AUSTRALIAN PRODUCT INFORMATION – JESPECT® [INACTIVATED JAPANESE ENCEPHALITIS VACCINE (ADSORDED)] SUSPENSION FOR INJECTION

1 NAME OF THE MEDICINE

Inactivated Japanese Encephalitis Vaccine (adsorbed).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

JESPECT® Japanese Encephalitis (JE) Virus, purified inactivated vaccine is a sterile, ready to use suspension for intramuscular (IM) injection. The vaccine is prepared by propagating Japanese encephalitis virus strain (SA_{14}-14-2) in Vero cells. No preservatives or antibiotics are added to the formulation.

JESPECT® is a clear liquid with white precipitate and when shaken before use a white/cloudy suspension forms. JESPECT® is supplied in pre-filled syringes without needles. Each 0.5 mL dose of vaccine contains 6 antigen units (AgU) of purified, inactivated JE virus. Each dose of vaccine also contains the following excipients: 0.1% aluminium hydroxide, hydrated corresponding to 0.25 mg aluminium, and Phosphate Buffered Saline.

3 PHARMACEUTICAL FORM

JESPECT® is supplied as a 0.5 mL suspension in a pre-filled syringe (Type I glass) with a plunger stopper (chlorobutyl elastomer) in a pack size of 1 needle-less syringe.

To attach needle, remove the syringe cap by gently twisting it. Do not attempt to snap or pull the tip off as this may damage the syringe.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

JESPECT® is indicated for active immunisation against Japanese Encephalitis (JE) virus for persons 18 years of age and older.

JESPECT® should be considered for use in persons who plan to reside in or travel to areas where JE is endemic (common) or epidemic (seasonal), especially during the transmission season.

JESPECT® is indicated for persons who work with JE virus in laboratories and in industry.

4.2 DOSE AND METHOD OF ADMINISTRATION

Primary vaccination

The primary vaccination series consists of a total of two doses of 0.5 mL each according to the following schedule:

- First dose at Day 0 (elected date).
- Second dose: 28 days after first dose.

It is recommended that persons who receive the first dose of JESPECT® complete the 2-dose primary vaccination course.

If the primary immunisation schedule of 2 doses is not completed, sufficient protection against Japanese encephalitis virus might not be achieved. Clinical trial data indicates that administration of the second dose up to 11 months after the first dose results in high seroconversion rates (see **5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials**, Incomplete primary immunisation).

Booster dose

Refer to **Clinical trials** for clinical trial data for potential booster doses.

The vaccine should be inspected visually for the particulate matter and discolouration prior to administration. Discard the product if particulates are present, if it appears discoloured or if the syringe appears to be physically damaged. Any unusual product or waste material should be disposed of in accordance with local requirements.

JESPECT® should be well shaken before administration to obtain a homogenous suspension. Once shaken, the vaccine should appear as a white cloudy suspension.

JESPECT® should be administered by IM injection into the deltoid muscle. It should never be injected IV.

In exceptional circumstances, for those patients with thrombocytopenia or bleeding disorders where bleeding may occur following IM administration, JESPECT® may be administered subcutaneously. Subcutaneous administration could lead to a suboptimal response to the vaccine.

JESPECT® pre-filled syringe is for single use only in one individual only. Inject the entire contents of the syringe.

4.3 CONTRAINDICATIONS

JESPECT® should not be administered to individuals who have previously experienced a serious reaction (e.g. anaphylaxis) to this vaccine or who are known to be hypersensitive to any of the vaccine components or to the residues protamine sulphate, formaldehyde, bovine serum albumin, host cell DNA, sodium metabisulphite or host cell protein. Individuals who show hypersensitivity reactions after receiving the first dose of the vaccine should not be given the second dose.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

As with other injectable vaccines, appropriate medical treatment and supervision should always be available in the event of anaphylactic reaction. Adrenaline should always be readily available whenever the injection is given.

JESPECT® will not protect against encephalitis caused by other organisms. As with any other vaccine, vaccination with JESPECT® may not result in protection in all cases. The primary vaccination series (2 doses) should be completed at least one week prior to potential exposure to Japanese Encephalitis virus. Seroconversion rates after one dose are limited (see **Clinical trials**, Table 3).

