Amsterdam, 16 October 2025
EMADOC-1700519818-2373718
Human Medicines Division

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006

Maviret

International non-proprietary name: Glecaprevir / Pibrentasvir

Procedure no.: EMA/PAM/0000291196

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	22 September 2025	19 September 2025
☐	CHMP comments	6 October 2025	6 October 2025
☐	Updated CHMP Rapporteur AR	9 October 2025	N/A
☒	CHMP outcome	16 October 2025	16 October 2025

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1. Introduction

On 30 July 2025, the MAH submitted a completed paediatric study for Maviret, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

Study P19-620 was conducted based on the GPSP Ordinance (Good Post-marketing Study Practice; Ministerial Ordinance No. 171 of the Ministry of Health, Labour and Welfare dated December 20, 2004).

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

Maviret is currently marketed and approved for the treatment of chronic hepatitis C virus (HCV) infection in adults and children aged 3 years and older.

The MAH stated that Study P19-620 is part of the clinical development program, generating additional effectiveness and safety data in daily practice in paediatric and adolescent patients infected with HCV in Japan.

2.2. Information on the pharmaceutical formulation used in the study<ies>

Two pharmaceutical formulations of Maviret exist:

- 100 mg glecaprevir and 40 mg pibrentasvir. film-coated tablets for adults, adolescents aged 12 years and older, or children weighing at least 45 kg
- 50 mg glecaprevir and 20 mg pibrentasvir. coated granules in sachets for children aged 3 years to less than 12 years and weighing 12 kg to less than 45 kg

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for Study P19-620 entitled "Real World Evidence of the Safety and Clinical Practice Use of Maviret in Pediatric and Adolescents Patients Infected with Chronic Hepatitis C virus (All case survey)".

2.3.2. Clinical study

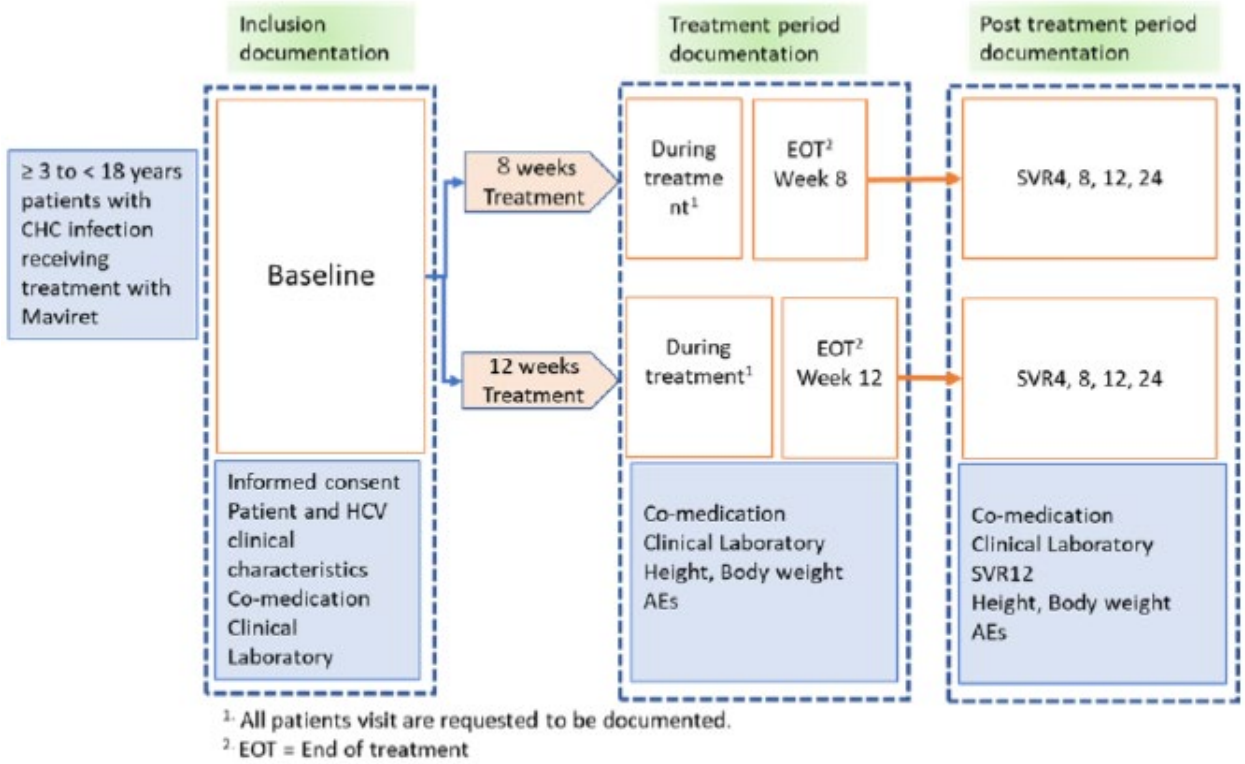
Study P19-620

Description

Study P19-620 was a prospective, central registration, multi-center observational study in pediatric (≥ 3 to < 12 years) and adolescent (≥ 12 to < 18 years) patients with chronic hepatitis C receiving Maviret.

