

Supplementary Table S1. Fourfold table of disproportionality analysis for rimegepant signal detection.

	Reports with target adverse event	Reports with other adverse events
Reports with rimegepant as the primary suspected drug	a	b
Reports with other drugs as the primary suspected drug	c	d

a, number of reports containing both rimegepant and target adverse event; b, number of reports containing other adverse events of rimegepant; c, number of reports containing target adverse event of other drugs; d, number of reports containing other drugs and other adverse events.

Supplementary Table S2. Equations and criteria of four algorithms for rimegepant signal detection.

Algorithms	Equation	Criteria
ROR	$ROR=(ad)/(bc)$	Lower limit of 95% CI>1, N≥2
	Lower limit of 95% CI= $e^{\ln(ROR)-1.96(1/a+1/b+1/c+1/d)^{0.5}}$ Upper limit of 95% CI= $e^{\ln(ROR)+1.96(1/a+1/b+1/c+1/d)^{0.5}}$	
PRR	$PRR=a(c+d)/c/(a+b)$ $\chi^2=[(ad-bc)^2(a+b+c+d)/[(a+b)(c+d)(a+c)(b+d)]$	PRR≥2, $\chi^2 \geq 4$, N≥3
BCPNN	$IC=\log_2 a(a+b+c+d)/(a+c)/(a+b)$ $IC025=E(IC)-2V(IC)^{0.5}$	IC025>0
MGPS	$EBGM=a(a+b+c+d)/(a+c)/(a+b)$ $EBGM05=e^{\ln(EBGM)-1.96(1/a+1/b+1/c+1/d)^{0.5}}$	EBGM05>2

N, number of reports; 95% CI, 95% confidence interval; IC, information component; IC025, lower limit of 95% confidence interval of IC; E(IC), IC expectation; V(IC), variance of IC; EBGM, empirical Bayesian geometric mean; EBGM05, lower limit of 95% confidence interval of EBGM.

Supplementary Table S3. Fourfold table of disproportionality analysis for difference detection of rimegepant signals.

	Reports with target adverse event	Reports with other adverse events
Factor 1	a	b
Factor 2	c	d

a, number of reports conforming to factor 1, containing the target adverse event with rimegepant identified as the primary suspected drug; b, number of reports conforming to factor 1, containing other adverse events with rimegepant identified as the primary suspected drug; c, number of reports conforming to factor 2, containing the target adverse event with rimegepant identified as the primary suspected drug; d, number of reports conforming to factor 2, containing other adverse events with rimegepant identified as the primary suspected drug.

Supplementary Table S4. Criteria of ROR and Fisher's exact test for difference detection of rimegepant signals.

	ROR	Fisher's exact test
Signals that factor 1 more likely to develop	ROR>1, Lower limit of 95% CI>1, N≥2	P<0.05
Signals that factor 2 more likely to develop	ROR<1, Upper limit of 95% CI<1, N≥2	P<0.05

Supplementary Table S5. Case number and signal strength of rimegepant at the SOC level.

SOC	Case Number	ROR	Lower limit of 95% CI	PRR	χ^2	IC	IC025	EBGM	EBGM05
General disorders and administration site conditions (SOC: 10018065) ^{abcd}	4501	3.69	3.55	2.50	4915.53	1.32	1.27	2.50	2.40
Gastrointestinal disorders (SOC: 10017947) ^{ac}	1542	2.13	2.02	1.96	785.13	0.97	0.89	1.96	1.86
Nervous system disorders (SOC: 10029205) ^{ac}	1256	1.83	1.72	1.73	412.06	0.79	0.70	1.72	1.63
Injury, poisoning and procedural complications (SOC: 10022117)	686	0.53	0.50	0.57	258.64	-0.82	-0.93	0.57	0.52
Skin and subcutaneous tissue disorders (SOC: 10040785)	446	0.83	0.76	0.84	14.23	-0.25	-0.39	0.84	0.76
Psychiatric disorders (SOC: 10037175)	349	0.60	0.54	0.61	90.30	-0.71	-0.86	0.61	0.55
Respiratory, thoracic and mediastinal disorders (SOC: 10038738)	180	0.38	0.33	0.40	173.93	-1.34	-1.55	0.40	0.34
Immune system disorders (SOC: 10021428) ^{ac}	179	1.61	1.39	1.60	40.42	0.68	0.45	1.60	1.38
Product issues (SOC: 10077536)	167	0.92	0.79	0.92	1.20	-0.12	-0.35	0.92	0.79
Musculoskeletal and connective tissue disorders (SOC: 10028395)	152	0.27	0.23	0.29	286.96	-1.81	-2.04	0.29	0.24
Investigations (SOC: 10022891)	128	0.20	0.17	0.21	399.19	-2.24	-2.49	0.21	0.18
Infections and infestations (SOC: 10021881)	117	0.20	0.16	0.21	378.10	-2.28	-2.53	0.21	0.17
Eye disorders (SOC: 10015919)	113	0.59	0.49	0.60	31.64	-0.75	-1.01	0.60	0.49
Vascular disorders (SOC: 10047065)	72	0.38	0.30	0.38	73.67	-1.39	-1.72	0.38	0.30
Ear and labyrinth disorders (SOC: 10013993) ^{ac}	69	1.71	1.35	1.71	20.28	0.77	0.41	1.71	1.35
Cardiac disorders (SOC: 10007541)	61	0.30	0.24	0.31	96.28	-1.70	-2.05	0.31	0.24
Metabolism and nutrition disorders (SOC: 10027433)	39	0.20	0.15	0.21	121.23	-2.28	-2.70	0.21	0.15
Reproductive system and breast disorders (SOC: 10038604)	25	0.42	0.28	0.42	19.98	-1.25	-1.78	0.42	0.28
Surgical and medical procedures (SOC: 10042613)	25	0.18	0.12	0.18	95.96	-2.49	-3.01	0.18	0.12
Renal and urinary disorders (SOC: 10038359)	25	0.13	0.08	0.13	152.42	-2.97	-3.49	0.13	0.09
Social circumstances (SOC: 10041244)	21	0.42	0.28	0.43	16.40	-1.23	-1.81	0.43	0.28
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (SOC: 10029104)	14	0.03	0.02	0.03	505.84	-5.18	-5.83	0.03	0.02
Hepatobiliary disorders (SOC: 10019805)	10	0.12	0.07	0.12	61.98	-3.00	-3.75	0.12	0.07
Congenital, familial and genetic disorders (SOC: 10010331)	5	0.19	0.08	0.19	17.91	-2.43	-3.40	0.19	0.08
Pregnancy, puerperium and perinatal conditions (SOC: 10036585)	5	0.15	0.06	0.15	24.64	-2.76	-3.71	0.15	0.06
Blood and lymphatic system disorders (SOC: 10005329)	4	0.02	0.01	0.02	166.59	-5.42	-6.40	0.02	0.01
Endocrine disorders (SOC: 10014698)	3	0.12	0.04	0.12	20.40	-3.11	-4.20	0.12	0.04