JESPECT® should be administered by IM injection into the deltoid muscle. It should never be injected IV. In exceptional circumstances, for those patients with thrombocytopenia or bleeding disorders where bleeding may occur following IM administration, JESPECT® may be administered subcutaneously. Subcutaneous administration could lead to a suboptimal response to the vaccine (see **4.2 DOSE AND METHOD OF ADMINISTRATION**).

As with other vaccines, JESPECT® should not be administered in persons with acute severe febrile illness.

Safety and efficacy of JESPECT® have not been established in persons with a history of flavivirus (including JE virus, Yellow Fever virus, Dengue virus and Murray Valley encephalitis virus) infection and/or vaccination against JE or Yellow fever (see **4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**).

Paediatric use

The safety and efficacy of JESPECT® in persons under 18 years of age have not been established.

Use in the elderly

Special studies in the geriatric population have not been performed; however, JESPECT® has been administered to 118 subjects ≥ 65 years of age. No overall differences in safety and effectiveness were observed between these subjects and younger subjects.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Concomitant administration of JESPECT® with inactivated hepatitis A vaccine (HAVRIX® 1440) has been explored in one clinical trial (study IC51-308). There was no interference with the immune response to the JE virus and HAV, respectively (see **5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials**).

Vaccination with JESPECT® in persons with vaccine induced tick born encephalitis (TBE) antibodies resulted in comparable SCR and GMT at Day 56 compared to TBE naive persons.

Vaccination with JESPECT® concurrently with or after administration of other flavivirus vaccines (including yellow fever vaccine) has not been assessed.

If co-administration with other vaccines is indicated, injections should be given into separate limbs. It should be noted that adverse reactions might be intensified.

In patients receiving immunosuppressive therapy or patients with immunodeficiency an adequate immune response may be diminished.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No significant effects on mating performance or fertility were observed in vaccine treated rats administered with IM JESPECT® prior to mating (3 weeks (regimen 1 only) and 1 week) during gestation (day 6). The effect of JESPECT® administration on male fertility has not been evaluated (see also Use in Pregnancy).

Use in pregnancy – Pregnancy Category B1

In a three phase reproductive study of female rats administered approximately the clinical IM dose of JESPECT® (5 µg) prior to mating (3 weeks (regimen 1 only) and 1 week) and during gestation (day 6), there were no significant toxicological effects in the dams. High JEV-specific antibody titres were detected in maternal blood during gestation (day 5 and 20) in fetal cord blood and at the end of gestation (day 20), and in pups at weaning (lactation day 21).

In a reproductive and pre-/post-natal toxicity study, no vaccine-related effects were detected on reproduction, foetal weight, survival and development of the off-springs. However, incomplete ossification of parts of the skeleton was observed in the group receiving 2 doses, but not in the group receiving 3 doses. There is currently no evidence that this phenomenon is treatment related.

There are limited data from the use of JESPECT® in pregnant women. The vaccine should be used during pregnancy only when clearly needed and the possible advantages outweigh the possible risks for the fetus.

Use in lactation

It is not known whether vaccine antigens or antibodies induced by the vaccine are excreted in human milk. Therefore, caution should be exercised when JESPECT® is administered to a nursing woman.

In a three phase reproductive study of maternal treatment of rats with IM JESPECT® prior to mating and during gestation, assessed to lactation day 21, high JEV-specific antibody titres were detected in maternal blood during gestation, in fetal cord blood at the end of gestation and in pups at weaning (see also **Use in pregnancy – Pregnancy Category B1**).

Adequate human data on JESPECT® use during lactation are not available. JESPECT® should be administered to women who are breastfeeding only when clearly needed.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive and use machines have been performed.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The safety of JESPECT® has been assessed in different controlled clinical trials in which more than 5,405 healthy adults were included of which 4,248 healthy adults received the vaccine.

Approximately 40% of treated subjects can be expected to experience adverse reactions. They usually occur within the first three days after vaccination, are usually mild and disappear within a few days. No increase in the number of undesirable reactions was noted between first and second doses. The incidence of systemic and local symptoms was less prominent after the second vaccination.

Most commonly reported adverse reactions included headache and myalgia occurring in approximately 20% and 13% of subjects, respectively. The treatment-related, treatment-emergent adverse events seen in clinical trials are described in Table 1.