Study period: 27 November 2020 to 26 September 2024

Figure 1 Study design



The prescription of a treatment regimen was in accordance with local label, was made independently from this observational study and preceded the decision to offer the patient the opportunity to participate in this study.

This study focused on collecting real-world data. Follow-up visits, treatment, procedures and diagnostic methods were followed in physicians' routine clinical practice.

Methods

Study participants

Patients with chronic HCV infection treated with Maviret in daily practice, who were ≥ 3 to < 18 years of age at start of Maviret treatment.

Treatments

The dosage and administration followed the dosage and administration described in the package insert.

Objectives and endpoints

Research question: What is the safety of Maviret in pediatric and adolescent patients with chronic hepatitis C (CHC) in a real world setting across clinical practice patient populations in Japan?

The objective of this study was to evaluate the safety and effectiveness of Maviret in pediatric and adolescent patients infected with HCV in daily practice as mandated by the Japanese regulatory authority.

- *The primary objective*: To describe the safety of Maviret in overall and subpopulations of interest.

- *Secondary objectives*: To describe in routine clinical practice the effectiveness of Maviret overall and by subpopulations of interest (e.g. HCV genotype, prior treatment experience, absence of cirrhosis/ presence of cirrhosis.) as evidenced by SVR12, to describe the percentage of patients achieving SVR at 4, 8, and 24 weeks after the last actual dose of Maviret, to describe the percentage of patients with on-treatment virologic failure (non-response, breakthrough), and to describe the percentage of patients with after-treatment virologic failure (relapse).

Endpoints

Primary Endpoint

The number and percentage of patients with ADRs in overall and subpopulations of interest. (Events were coded and tabulated by MedDRA SOC and PT). If any patients who developed "HBV reactivation" and "Hepatic dysfunction and Jaundice" were observed, the seriousness, onset, etc. were also analyzed.

Secondary Endpoint

1. The percentage of patients achieving SVR12 in effectiveness population and subpopulations of interest.

2. The percentage of patients achieving SVR at 4, 8 and 24 weeks after the last actual dose of Maviret in effectiveness population and effectiveness population in accordance with approved local label.

3. The percentage of patients with on-treatment virologic failure (non-response, breakthrough).

4. The percentage of patients with after-treatment virologic failure (relapse).

Statistical Methods

Descriptive and exploratory statistical methods were used to analyze the data of the study.

All baseline and disease characteristics were summarized for the safety population and effectiveness population stratified by the analysis groups based on HCV genotype/subtype and cirrhosis status, which are relevant for scheduled treatment duration (8 or 12 weeks).

Subgroup analysis by formulation (tablet or sachet) and age (pediatric group who are ≥ 3 to < 12 years old and adolescent group who are ≥ 12 to < 18 years old) was also executed.

ADRs or SAEs are described in the table with number, rate and 95% CI. SVR12 is described in the table with number, rate and 95% CI. The percentage of patients achieving SVR12 is described with the 95% CI using Wilson's score method.

Further details of analysis populations were specified in the statistical analysis plan (SAP). All safety variables were summarized for patients in the safety population using descriptive statistical methods stratified by the scheduled treatment duration.

Results

Participant flow

A total of 103 subjects with chronic hepatitis C were enrolled into this observational study in Japan.

Recruitment

Inclusion criteria

Patients who met the following inclusion criteria were included in this study:

- Patients with chronic HCV infection treated in daily practice with Maviret.
- ≥ 3 to < 18 years of age at start of Maviret treatment.

- Patients who were enrolled after treatment initiation.
- The legal guardian of the patient agreed with patient authorization or informed consent to use and/or disclose his/her anonymized health data prior to inclusion into the study.
- No prior treatment with Maviret.

Exclusion criteria

None

Assessor's comment:

Eligibility criteria are consistent with the study objectives and endpoints.

Baseline data

Demographics and baseline disease characteristics

Table 1 Patient demographics

Item	Level		Safety analysis population		Efficacy analysis population	
			n	(%)	n	(%)
Sex	Male		48	(46.60)	43	(46.74)
	Female		55	(53.40)	49	(53.26)
	Pregnancy and breastfeeding *1	No	54	(98.18)	48	(97.96)
		Unknown, not specified, etc.	1	(1.82)	1	(2.04)
	Unknown, not specified, etc.		0	(0)	0	(0)
Age [years]	N		103		92	
	Mean±SD		12.4±3.2		12.2±3.4	
	Median		12.0		12.0	
	Min-Max		3-17		3-17	
	Q1-Q3		11.0-15.0		11.0-15.0	
	3≦ <12		26	(25.24)	26	(28.26)
	12≦ <15		46	(44.66)	38	(41.30)
	15≦ 18		31	(30.10)	28	(30.43)
	<15		72	(69.90)	64	(69.57)
	15≦ 18		31	(30.10)	28	(30.43)
Weight [kg]	N		75		70	
	Mean±SD		43.43±13.99		43.45±14.46	
	Median		43.60		43.85	
	Min-Max		14.3-82.3		14.3-82.3	
	Q1-Q3		34.20-52.50		32.50-52.70	
	<12		0	(0)	0	(0)
	12≦ <20		4	(3.88)	4	(4.35)
	20≦ <30		11	(10.68)	11	(11.96)
	30≦ <45		29	(28.16)	25	(27.17)
	45≦		31	(30.10)	30	(32.61)
	Test not performed		18	(17.48)	14	(15.22)
	Unknown, not specified, etc.		10	(9.71)	8	(8.70)
Height [cm]	N		71		66	
	Mean±SD		148.10±16.56		147.73±17.08	
	Median		151.00		150.10	
	Min-Max		94.0-176.0		94.0-176.0	
	Q1-Q3		142.70-159.40		138.60-159.40	
	<85		0	(0)	0	(0)
	85≦ <100		1	(0.97)	1	(1.09)
	100≦ <115		2	(1.94)	2	(2.17)
	115≦ <130		8	(7.77)	8	(8.70)
	130≦ <145		11	(10.68)	11	(11.96)

