccines (see section 5.1).

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

Paediatric population
The safety and efficacy of VidPrevtyn Beta in children and adolescents less than 18 years of age have not yet been established. No data are available.

Method of administration
VidPrevtyn Beta is for intramuscular injection only after mixing. The preferred site is 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 mixing, 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, or to octylphenol ethoxylate (trace residual).

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
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. 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 an intramuscular administration in these individuals.

Immunocompromised individuals
The efficacy, safety and immunogenicity of the vaccine have not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The immune response of VidPrevtyn Beta may be lower in immunosuppressed 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 VidPrevtyn Beta may not protect all vaccine recipients.

Excipients
Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Concomitant administration of VidPrevtyn Beta with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is limited experience with use of VidPrevtyn Beta in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, parturition or post-natal development (see section 5.3).

Administration of VidPrevtyn Beta during pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

Breast-feeding
It is unknown whether VidPrevtyn Beta 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 VidPrevtyn Beta 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

VidPrevtyn Beta 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 safety of VidPrevtyn Beta administered as a first booster in individuals previously vaccinated with a primary series of mRNA-based, adenovirus-vectored or protein-based COVID-19 vaccines was evaluated in an ongoing phase 3 clinical study. This study involved 705 participants 18 years of age and older who received the vaccine 4 to 10 months after receiving primary vaccination. Due to the size of the safety database for VidPrevtyn Beta, uncommon adverse reactions (≥ 1/1,000 to < 1/100) may not be detected. The median duration of safety follow-up was 145 days, with 610 (86.5%) participants completing more than 2 months safety follow-up after booster injection.

The most common adverse reactions with VidPrevtyn Beta were injection site pain (76.2%), headache (41.4%), myalgia (37.8%), malaise (33.0%), arthralgia (28.7%), and chills (19.9%).

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.

Supportive safety data were collected in 7093 participants 18 years of age and older having received primary or booster vaccine formulation containing the same Beta antigen (monovalent (B.1.351)/ bivalent (B.1.351 + D614)) and AS03 adjuvant. In general, the safety profile based on these supportive data is in accordance with the most common adverse reactions detected based on the VidPrevtyn Beta safety database (N=705). The majority of these participants received primary immunisation with bivalent (B.1.351 + D614) vaccine.

Tabulated list of adverse reactions

Adverse reactions observed during clinical studies are listed below according to the following frequency convention: 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).

Within each System Organ Class, adverse reactions are presented in order of decreasing frequency and then by decreasing seriousness (Table 1).

Table 1: Adverse reactions

MedDRA System Organ Class	**Frequency**	**Adverse reaction**
Blood and lymphatic system disorders	Uncommon	Lymphadenopathy
Nervous system disorders	Very common	Headache
Gastrointestinal disorders	Common	Nausea Diarrhoea
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
General disorders and administration site conditions	Very common	Malaise Chills Injection site pain
	Common	Fever Fatigue Injection site swelling Injection site erythema
	Uncommon	Injection site pruritus Injection site bruising Injection site warmth

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 Medicines and Healthcare products Regulatory Agency (MHRA), Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There is no specific treatment for an overdose with VidPrevtyn Beta. 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
VidPrevtyn Beta is an adjuvanted vaccine composed of the soluble trimeric SARS-CoV-2 recombinant spike (S) protein (B.1.351 strain) stabilised in its prefusion conformation and deleted of its transmembrane and intracellular domains. The combination of antigen and adjuvant enhances the magnitude of immune response, which may contribute to protection against COVID-19.

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

The clinical immunogenicity of VidPrevtyn Beta given as a first booster injection is being evaluated in two clinical studies: VAT00013 (Study 1) in COVID-19 mRNA vaccine-primed participants and VAT00002 Cohort 2, Beta arm (Study 2) that included participants primed with various types of COVID-19 vaccines.

Immunogenicity results from Study 1
Study 1 is a randomised, single-blinded multicentre investigator-initiated clinical study, which evaluated the immune response induced by a booster dose of either VidPrevtyn Beta or COVID-19 mRNA vaccine (nucleoside modified/tozinameran) in individuals previously vaccinated with 2 doses of COVID-19 mRNA vaccine (tozinameran). The per-protocol analysis population included 143 participants 18 years of age and older primed with 2 doses of COVID-19 mRNA vaccine (tozinameran) 3 to 7 months prior to receiving VidPrevtyn Beta (N=67) or COVID-19 mRNA vaccine (tozinameran) (N=76). The mean age was comparable across groups with 41.4 and 40.4 years for VidPrevtyn Beta and COVID-19 mRNA vaccine (tozinameran), respectively. Age ranged from 20.0 to 69.0 years. The mean duration between the second dose of the primary series and the booster dose was comparable across groups, being 171.0 and 174.5 days for VidPrevtyn Beta and COVID-19 mRNA vaccine (tozinameran), respectively.