Table 1 Treatment-Related Treatment-Emergent Adverse Events: Pooled Safety Population

TEAE system organ class and preferred term	JESPECT® N=4043[1]		Placebo N=657[2]	
	n	(%)	n	(%)
Any treatment-related TEAE[3]	**1557**	**(38.5)**	**255**	**(38.8)**
Nervous system disorders	**806**	**(19.9)**	**135**	**(20.5)**
Headache	779	(19.3)	132	(20.1)
Dizziness	16	(0.4)	4	(0.6)
Migraine	11	(0.3)	0	(0)
Paraesthesia	6	0.2	0	(0)
General disorders and administration site conditions[4]	**738**	**(18.3)**	**119**	**(18.1)**
Fatigue	395	(9.8)	65	(9.9)
Influenza-like illness	363	(9.0)	57	(8.7)
Pyrexia	84	(2.1)	15	(2.3)
Chills	5	(0.1)	3	(0.5)
Malaise	5	(0.1)	0	(0)
Oedema peripheral	1	(0.02)	0	(0)
Injection site reactions				
Injection site haemorrhage	12	(0.3)	0	(0)
Injection site bruising	27	(0.7)	1	(0.2)

Musculoskeletal and connective tissue disorders	**541**	**(13.4)**	**101**	**(15.4)**
Myalgia	524	(13.0)	94	(14.3)
Muscoskeletal stiffness	5	(0.1)	0	(0)
Pain in extremity	3	(0.1)	0	(0)
Arthralgia	2	(0.1)	0	(0)
Gastrointestinal disorders	**228**	**(5.6)**	**40**	**(6.1)**
Nausea	193	(4.8)	37	(5.6)
Vomiting	27	(0.7)	7	(1.1)
Diarrhoea	23	(0.6)	4	(0.6)
Abdominal pain	4	(0.1)	0	(0)
Infections and infestations	**76**	**(1.9)**	**10**	**(1.5)**
Nasopharyngitis	33	(0.8)	4	(0.6)
Rhinitis	15	(0.4)	1	(0.2)
Skin and subcutaneous tissue disorders	**59**	**(1.5)**	**8**	**(1.2)**
Rash	39	(1.0)	4	(0.6)
Pruritus	4	(0.1)	1	(0.2)
Erythema	3	(0.1)	0	(0)
Urticaria	1	(0.02)	0	(0)
Respiratory, thoracic and mediastinal disorders	**32**	**(0.8)**	**8**	**(1.2)**
Pharyngolaryngeal pain	14	(0.4)	5	(0.8)
Dyspnoea	2	(0.1)	0	(0)
Investigations	**34**	**(0.8)**	**3**	**(0.5)**
Increased hepatic enzymes	9	(0.2)	0	(0)
Ear and labyrinth disorders	**18**	**(0.4)**	**1**	**(0.2)**
Vertigo	16	(0.4)	1	(0.2)
Cardiac disorders	**6**	**(0.2)**	**0**	**(0)**
Palpitations	2	(0.1)	0	(0)
Tachycardia	2	(0.1)	0	(0)
Blood and lymphatic system disorders	**19**	**(0.5)**	**5**	**(0.8)**
Lymphadenitis	2	(0.1)	0	(0)
Lymphadenopathy	8	(0.2)	0	(0)
Thrombocytopaenia	1	(0.02)	0	(0)

[1]Data taken from different pooled analyses of clinical trials

[2]Placebo was Phosphate Buffered Saline +aluminum hydroxide adjuvant

[3]Events with a causality reported as probable or possible or with a missing classification were considered related to study medication.

[4]Only injection site reactions not solicited in subject diaries are displayed here. For solicited local reactions see Table 2.

Abbreviations: N=number of subjects in group; n=number of subjects with event; %=percentage of subjects based on number of subjects in the group; TEAE=treatment-emergent adverse event.

The incidence of local symptoms from a pooled safety population is described in Table 2. Please note the results are from subject diary cards on the day of first and second vaccination.