Item	Level	Safety analysis population		Efficacy analysis population	
		n	(%)	n	(%)
	145≦ <160	33	(32.04)	28	(30.43)
	160≦ <175	14	(13.59)	14	(15.22)
	175≦	2	(1.94)	2	(2.17)
	Test not performed	22	(21.36)	18	(19.57)
	Unknown, not specified, etc.	10	(9.71)	8	(8.70)
BMI[kg/m^2]	N	71		66	
	Mean±SD	19.54±3.55		19.62±3.64	
	Median	18.85		18.85	
	Min-Max	13.5-28.4		13.5-28.4	
	Q1-Q3	16.89-21.86		16.89-22.35	
	<18.5	31	(30.10)	29	(31.52)
	18.5≦ <25	33	(32.04)	30	(32.61)
	25≦ <30	7	(6.80)	7	(7.61)
	30≦ <35	0	(0)	0	(0)
	35≦	0	(0)	0	(0)
	Test not performed	22	(21.36)	18	(19.57)
	Unknown, not specified, etc.	10	(9.71)	8	(8.70)
Visit category	Outpatient	102	(99.03)	91	(98.91)
	Hospitalization	1	(0.97)	1	(1.09)
	Unknown, not specified, etc.	0	(0)	0	(0)
Concomitant conditions	No	91	(88.35)	82	(89.13)
	Yes	12	(11.65)	10	(10.87)
History of hepatitis B virus infection	No	103	(100)	92	(100)
	Yes	0	(0)	0	(0)
eGFR [mL/min/1.73m^2]	N	79		75	
	Mean±SD	174.84±73.69		174.88±74.52	
	Median	154.92		154.92	
	Min-Max	82.6-528.3		82.6-528.3	
	Q1-Q3	122.28-209.35		122.28-209.35	
	<15	0	(0)	0	(0)
	15≦ <30	0	(0)	0	(0)
	30≦ <45	0	(0)	0	(0)
	45≦ <60	0	(0)	0	(0)
	60≦ <90	2	(1.94)	2	(2.17)
	90≦	77	(74.76)	73	(79.35)
	Test not performed	15	(14.56)	10	(10.87)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)
Diabetes mellitus	Yes	1	(0.97)	1	(1.09)
	No/Unknown	102	(99.03)	91	(98.91)
Cardiac disorders (SOC)	Yes	0	(0)	0	(0)
	No/Unknown	103	(100)	92	(100)
Dialysis	Yes	0	(0)	0	(0)
	No/Unknown	103	(100)	92	(100)
HIV infection	Yes	0	(0)	0	(0)
	No/Unknown	103	(100)	92	(100)
Hepatitis B virus infection	Yes	0	(0)	0	(0)
	No/Unknown	103	(100)	92	(100)

Item	Level		Safety analysis population		Efficacy analysis population	
			n	(%)	n	(%)
Compensated cirrhosis type C	No		103	(100)	92	(100)
	Yes		0	(0)	0	(0)
	Child-Pugh classification *2	A	0	-	0	-
		B	0	-	0	-
		C	0	-	0	-
		Unknown, not specified, etc.	0	-	0	-
	Unknown, not specified, etc.		0	(0)	0	(0)
Reason for using this drug	Serogroup 1 (genotype 1) or serogroup 2 (genotype 2) chronic hepatitis C		100	(97.09)	91	(98.91)
	Compensated cirrhosis type C with serogroup 1 (genotype 1) or serogroup 2 (genotype 2)		0	(0)	0	(0)
	Chronic hepatitis C with or without compensated cirrhosis that is neither serogroup 1 (genotype 1) nor serogroup 2 (genotype 2)		2	(1.94)	0	(0)
	Other		1	(0.97)	1	(1.09)
	Unknown, not specified, etc.		0	(0)	0	(0)
Prior IFN and DAA use	No		98	(95.15)	87	(94.57)
	Yes		5	(4.85)	5	(5.43)
Prior DAA treatment	No		103	(100)	92	(100)
	Yes		0	(0)	0	(0)
Contraindicated drug used	No		103	(100)	92	(100)
	Yes		0	(0)	0	(0)
Use of drugs to be used with caution	No		103	(100)	92	(100)
	Yes		0	(0)	0	(0)
Fibrosis stage of liver (Fib-4 index)	N		79		75	
	Mean±SD		0.243±0.099		0.243±0.102	
	Median		0.232		0.230	
	Min-Max		0.04-0.59		0.04-0.59	
	Q1-Q3		0.183-0.303		0.180-0.303	
	<1.45		79	(76.70)	75	(81.52)
	1.45≦ ≦3.25		0	(0)	0	(0)
	3.25<		0	(0)	0	(0)
	Unknown, not specified, etc.		24	(23.30)	17	(18.48)
Baseline HCV-RNA level [LogIU/mL]	N		96		92	
	Mean±SD		6.24±0.79		6.23±0.78	
	Median		6.45		6.40	
	Min-Max		2.9-7.3		2.9-7.3	
	Q1-Q3		5.90-6.80		5.90-6.80	
	<5		7	(6.80)	6	(6.52)
	5≦ <6		19	(18.45)	19	(20.65)
	6≦ <7		57	(55.34)	55	(59.78)
	7≦		13	(12.62)	12	(13.04)
	Test not performed		5	(4.85)	0	(0)
	Unknown, not specified, etc.		2	(1.94)	0	(0)