Among this per-protocol population, samples from prior to vaccination and 28 days after booster of 114 participants (54 from VidPrevtyn Beta and 60 from COVID-19 mRNA vaccine (tozinameran)) were tested by Pseudovirus Neutralisation Assay. The Geometric Mean Titers (GMT) of neutralising antibodies 28 days after VidPrevtyn Beta or COVID-19 mRNA vaccine (tozinameran) booster in COVID-19 mRNA vaccine-primed participants were compared.

Superiority of GMT against Omicron BA.1 was demonstrated for VidPrevtyn Beta group in comparison with COVID-19 mRNA vaccine (tozinameran) group, see Table 2.

Table 2: Post-booster GMT ratio for VidPrevtyn Beta versus COVID-19 mRNA vaccine (tozinameran) with individual neutralisation titres against Omicron BA.1 - 28 days post-booster dose – per-protocol analysis subset

VidPrevtyn Beta (N=54)			COVID-19 mRNA vaccine (tozinameran) (N=60)			VidPrevtyn Beta / COVID-19 mRNA vaccine (tozinameran)		
M	**GMT**	**(95% CI)**	**M**	**GMT**	**(95% CI)**	**GMT ratio**	**(95% CI)**	**Superiority demonstrated†**
54	1327.5	(1005.0; 1753.4)	58	524.0	(423.3; 648.6)	2.53	(1.80; 3.57)	Yes

M: number of participants with available data for the relevant endpoint;
N: number of participants in per-protocol analysis subset 28 days post-booster dose;
† Superiority is concluded if the lower limit of the 2-sided 95% Confidence Interval (CI) of the GMT ratio > 1.2.

Non-inferiority of seroresponse rate against Omicron BA.1 and D614G strains for VidPrevtyn Beta compared to COVID-19 mRNA vaccine (tozinameran) was demonstrated (see Table 3). Seroresponse rate was defined as a 4-fold or greater rise in serum neutralisation titre 28 days post-booster dose relative to pre-booster dose.

Table 3: Seroresponse rate (SR) for VidPrevtyn Beta versus COVID-19 mRNA vaccine (tozinameran) with individual neutralisation titre against Omicron BA.1 and D614G - 28 days post-booster dose - per-protocol analysis subset

	VidPrevtyn Beta (N=54)			COVID-19 mRNA vaccine (tozinameran) (N=60)			VidPrevtyn Beta / COVID-19 mRNA vaccine (tozinameran)		
	n/M	**SR (%)**	**(95% CI)**	**n/M**	**SR (%)**	**(95% CI)**	**Difference (%)**	**(95% CI)**	**Non-inferiority demonstrated†**
D614G	51/53	96.2	(87.0; 99.5)	55/59	93.2	(83.5; 98.1)	3.0	(-6.9;12.8)	Yes
Omicron BA.1	50/50	100.0	(92.9; 100.0)	51/53	96.2	(87.0; 99.5)	3.8	(-3.9;12.8)	Yes

M: number of participants with available data for the relevant endpoint;
N: number of participants in per-protocol analysis subset 28 days post-booster dose;
n: Number of participants who achieve seroresponse;
† Non-inferiority is concluded if the lower limit of the 2-sided 95% Confidence Interval (CI) of the difference in seroresponse rate between groups is > -10%.

Levels of neutralising antibody titres against D614G 28 days post-booster dose observed in VidPrevtyn Beta group were higher than in COVID-19 mRNA vaccine (tozinameran) group, with the GMT ratio of 1.43 (95%CI 1.06; 1.94), see Table 4.

Table 4: Neutralising antibody Geometric Mean Titres (GMT) against D614G - 28 days post-booster dose - per-protocol analysis subset

VidPrevtyn Beta			COVID-19 mRNA vaccine (tozinameran)			VidPrevtyn Beta / COVID-19 mRNA vaccine (tozinameran)	
N	**GMT**	**(95% CI)**	**N**	**GMT**	**(95% CI)**	**GMT Ratio**	**(95% CI)**
54	6459	(5103; 8174)	60	4507	(3695; 5498)	1.43	(1.06; 1.94)

N: number of participants in per-protocol analysis subset 28 days post-booster dose;
CI: Confidence Interval

Immunogenicity results from Study 2

VidPrevtyn Beta given as a booster is being evaluated in an ongoing multicentre phase 3 clinical study in participants 18 years of age and older. Per-protocol analysis population included 543 participants who received VidPrevtyn Beta 4 to 10 months after receiving primary vaccination with 2 doses of COVID-19 mRNA vaccine (tozinameran) (n=325) or COVID-19 mRNA Vaccine (nucleoside modified/elasomeran) (n=93), COVID-19 Vaccine (ChAdOx1-S [recombinant]) (n=94), or with 1 dose of COVID-19 vaccine (Ad26.COV2-S [recombinant]) (n=31).