Table 2 Subject Diary Local Tolerability on Day of Vaccination: Pooled Safety Population

Symptom	Vaccination	JESPECT® N=4043[1]		Placebo N=657[2]	
		n	(%)	n	(%)
Any symptom	First (Day 0)	1342	(35.3)	219	(34.1)
	Second (Day 28)	823	(25.1)	192	(27.6)
Local pain	First	768	(20.2)	129	(20.1)
	Second	469	(13.0)	112	(16.1)
Local tenderness [3]	First	693	(19.3)	120	(18.7)
	Second	570	(16.2)	110	(15.8)
Redness	First	174	(4.6)	17	(2.6)
	Second	116	(3.2)	24	(3.5)
Hardening	First	144	(3.8)	19	(3.0)
	Second	114	(3.2)	17	(2.4)
Swelling	First	82	(2.2)	11	(1.7)
	Second	67	(1.8)	11	(1.6)
Itching	First	36	(1.0)	10	(1.6)
	Second	33	(1.0)	11	(1.6)

[1]Data taken from different pooled analyses of clinical trials

[2]Placebo was Phosphate Buffered Saline +aluminum hydroxide adjuvant

[3] Tenderness was not assessed in study IC51-304, included in the pooled safety population.

Abbreviations: N=number of subjects in group; n=number of subjects with event; %=percentage of subjects based on number of subjects in the respective treatment group with a response (yes/no).

Post marketing experience

The following adverse events have been reported during post marketing use of JESPECT®. Because these events are reported voluntarily, it is not possible to estimate frequency.

Nervous system disorders: paraesthesia, neuritis, syncope.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 Overdose

There have been no cases of overdosage reported.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

No data available.

Clinical trials

Efficacy (immunogenicity) of JESPECT® has been studied in approximately 2,228 healthy, adult subjects in 10 multi-centre clinical trials conducted in the US and Europe.

Immunogenicity of the vaccine was evaluated in a randomized, active-controlled, observer-blinded, multicenter Phase 3 clinical trial (trial IC51-301) conducted in the US, Germany and Austria in healthy male and female subjects ≥ 18 years of age (mean age: 41.3 years; 60.8% female; race: Caucasian 80.8%, Asian 0.8%, Black/African American 13.1%, and Other 5.3%). Subjects were randomised to receive either two separate doses of 6 µg/0.5 mL of JESPECT® (on a 0, 28-day schedule by IM injection) (n = 430) or three separate doses of 1.0 mL of the JE vaccine JE-VAX® (on a 0, 7 and 28 day schedule by subcutaneous injection) (n = 437). The co-primary endpoint was seroconversion rate (anti-JE virus antibody titer ≥1:10) and geometric mean titer (GMT) at Day 56 as assessed by a Plaque Reduction Neutralisation Test (PRNT) for the entire study population.

By Day 56, the proportion of subjects who had seroconverted was similar for both treatment groups (96.4% vs. 93.8% for JESPECT® and JE-VAX®, respectively) (Table 3). Geometric mean titers increased by Day 56 to 243.6 for JESPECT® and to 102.0 for JE-VAX®, respectively. The immune responses elicited by JESPECT® were non-inferior to those induced by JE-VAX® (Table 3).

Table 3 Seroconversion Rates and Geometric Mean Titers of JESPECT® and JE-VAX® in per protocol population (trial IC51-301)

Seroconversion Rate			
Timepoint	**JESPECT® N=365 n (%)**	**JE-VAX® N=370 n (%)**	**Risk difference estimator [95% CI]**
Visit 0 (Screening)	0	0	
Visit 3 (Day 28)	197 (54)	321 (86.8)	
Visit 4 (Day 56)	352 (96.4)	347 (93.8)	1.05 [-1.33, 3.43]
Geometric Mean Titer (GMT) (by Plaque Reduction Neutralisation Test)			
Timepoint	**JESPECT® N=365 n (GMT)**	**JE-VAX® N=370 n (GMT)**	**GMT ratio estimator [95% CI]**
Visit 0 (Screening)	365 (5.0)	370 (5.0)	
Visit 3 (Day 28)	363 (17.4)	367 (76.9)	
Visit 4 (Day 56)	361 (243.6)	364 (102.0)	2.3257 [1.9666, 2.7505]

The effect of age on the immune response to JESPECT® and JE-VAX® was assessed as a secondary endpoint (trial IC51-301), comparing subjects 50 years of age or older (N = 262, mean age 59.8) with those below 50 years of age (N = 605, mean age 33.9). There was no significant difference between seroconversion rates of JESPECT® and JE-VAX® in subjects aged <50 years compared to those aged ≥50 years at Day 28 or Day 56 following vaccination. Geometric mean titers were significantly higher at Day 28 in subjects aged <50 years than those aged ≥50 years in the JE-VAX® group (80.9 vs. 46.9, p=0.0236) but there was no significant difference at Day 56 for this treatment group. In addition there were no significant effects of age on GMT in the group receiving JESPECT® and no significant difference between seroconversion rates in subjects aged <50 years compared to those aged ≥50 years at Day 28 or Day 56 for either treatment group.