Item	Level	Safety analysis population		Efficacy analysis population	
		n	(%)	n	(%)
Baseline AFP[ng/mL]	N	64		62	
	Mean±SD	3.30±8.78		3.35±8.92	
	Median	2.00		2.00	
	Min-Max	0.0-72.0		0.0-72.0	
	Q1-Q3	1.80-2.55		1.80-2.60	
	≦10	63	(61.17)	61	(66.30)
	10< ≦50	0	(0)	0	(0)
	50< ≦100	1	(0.97)	1	(1.09)
	100<	0	(0)	0	(0)
	Test not performed	30	(29.13)	23	(25.00)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)
Baseline M2BPGi	N	52		51	
	Mean±SD	0.954±0.800		0.968±0.802	
	Median	0.750		0.760	
	Min-Max	0.28-5.50		0.28-5.50	
	Q1-Q3	0.575-1.075		0.580-1.120	
	<1.00	38	(36.89)	37	(40.22)
	1.00≦ <3.00	12	(11.65)	12	(13.04)
	3.00≦	2	(1.94)	2	(2.17)
	Test not performed	42	(40.78)	34	(36.96)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)
Baseline AST[U/L]	N	80		76	
	Mean±SD	32.7±22.9		33.1±23.4	
	Median	27.5		28.0	
	Min-Max	14-198		14-198	
	Q1-Q3	22.0-34.5		22.0-35.0	
	≦40	68	(66.02)	64	(69.57)
	40< ≦120	11	(10.68)	11	(11.96)
	120< ≦200	1	(0.97)	1	(1.09)
	200<	0	(0)	0	(0)
	Test not performed	14	(13.59)	9	(9.78)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)
Baseline ALT[U/L]	N	80		76	
	Mean±SD	38.6±37.9		39.5±38.7	
	Median	27.0		28.0	
	Min-Max	8-262		8-262	
	Q1-Q3	19.0-42.5		19.5-44.0	
	≦45	63	(61.17)	59	(64.13)
	45< ≦135	15	(14.56)	15	(16.30)
	135< ≦225	1	(0.97)	1	(1.09)
	225<	1	(0.97)	1	(1.09)
	Test not performed	14	(13.59)	9	(9.78)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)

Item	Level	Safety analysis population		Efficacy analysis population	
		n	(%)	n	(%)
Baseline	N	24		22	
ALP[U/L]	Mean±SD	713.3±384.6		682.3±371.4	
	Median	699.0		696.5	
	Min-Max	146-1409		146-1227	
	Q1-Q3	331.5-1017.5		315.0-1005.0	
	≦338	6	(5.83)	6	(6.52)
	338< ≦845	9	(8.74)	8	(8.70)
	845< ≦1690	9	(8.74)	8	(8.70)
	1690<	0	(0)	0	(0)
	Test not performed	70	(67.96)	63	(68.48)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)
Baseline	N	78		74	
Albumin [g/dL]	Mean±SD	4.46±0.28		4.45±0.29	
	Median	4.50		4.50	
	Min-Max	3.6-5.4		3.6-5.4	
	Q1-Q3	4.30-4.60		4.30-4.60	
	<2.0	0	(0)	0	(0)
	2.0≦ <3.0	0	(0)	0	(0)
	3.0≦ <3.7	1	(0.97)	1	(1.09)
	3.7≦	77	(74.76)	73	(79.35)
	Test not performed	16	(15.53)	11	(11.96)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)
Baseline	N	79		75	
Total bilirubin [mg/dL]	Mean±SD	0.66±0.31		0.67±0.31	
	Median	0.60		0.60	
	Min-Max	0.2-1.7		0.2-1.7	
	Q1-Q3	0.40-0.80		0.40-0.80	
	≦1.2	74	(71.84)	70	(76.09)
	1.2< ≦3.0	5	(4.85)	5	(5.43)
	3.0< ≦3.6	0	(0)	0	(0)
	3.6<	0	(0)	0	(0)
	Test not performed	15	(14.56)	10	(10.87)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)
Baseline	N	54		53	
Direct Bilirubin [mg/dL]	Mean±SD	0.14±0.10		0.14±0.10	
	Median	0.10		0.10	
	Min-Max	0.0-0.4		0.0-0.4	
	Q1-Q3	0.10-0.20		0.10-0.20	
	≦0.4	54	(52.43)	53	(57.61)
	0.4< ≦0.5	0	(0)	0	(0)
	0.5< ≦1.2	0	(0)	0	(0)
	1.2<	0	(0)	0	(0)
	Test not performed	40	(38.83)	32	(34.78)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)