In the per-protocol analysis population primed with mRNA vaccines and receiving VidPrevtyn Beta booster, the mean age of participants was 41.2 years (range 18-83 years); 347 (83.0%) were 18 to 55 years of age, 71 (17.0%) were 56 years of age and older, 25 (6.0%) were 65 years of age and older. Among them, 44.0% were male, 56.0% were female, 67.7% were White, 13.2% were Black or African American, 2.6% were Asian, and 1.0% were American Indian or Alaska Native.

In the per-protocol analysis population primed with adenoviral vector vaccines and receiving VidPrevtyn Beta booster, the mean age of participants was 50.4 years (range 24-77 years); 84 (67.2%) were 18 to 55 years of age, 41 (32.8%) were 56 years of age and older, 17 (13.6%) were 65 years of age and older. Among them, 52.8% were male, 47.2% were female, 78.4% were White, 13.6% were Black or African American, 4.0 % were Asian, and 2.4% were American Indian or Alaska Native.

Immunogenicity was assessed by measuring neutralising antibody titres (ID50) against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate with the D614G mutation and B.1.351 variant using a SARS-CoV-2 Pseudovirus Neutralisation Assay.

A booster response to VidPrevtyn Beta was demonstrated regardless of the vaccine used for primary vaccination with the Geometric Mean Titres Ratio (GMTR, fold increase) 14 days post-booster relative to pre-booster against B.1.351 strain ranging from 38.5 to 72.3, and from 14.5 to 28.6 for D614G strain, see Table 5.

Table 5: Neutralising antibody Geometric Mean Titres (ID50) at 14 days post-booster dose and Geometric Mean Titres Ratio (14 days post-booster dose relative to pre-booster dose) against a pseudovirus expressing the SARS-CoV-2 Spike protein in participants 18 years of age and older - per-protocol analysis set

	mRNA primed[1] (N=418)			**Ad-vector primed[2] (N=125)**		
Pre-booster GMT						
	M	**GMT**	**(95% CI)**	**M**	**GMT**	**(95% CI)**
D614G	407	751	(633; 892)	118	228	(159; 325)
Beta	383	191	(158; 231)	117	69.9	(50.3; 97.2)
GMT at 14 days post-booster dose						
	M	**GMT**	**(95% CI)**	**M**	**GMT**	**(95% CI)**
D614G	418	10814	(9793; 11941)	125	6565	(5397;7986)
Beta	418	7501	(6754; 8330)	124	5077	(4168; 6185)
GMT ratio - 14 days post-booster dose relative to pre-booster dose						
	M	**GMTR**	**(95% CI)**	**M**	**GMTR**	**(95% CI)**
D614G	407	14.5	(12.2;17.2)	118	28.6	(21.1;38.9)
Beta	383	38.5	(31.8; 46.6)	116	72.3	(52.4; 99.8)

M: number of participants with available data for the relevant endpoint;
N: number of participants in per-protocol analysis set
CI: Confidence Interval
ID50- serum dilution conferring 50% inhibition of pseudovirus infection
GMTR (geometric mean titre ratio): geometric mean of individual titre ratios (post-vaccination/pre-vaccination)
[1-2] - Priming vaccines: [1-] COVID-19 mRNA vaccine (tozinameran) and COVID-19 mRNA vaccine (elasomeran); [2] - COVID-19 Vaccine (ChAdOx1-S [recombinant]) and COVID-19 vaccine (Ad26.COV2-S [recombinant])

Paediatric population

The licensing authority has deferred the obligation to submit the results of studies with VidPrevtyn Beta in one or more subsets of the paediatric population in 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 and toxicity to reproduction and development.

Genotoxicity and carcinogenicity
No genotoxicity was observed for the adjuvant based on *in vitro* and *in vivo* tests. Genotoxicity of the antigen was not evaluated, as its biological nature is not expected to have genotoxic potential. Carcinogenicity studies were not performed.