Antibody persistence

Antibody persistence was assessed in an uncontrolled Phase 3 follow-up clinical trial (trial IC51-303) of subjects who completed the pivotal immunogenicity study (trial IC51-301) or the pivotal safety study (trial IC51-302), and who received at least one dose of JESPECT®. The primary objective of the study was the evaluation of the immune response (seroconversion rate) to JESPECT® 24 months after the first vaccination. Secondary objectives included the evaluation of the immune response to JESPECT® 6, 12, 24 and 36 months after the first vaccination and to evaluate the safety of JESPECT® during the

respective study period (see **4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)**. A total of 3,258 healthy male and female subjects were enrolled (mean age: 35.6 years, 56.5% female, race: Caucasian 90.2%, Asian 1.7%, Black/African American 4.9%, Other 3.2%) of which 2,283 subjects received JESPECT®, 338 subjects received JE-VAX®, and 637 subjects received placebo in the respective previous study. Long-term immunogenicity to JESPECT® was assessed in a subset of 181 subjects up to 24 months, and a subset of 152 subjects at 36 months (ITT population). Immunogenicity data covering a period up to 36 months after the first vaccination are described below:

Seroconversion rates for anti-JE virus antibodies at Months 2, 6, 12, 24 and 36 are summarized in Table 4 for the ITT population. At Month 2, 98.9% of subjects had seroconverted (95% CI: 96.06, 99.70), at Month 6 95.0% of subjects had seroconverted (95% CI: 90.82, 97.36). By Month 12, the percentage of subjects who had seroconverted was 83.4% (95% CI: 77.33, 88.14). Seroconversion at 24 months and 36 months was 81.8% (95% CI: 75.50, 86.71) and 84.9% (95% CI: 78.32, 89.70) respectively.

In the ITT2 population, which is a subset of the ITT population with positive PRNT results at Month 2, per definition, 100% of the subjects (N=179) had seroconverted at Month 2 (95% CI: 97.90%, 100.00%). By Month 6 and Month 12, the number of subjects of the ITT2 population who had seroconverted was 95.5% (95% CI: 91.43, 97.72) and 83.8% (95% CI: 77.70, 88.48) respectively (Table 4). The number of subjects of the ITT2 population who had seroconverted at 24 months was 82.1% ((95% CI: 75.85, 87.04) and at 36 months was 84.8% (95% CI: 78.18, 89.63).

Table 4 Seroconversion Rates at Month 2, 6, 12, 24 and 36 after Vaccination with JESPECT® (ITT and ITT2 Populations) (trial IC51-303)

Time		ITT Population		ITT2 Population	
		N=181 n (%)	95% Confidence Interval	N=179 n (%)	95% Confidence Interval
Month 2	Seroconverted Not seroconverted Missing	179 (98.9) 1 (0.6) 1 (0.6)	[96.06, 99.70]	179 (100)	[97.90, 100.00]
Month 6	Seroconverted Not seroconverted	172 (95.0) 9 (5.0)	[90.82, 97.36]	171 (95.5) 8 (4.5)	[91.43, 97.72]
Month 12	Seroconverted Not seroconverted	151 (83.4) 30 (16.6)	[77.33, 88.14]	150 (83.8) 29 (16.2)	[77.70, 88.48]
Month 24	Seroconverted Not seroconverted	148 (81.8) 33 (18.2)	[75.50, 86.71]	147 (82.1) 32 (17.9)	[75.85, 87.04]
		N=152 n (%)	95% Confidence Interval	N=151 n (%)	95% Confidence Interval
Month 36	Seroconverted Not seroconverted	129 (84.9) 23 (15.1)	[78.32, 89.70]	128 (84.8) 23 (15.2)	[78.18, 89.63]