Item	Level	Safety analysis population		Efficacy analysis population	
		n	(%)	n	(%)
Baseline Creatinine/Male [mg/dL] *3	N	37		35	
	Mean±SD	0.603±0.158		0.611±0.158	
	Median	0.640		0.640	
	Min-Max	0.30-0.93		0.30-0.93	
	Q1-Q3	0.470-0.730		0.470-0.740	
	≦1.1	37	(77.08)	35	(81.40)
	1.1< ≦1.6	0	(0)	0	(0)
	1.6< ≦3.3	0	(0)	0	(0)
	3.3<	0	(0)	0	(0)
	Test not performed	7	(14.58)	4	(9.30)
	Unknown, not specified, etc.	4	(8.33)	4	(9.30)
Baseline Creatinine/Female [mg/dL] *1	N	42		40	
	Mean±SD	0.501±0.113		0.497±0.113	
	Median	0.480		0.475	
	Min-Max	0.26-0.80		0.26-0.80	
	Q1-Q3	0.410-0.570		0.410-0.570	
	≦0.82	42	(76.36)	40	(81.63)
	0.82< ≦1.2	0	(0)	0	(0)
	1.2< ≦2.5	0	(0)	0	(0)
	2.5<	0	(0)	0	(0)
	Test not performed	8	(14.55)	6	(12.24)
	Unknown, not specified, etc.	5	(9.09)	3	(6.12)
Baseline Platelet count [10^4/uL]	N	79		75	
	Mean±SD	30.37±21.82		30.50±22.38	
	Median	27.60		27.50	
	Min-Max	15.7-213.0		15.7-213.0	
	Q1-Q3	23.00-32.80		23.00-32.90	
	<5.0	0	(0)	0	(0)
	5.0≦ <10.0	0	(0)	0	(0)
	10.0≦ <15.0	0	(0)	0	(0)
	15.0≦	79	(76.70)	75	(81.52)
	Test not performed	15	(14.56)	10	(10.87)
	Unknown, not specified, etc.	9	(8.74)	7	(7.61)

*1: The denominator for the proportion was "female."
*2: Subjects with chronic hepatitis C and compensated cirrhosis "Yes" were used as the denominator for the proportion.
*3: The denominator for the proportion was male subjects.

More females (53.4%) were enrolled than males (46.6%). The age range was 3 to 17 years of age, with a median age of 12. The median weight of the patients was 43.6 kg, and the median BMI was 18.9. The majority of patients (88.4%) reported no concomitant conditions.Table 1

Table 2 Distribution of serogroups and genotypes

Serogroup Genotype		Safety analysis set		Efficacy analysis set	
		n	(%)	n	(%)
Number of subjects		103		92	
Serogroup 1 or genotype 1		41	(39.81)	39	(42.39)
	1a	3	(2.91)	3	(3.26)
	1b	28	(27.18)	27	(29.35)
	Other	0	(0)	0	(0)
	Unknown, not specified, etc.	1	(0.97)	0	(0)
	Genotype test not performed	9	(8.74)	9	(9.78)
Serogroup 2 or genotype 2		57	(55.34)	51	(55.43)
	2a	24	(23.30)	21	(22.83)
	2b	21	(20.39)	20	(21.74)
	Superinfection (2a+2b)	1	(0.97)	1	(1.09)
	Other	0	(0)	0	(0)
	Unknown, not specified, etc.	0	(0)	0	(0)
	Genotype test not performed	11	(10.68)	9	(9.78)
GT3, 4, 5, or 6		0	(0)	0	(0)
Indeterminate		5	(4.85)	2	(2.17)

Table 3 Prior treatment for HCV

History of prior treatment for chronic hepatitis C (total)	Safety analysis set		Efficacy analysis set	
	n	(%)	n	(%)
Number of subjects	103		92	
No	98	(95.15)	87	(94.57)
Yes	5	(4.85)	5	(5.43)
IFN/Peg-IFN	5	(4.85)	5	(5.43)
With DAA+Peg-IFN+ ribavirin therapy	0	(0)	0	(0)
With IFN-free DAA therapy	0	(0)	0	(0)
Other	0	(0)	0	(0)

The denominator for the proportion of patients with detailed history of prior treatment for chronic hepatitis C was the "number of patients."

Hepatitis B virus testing prior to the treatment of Maviret

Table 4 HBV testing

Hepatitis B virus test	Safety analysis set	
	n	(%)
Number of subjects	103	
HBs antigen test		
Testing not performed	20	(19.42)
Test performed	83	(80.58)
Positive	0	(0)
Negative	83	(100)
Indeterminate	0	(0)
HBs antibody test		
Testing not performed	68	(66.02)
Test performed	35	(33.98)
Positive	4	(11.43)
Negative	31	(88.57)
Indeterminate	0	(0)
HBc antibody test		
Testing not performed	54	(52.43)
Test performed	49	(47.57)
Positive	0	(0)
Negative	49	(100)
Indeterminate	0	(0)
HBV DNA quantification test		
Testing not performed	99	(96.12)
Test performed	4	(3.88)
Below the quantitation limit	4	(100)
Not less than quantitation limit	0	(0)

The denominator of the test results was the number of subjects who underwent the test.