Reproductive toxicity and fertility
In a developmental and reproductive toxicity study, 0.5 mL of a vaccine formulation containing up to 15 micrograms (three human doses) of recombinant protein adjuvanted with AS03 was administered to female rabbits by intramuscular injection on five occasions: 24 and 10 days prior to mating and on gestation days 6, 12 and 27. No vaccine-related adverse effects on female fertility, embryo/fetal or postnatal development were observed up to postnatal day 35. In this study, high S-specific anti-SARS-CoV-2 IgG response was detected in maternal animals, as well as in fetuses and pups, indicating placental transfer of the maternal antibodies. No data are available on vaccine excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Antigen vial
Sodium dihydrogen phosphate monohydrate
Disodium phosphate dodecahydrate
Sodium chloride
Polysorbate 20
Water for injections

Adjuvant vial
Sodium chloride
Disodium hydrogen phosphate
Potassium dihydrogen phosphate
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

1 year.

After mixing, the product should be used within 6 hours, if stored at 2°C – 8°C and **protected from light.**

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 mixing of the medicinal product, see section 6.3.

6.5 Nature and contents of container

VidPrevtyn Beta is presented as:

- 2.5 mL antigen solution in a multidose vial (type 1 glass) with a stopper (chlorobutyl) and an aluminium seal with a green plastic flip-off cap;
- 2.5 mL adjuvant emulsion in a multidose vial (type 1 glass) with a stopper (chlorobutyl) and an aluminium seal with a yellow plastic flip-off cap.

Each pack contains: 10 multidose antigen vials and 10 multidose adjuvant vials.

6.6 Special precautions for disposal and other handling

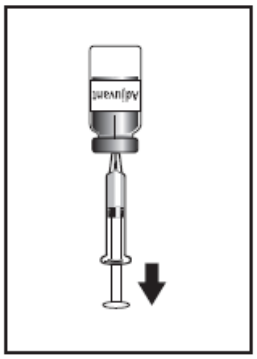
Handling instructions
This vaccine should be handled by a healthcare professional using aseptic technique to ensure the sterility of each dose.

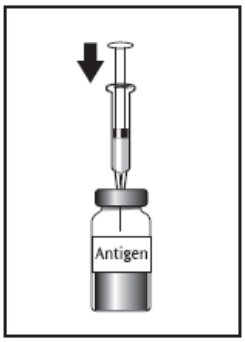
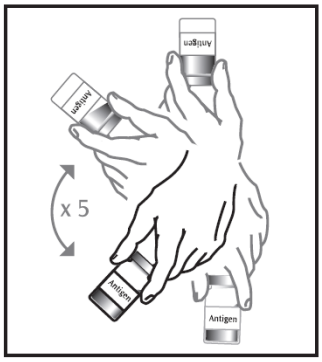
Instructions for mixing
VidPrevtyn Beta is supplied as 2 separate vials: an antigen vial and an adjuvant vial.
Prior to administration, the two components must be mixed as per steps below.

Step 1: Place the vials at room temperature (up to 25 °C) for a minimum of 15 minutes before mixing, **protecting them from light.**

Step 2: Invert (without shaking) each vial and inspect them visually for any particulate matter or discolouration. If either of these conditions exist, do not administer the vaccine.

Step 3: After removing the flip-off caps, cleanse both vial stoppers with antiseptic swabs.

Step 4  **Vial 2 of 2**	Using a sterile 21-gauge or narrower needle and a sterile syringe, withdraw the entire contents from the adjuvant vial (yellow cap) into a syringe. Invert the adjuvant vial to facilitate the withdrawal of the full contents.

Step 5  **Vial 1 of 2**	Transfer the full syringe contents into the antigen vial (green cap).
Step 6  **Vial 1 of 2**	Remove the syringe with the needle from the antigen vial. Mix the contents by inverting the vial 5 times. Do not shake. The mixed vaccine is a whitish to yellowish homogeneous milky liquid emulsion.

Step 7: Record the discard date and time (6 hours after mixing) on designated area of vial label.

The volume of the vaccine after mixing is at least 5 mL. It contains 10 doses of 0.5 mL.
An additional overfill is included in each vial to ensure that 10 doses of 0.5 mL can be delivered.

After mixing, administer immediately or store the vaccine at 2°C to 8°C, **protected from light**, and use within 6 hours (see section 6.3). After this time period, discard the vaccine.

Preparation of individual doses
Prior to each administration, mix the vial thoroughly by inversion 5 times. Do not shake.
Visually inspect it for any particulate matter and discolouration (see Step 6 for the aspect of the vaccine). If either of these conditions exists, do not administer the vaccine.

Using appropriate syringe and needle, withdraw 0.5 mL from the vial containing the mixed vaccine and administer intramuscularly (see section 4.2).

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

7. MARKETING AUTHORISATION HOLDER

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69007 Lyon
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Distributed in the UK by:

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8. MARKETING AUTHORISATION NUMBER(S)

PLGB 46602/0028

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20/12/2022

10. DATE OF REVISION OF THE TEXT