Geometric mean titers at Months 2, 6, 12, 24 and 36 after vaccination with JESPECT® are summarized in Table 5. At Month 2, the GMT was 310.8 (95% CI: 268.76, 359.44) which decreased to 83.5 (95% CI: 70.89, 98.38) at Month 6 and to 41.2 (95% CI: 34.39, 49.33) at Month 12 after vaccination with JESPECT®. At Month 24 and 36, the GMT was 44.3 (95% CI: 36.72, 53.44) and 43.8 (95% CI: 36.49, 52.56) respectively.

Table 5 Geometric Mean Titers at Months 2, 6, 12, 24 and 36 after Vaccination with JESPECT® (ITT and ITT2 Populations) (trial IC51-303)

Time	ITT Population		ITT2 Population	
	N=181	95% Confidence Interval	N=179	95% Confidence Interval
Month 2	310.8	[268.76, 359.44]	318.1	[276.83, 365.43]
Month 6	83.5	[70.89, 98.38]	84.9	[72.18, 99.95]
Month 12	41.2	[34.39, 49.33]	41.6	[34.73, 49.87]
Month 24	44.3	[36.72, 53.44]	44.9	[37.15, 54.14]
	N=152	95% Confidence Interval	N=151	95% Confidence Interval
Month 36	43.8	[36.49, 52.56]	43.5	[36.21, 52.23]

The results were confirmed in the ITT2 population.

Vaccination with inactivated JE vaccine is known to produce antibodies that decline with time in a proportion of the vaccinated population. The observed decline in GMT is therefore as expected and compares well with data from other inactivated JE vaccines.

Results of another Phase 3 follow-up clinical trial (trial IC51-305) support these findings. In this study, 58.3% and 48.3% of subjects who received the recommended primary vaccination series (see **4.2 DOSE AND METHOD OF ADMINISTRATION**) showed persisting protective antibodies 12 and 24 months (respectively) after completion of primary vaccination. See also **Incomplete primary immunisation**.

Booster immunisation

The effect of booster vaccination of JESPECT® on long term immunogenicity was investigated in an uncontrolled, open label, Phase 3 clinical trial in healthy male and female adults (trial IC51-311). Subjects (n=198) were administered one 6 µg/0.5 mL dose of JESPECT® 15 months after their first dose (Day 0) of the recommended primary vaccination series (see **4.2 DOSE AND METHOD OF ADMINISTRATION)**. The primary endpoint was assessment of the effect of booster vaccination on immunogenicity in terms of seroconversion rate 12 months after administration of the booster dose (equivalent to 27 months after first dose (Day 0) of the recommended primary vaccination series). Secondary endpoints included assessment of seroconversion 28 days and 6 months after administration of the booster dose, and GMT 28 days, 6 months and 12 months after booster vaccination (equivalent to 16, 21 and 27 months after first dose (Day 0) of the recommended primary vaccination series).

Pre-booster vaccination, 69.2% of subjects had seroconverted and GMT was 22.5 (95% CI: 19.0, 26.7).

Seroconversion was 100% at 28 days after administration of the booster vaccination and remained high (98.5%) to 12 months after administration of the booster vaccination (equivalent to 27 months after first dose (Day 0) of the recommended primary vaccination series) (Table 6).

Geometric mean titers were highest 28 days after receiving the booster vaccination and declined to 361.4 after 12 months (equivalent to 27 months after first dose (Day 0) of the recommended primary vaccination series) (Table 6).

Table 6 Seroconversion rates and Geometric Mean Titers at Day 28 and Months 6 and 12 after Booster Vaccination with JESPECT® (ITT Population) (trial IC51-311)

	Seroconversion rate		**GMT**	
	%	95% CI		95% CI
Pre-booster (n=198)	69.2	[62.4, 75.2]	22.5	[19.0, 26.7]
Day 28 (n=198)	100.0	[98.1, 100.0]	900.1	[742.4, 1091.3]
Month 6 (n=197)	98.5	[95.6, 99.5]	487.4	[390.7, 608.1]
Month 12 (n=194)	98.5	[95.6, 99.5]	361.4	[294.5, 443.5]