HCV testing

Table 5 HCV drug resistance mutation testing (GT1b-infected patients)

GT1b	Safety analysis set		Efficacy analysis set	
	n	(%)	n	(%)
Number of subjects	28		27	
Testing not performed	24	(85.71)	23	(85.19)
Test performed	4	(14.29)	4	(14.81)
D168				
None of the resistance test items performed	1	(25.00)	1	(25.00)
No mutation	2	(50.00)	2	(50.00)
Mutated	0	(0)	0	(0)
Unknown	1	(25.00)	1	(25.00)
L31				
None of the resistance test items performed	2	(50.00)	2	(50.00)
No mutation	0	(0)	0	(0)
Mutated	1	(25.00)	1	(25.00)
Unknown	1	(25.00)	1	(25.00)
Y93				
None of the resistance test items performed	2	(50.00)	2	(50.00)
No mutation	0	(0)	0	(0)
Mutated	1	(25.00)	1	(25.00)
Unknown	1	(25.00)	1	(25.00)
L31 and Y93				
Both mutated	1	(25.00)	1	(25.00)
Other	3	(75.00)	3	(75.00)
P32 deletion				
None of the resistance test items performed	2	(50.00)	2	(50.00)
No defects	1	(25.00)	1	(25.00)
Missing	0	(0)	0	(0)
Unknown	1	(25.00)	1	(25.00)

The denominator of the test results was the number of subjects who underwent the test.

Table 6 HCV drug resistance mutation testing (non-GT1b patients)

Non-GT1b	Safety analysis set		Efficacy analysis set	
	n	(%)	n	(%)
Number of subjects	75		65	
Testing not performed	63	(84.00)	53	(81.54)
Test performed	12	(16.00)	12	(18.46)
No mutation	2	(16.67)	2	(16.67)
Mutated	1	(8.33)	1	(8.33)
Unknown	9	(75.00)	9	(75.00)

The denominator of the test results was the number of subjects who underwent the test.

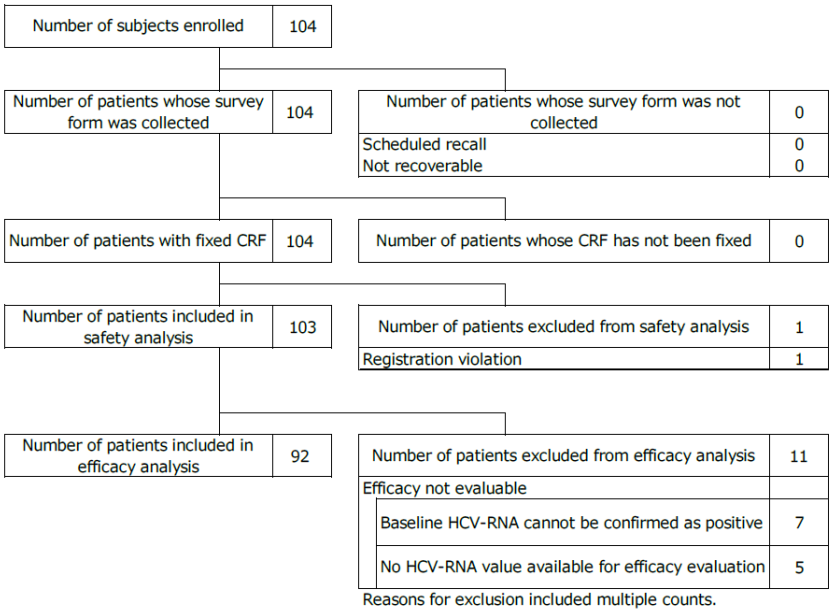
Concomitant use

Item		Safety analysis set		Efficacy analysis set	
		n	(%)	n	(%)
Number of subjects		103		92	
Drugs other than Maviret	No	101	(98.06)	90	(97.83)
	Yes	2	(1.94)	2	(2.17)
Drugs for chronic hepatitis C	No	103	(100)	92	(100)
	Yes *1	0	(0)	0	(0)
	Interferon	0	(0)	0	(0)
	Ribavirin preparations	0	(0)	0	(0)
	Drugs that improve liver function (hepatoprotective drugs)	0	(0)	0	(0)

*1: The denominator for the proportion of chronic hepatitis C medications was the number of subjects.

Number analysed

Figure 2 Patients disposition



Reasons for exclusion included multiple counts.

2.3.2.1. Efficacy results

Of the 92 patients included in the efficacy analysis (patients for which efficacy was evaluable), the SVR12 rate and treatment response are shown in Table 7. A total of 91 patients (98.91%) achieved SVR12, while 1 patient (1.09%) experienced a relapse within 12 weeks after the end of treatment. The percentage of patients confirmed HCV-RNA negative at the final observation was also 98.91%.

Details for the patient who observed relapse are as follows:
(A male patient, age 5-10 years old with genotype 2a chronic hepatitis C. This patient had no prior experience with hepatitis C treatment and did not have liver cirrhosis. After initiating treatment, the patient adhered to the regimen by taking 4 paediatric sachets of Maviret once daily for 56 days, as outlined in the package insert.
Detected HCV-RNA levels exceeding 1.2 log IU/mL at 4 weeks, 12 weeks, and 24 weeks after the end of treatment (no measurement at 8 weeks after the end of treatment).
HCV drug resistance mutation testing was not conducted before the commencement of drug administration; post-treatment testing confirmed "no mutations."

Table 7: SVR12 rate and treatment response

Analysis set: Efficacy analysis set

Serogroup Genotype	Number of subjects	Response															
		SVR12		95% CI	non-SVR12 (virologic failure)												
					Overall		Unresponsive		Partial response		Breakthrough		Relapse (End of Treatment)		Other		
		n	(%)		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
Overall	92	91	(98.91)	94.09-99.97	1	(1.09)	0	(0)	0	(0)	0	(0)	1	(1.09)	0	(0)	
Serogroup 1 or genotype 1	39	39	(100)	90.97-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	
1a	3	3	(100)	29.24-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	
1b	27	27	(100)	87.23-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	
Other	0	0	(-)	-	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	
Unknown, not specified, etc.	0	0	(-)	-	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	
Genotype test not performed	9	9	(100)	66.37-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	
Serogroup 2 or genotype 2	51	50	(98.04)	89.55-99.95	1	(1.96)	0	(0)	0	(0)	0	(0)	1	(1.96)	0	(0)	
2a	21	20	(95.24)	76.18-99.88	1	(4.76)	0	(0)	0	(0)	0	(0)	1	(4.76)	0	(0)	
2b	20	20	(100)	83.16-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	
Superinfection (2a+2b)	1	1	(100)	2.50-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	
Other	0	0	(-)	-	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	
Unknown, not specified, etc.	0	0	(-)	-	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	0	(-)	
Genotype test not performed	9	9	(100)	66.37-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	
Indeterminate	2	2	(100)	15.81-100.00	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	

***Rapporteur's comment**:*

No new relevant efficacy data is identified in these study results. Most of important efficacy results have already been discussed within the type II variation II12 (extension of indication in adolescents) and in the line extension X33G (extension of indication in paediatric patients aged ≥ 3years to < 12 years).

2.3.2.2. Safety results

Among the 103 patients in the safety analysis set, AEs were observed in 12 patients, all of whom were in the ≥ 12 to < 18 years (adolescent) subgroup. Among the patients with AEs, one patient had a treatment history of chronic hepatitis C with IFN treatment. Notably, all 16 of the observed AEs were non-serious. The incidence of AEs is shown in Table 8 and Table 9 below.

Table 8 Incidence of AEs

Analysis set: Safety analysis set

Number of subjects	103	
Number of subjects with adverse events	12	
Number of adverse events	16	
Incidence of adverse events (% [95%CI])	11.65[6.17-19.47]	
Adverse Event (n,%)		
Infections and infestations	2	(1.94)
Herpes zoster	1	(0.97)
Otitis media chronic	1	(0.97)
Gastrointestinal disorders	3	(2.91)
Abdominal pain	1	(0.97)
Nausea	2	(1.94)
Hepatobiliary disorders	2	(1.94)
Hepatic function abnormal	1	(0.97)
Hyperbilirubinaemia	1	(0.97)
Skin and subcutaneous tissue disorders	5	(4.85)
Eczema	1	(0.97)
Pruritus	4	(3.88)
Renal and urinary disorders	1	(0.97)
Renal disorder	1	(0.97)
General disorders and administration site conditions	2	(1.94)
Malaise	1	(0.97)
Pyrexia	1	(0.97)
Investigations	1	(0.97)
Weight decreased	1	(0.97)

Table 9: Incidence of AEs (patient-years)

Number of subjects	103	
Number of subjects with adverse events	12	
Number of adverse events	16	
Administration period of this drug [year] 1)	15.9	
Number of events per 100 patient-year (PYs)	100.71	
Adverse Events	Number of events	Number of events per 100
Infections and infestations	2	12.59
Herpes zoster	1	6.29
Otitis media chronic	1	6.29
Gastrointestinal disorders	3	18.88
Abdominal pain	1	6.29
Nausea	2	12.59
Hepatobiliary disorders	2	12.59
Hepatic function abnormal	1	6.29
Hyperbilirubinaemia	1	6.29
Skin and subcutaneous tissue disorders	5	31.47
Eczema	1	6.29
Pruritus	4	25.18
Renal and urinary disorders	1	6.29
Renal disorder	1	6.29
General disorders and administration site conditions	2	12.59
Malaise	1	6.29
Pyrexia	1	6.29
Investigations	1	6.29
Weight decreased	1	6.29

MedDRA/J version(27.1)

1)Total number of days of administration of this drug for all subjects/365

Among the 103 patients in the safety analysis set, ADRs were observed in 9 patients. None of the patients with observed ADRs had a treatment history for chronic hepatitis C. The incidence of ADRs is shown in Table 10 and Table 11.