Incomplete primary immunisation

Immunogenicity following incomplete primary vaccination was investigated in a non-randomized, open label, multicenter Phase 3 clinical trial (trial IC51-305) conducted in healthy male and female adults (n=349). Subjects received either the recommended primary vaccination schedule (see **4.2 DOSE AND METHOD OF ADMINISTRATION**); one 6 µg/0.5 mL dose of JESPECT® on Day 0 and a second 6 µg/0.5 mL dose of JESPECT® on Day 28) (n=116), or one single dose of 6 µg/0.5 mL dose of JESPECT® (on Day 0) (n=117), or one 12 µg/0.5 mL dose of JESPECT® (on Day 0) (n=116). Those subjects that were seronegative ($PRNT_{50}$ titers < 1:10) at Month 6 received a single 6 µg/0.5 mL booster dose at 11 months after the first dose (Day 0). Those subjects that were seronegative at Month 12 received a single 6 µg/0.5 mL booster dose at 23 months after the first dose (Day 0).

Administration of the second injection of the primary immunisation series up to 11 months after the first dose results in 99% seroconversion and GMT of 504.3 (95% CI 367.3, 692.3) (Table 7).

Table 7 **Seroconversion rates and Geometric Mean Titers 4 weeks after a single 6 µg/0.5mL booster dose is administered to subjects that are seronegative at Month 11 or Month 23 after complete primary immunisation (2 x 6 µg/0.5 mL) or incomplete primary immunisation (1 x 6 µg/0.5 mL)with JESPECT® (ITT Population) (trial IC51-305)**

	SCR (%)	GMT	
			95% CI
Complete primary immunisation (2 x 6 µg/0.5 mL dose)			
+Booster at Month 11 (n=17)	100	673.6	[378.7, 1198.2]
+ Booster at Month 23 (n=27)	100	2536.7	[1467.7, 4384.4]
Incomplete primary immunisation (1 x 6 µg/0.5 mL dose)			
+Booster at Month 11 (n=100)	99	504.3	[367.3, 692.3]
+Booster at Month 23 (n=5)	100	571.4	[88.2, 3702.9]

Concomitant use

The concomitant use of JESPECT® with inactivated Hepatitis A Virus (HAV) vaccine (HAVRIX® 1440) has been explored in one clinical trial (study IC51-308). There was no interference with the immune response to the JE virus and HAV, respectively. Concomitant administration of JESPECT® and inactivated hepatitis A vaccine was shown to be non-inferior to single vaccinations with regard to GMT of anti-JE virus neutralising antibody and HAV antibody, and for seroconversion rates of both antibody types.

5.2 PHARMACOKINETIC PROPERTIES

No data available

5.3 PRECLINICAL SAFETY DATA

Animal studies in mice, rats and rabbits have shown that the JESPECT® vaccine induces the immune system to produce neutralising antibodies against Japanese encephalitis virus which correlate with protection and survival. Mice treated with JESPECT® vaccine or human JESPECT® antisera demonstrated protection against lethal Japanese encephalitis challenge from several different (SA_{14}, Beijing and KE-093) strains in a generally dose- or titre-dependent manner, respectively.

Genotoxicity

JESPECT® has not been evaluated for genotoxic potential.

Carcinogenicity

JESPECT® has not been evaluated for carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Refer to Section 2 - Qualitative and quantitative composition

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store in a refrigerator at 2° to 8° C. **Do not freeze**. Store in the original package in order to protect from light.

Do not use if the package is torn or damaged.

Do not use the vaccine after the expiration date shown on the label.

Upon storage, a fine white deposit with a clear colourless supernatant can be observed.
Shake well before use.

6.5 NATURE AND CONTENTS OF CONTAINER

Packed in a pre-filled syringe (Type I glass) with a plunger stopper (chlorobutyl elastomer).

JESPECT® is available in a pack size of 1 needle-less syringe containing 0.5mL dose.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

No data available

CAS number

Not applicable

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

30 January 2009

10 DATE OF REVISION

12 October 2018

JESPECT® is a registered trademark of Valneva Scotland Ltd.

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
N/A	Product information reformatted as per the current TGA Form for providing product information
4.8	Adverse reaction ‘syncope’ is added to reflect the change in the SmPC informed by the Licensor
10	Date of revision updated