Table 10 : Incidence of ADRs

Number of subjects	103	
Number of patients with adverse reactions	9	
Number of adverse reactions	11	
Incidence of ADRs (% [95%CI])	8.74[4.07-15.94]	
Adverse Reaction (n,%)		
Gastrointestinal disorders	3	(2.91)
Abdominal pain	1	(0.97)
Nausea	2	(1.94)
Hepatobiliary disorders	1	(0.97)
Hyperbilirubinaemia	1	(0.97)
Skin and subcutaneous tissue disorders	4	(3.88)
Pruritus	4	(3.88)
Renal and urinary disorders	1	(0.97)
Renal disorder	1	(0.97)
General disorders and administration site conditions	1	(0.97)
Malaise	1	(0.97)
Investigations	1	(0.97)
Weight decreased	1	(0.97)

MedDRA/J version(27.1)

Table 11: Incidence of ADRs (patient-years)

Number of subjects		103	
Number of patients with adverse reactions		9	
Number of adverse reactions		11	
Administration period of this drug [year] [1)]		15.9	
Number of events per 100 patient-year (PYs)		69.24	
Adverse Reaction		Number of events	Number of events per 100 Pys
Gastrointestinal disorders		3	18.88
	Abdominal pain	1	6.29
	Nausea	2	12.59
Hepatobiliary disorders		1	6.29
	Hyperbilirubinaemia	1	6.29
Skin and subcutaneous tissue disorders		4	25.18
	Pruritus	4	25.18
Renal and urinary disorders		1	6.29
	Renal disorder	1	6.29
General disorders and administration site conditions		1	6.29
	Malaise	1	6.29
Investigations		1	6.29
	Weight decreased	1	6.29

MedDRA/J version(27.1)

1)Total number of days of administration of this drug for all subjects/365

A total of 11 non-serious ADRs occurred in the adolescent group (ages ≥ 12 to < 18 years). These included 4 events of pruritus, 2 events of nausea, and 1 event each of abdominal pain, hyperbilirubinemia, renal disorder, malaise, and weight decreased.

MAH Conclusions: The results from P19-620 support the safety and effectiveness of Maviret for pediatric and adolescent patients with HCV in a real world setting in Japan. The safety results are consistent with the current safety profile as described in the product label and no changes to the label were required based on the results of this study. The benefit-risk of Maviret is unchanged, and no update to the Summary of Product Characteristics is being proposed as a result of these data.

***Assessor's comment**:*

Among the 103 participants for safety data, 9 patients (all in the ≥ 12 to < 18 years subgroup) reported adverse reactions (ADRs) for a total of 11 ADRs. All ADRs were non-serious and are resolved or recovering. After review of these adverse reactions, they were either consistent with the current known safety profile of Maviret and/or does not raise new safety concerns.

The mainly ADRs reported were nausea and pruritus (already listed in Maviret product information).

There was also:

- One adverse reaction of hyperbilirubinaemia (a 12-18 year-old, male), this ADR is already listed in the Maviret product information

- One adverse reaction of Weigh decreased (a 12-18 -year-old male), a transient weight loss of up to 4.4 kg was observed, occurring on Day 41 and resolved during the treatment administration. The reporting physician commented that "during Maviret administration, the patient's body weight decreased by about 3 kg without any cause other than Maviret, and quickly increased thereafter," and determined that there was a causal relationship between Maviret and "Weight decreased". However, this single non-serious event quickly resolved without changes regarding the administration of Maviret (there was no modification/discontinuation, the treatment was completed), and also there is a missing information regarding the patient weight at the start of the treatment (the reference weight was measured 24 days before the start of treatment but not on the day of treatment). Thus, no major safety issue is identified.

- One adverse reaction of renal disorder (a 12-18 year-old, female) with elevation of creatinine, an increase up to 0.82 mg/dL (usual values between 0.3 and 0.6 mg/dL) on Day 36 and recovered on the

day 123 after onset. This single non-serious event resolved without changes in the treatment administration due to ADR, the treatment was completed. No new safety concern is identified.

The MAH concluded that the safety results are consistent with the current safety profile as described in the product label and no changes to the label were required based on the results of this study which is endorsed.

Overall, the CHMP rapporteur endorses that the safety data provided are consistent with the known safety profile of Maviret and/or do not raise new relevant safety concerns. Also, to note, the safety profile of the paediatric population will continue to be assessed and discussed in the next PSUR, as requested by the PRAC rapporteur in the last Maviret PSUSA procedure (PSUSA/00010620/202207)

2.3.2.3. Discussion on clinical aspects

No new relevant efficacy data is identified in these study results.

The safety results are consistent with the known current safety profile of Maviret and/or does not raise new relevant safety concerns.

3. Rapporteur's overall concluson and recommendation

The MAH submitted a final report for Study P19-620, a prospective, central registration, multi-center observational study in patients ≥ 3 to < 18 years of age with chronic hepatitis C receiving the Maviret regimen under GPSP Ordinance to evaluate the safety and effectiveness of Maviret in daily practice in Japan.

Following the results from P19-620 study no new relevant efficacy data is identified and no new safety concern is raised.

The benefit-risk balance of Maviret remains unchanged.

☒ **Fulfilled:**

No regulatory action required.