^a: SOCs met the criteria of ROR algorithm. ^b: SOCs met the criteria of PRR algorithm. ^c: SOCs met the criteria of BCPNN algorithm. ^d: SOCs met the criteria of MGPS algorithm. The colors of the individual table cells represent the values of each index.

Supplementary Table S6. Case number and signal strength of 33 rimegepant-unrelated signals at the PT level.

PT	Case Number	ROR	Lower limit of 95% CI	PRR	χ^2	IC	IC025	EBGM	EBGM05
Product issues (SOC: 10077536)									
Product physical issue (PT: 10071134)	33	10.65	7.56	10.62	285.48	3.40	2.54	10.55	7.48
Product taste abnormal (PT: 10069227)	24	10.85	7.26	10.83	212.53	3.43	2.37	10.75	7.19
Product packaging quantity issue (PT: 10069299)	15	7.64	4.60	7.63	85.99	2.93	1.70	7.60	4.57
Product solubility abnormal (PT: 10069229)	14	16.53	9.76	16.51	201.66	4.03	2.26	16.33	9.64
Product packaging issue (PT: 10069405)	13	8.28	4.80	8.27	82.66	3.04	1.67	8.23	4.77
Product after taste (PT: 10086446)	11	47.59	26.09	47.54	484.81	5.52	2.43	46.02	25.23
Product packaging difficult to open (PT: 10079403)	9	12.34	6.40	12.33	92.92	3.61	1.61	12.24	6.35
Product dosage form issue (PT: 10069232)	6	73.97	32.54	73.93	410.09	6.14	1.57	70.28	30.92
Packaging design issue (PT: 10079080)	3	31.46	10.02	31.45	86.50	4.94	0.40	30.78	9.80
Injury, poisoning and procedural complications (SOC: 10022117)									
Exposure during pregnancy (PT: 10073513)	56	4.91	3.77	4.89	172.81	2.29	1.81	4.88	3.75
Product use complaint (PT: 10079400)	43	12.58	9.31	12.53	452.29	3.64	2.86	12.43	9.20
Incorrect route of product administration (PT: 10081202)	25	5.31	3.58	5.30	86.89	2.40	1.61	5.28	3.56
Incorrect drug administration rate (PT: 10064306)	6	7.61	3.41	7.61	34.25	2.92	0.87	7.57	3.39
Consistent with indications									
Migraine (PT: 10027599)	267	17.96	15.89	17.51	4112.58	4.11	3.85	17.31	15.32
Headache (PT: 10019211)	256	2.82	2.49	2.77	292.22	1.47	1.28	2.77	2.45
Dizziness (PT: 10013573)	181	2.65	2.29	2.62	182.72	1.39	1.16	2.62	2.26
Vertigo (PT: 10047340)	29	3.64	2.53	3.63	55.25	1.86	1.21	3.63	2.52
Medication overuse headache (PT: 10072720)	20	128.53	81.28	128.28	2314.47	6.88	3.51	117.63	74.39
Tension headache (PT: 10043269)	12	20.43	11.55	20.41	218.31	4.33	2.22	20.13	11.38
Aura (PT: 10003791)	11	51.73	28.33	51.68	527.28	5.64	2.45	49.88	27.32
Migraine with aura (PT: 10027607)	8	19.36	9.63	19.34	137.26	4.25	1.69	19.09	9.50
Therapeutic product effect									
Drug ineffective (PT: 10013709)	2499	14.09	13.46	10.88	22763.10	3.43	3.36	10.80	10.33
Therapeutic product effect incomplete (PT: 10082200)	422	17.15	15.55	16.48	6082.43	4.03	3.83	16.31	14.78
Therapeutic product effect decreased (PT: 10082201)	160	10.38	8.88	10.23	1325.63	3.35	3.04	10.17	8.69
Therapeutic product effect variable (PT: 10082204)	157	127.25	107.96	125.30	17776.85	6.85	5.82	115.12	97.67
Therapeutic product effect delayed (PT: 10082202)	91	62.97	51.00	62.42	5266.07	5.90	4.88	59.80	48.43
Drug ineffective for unapproved indication (PT: 10051118)	55	5.50	4.22	5.47	200.57	2.45	1.95	5.46	4.18
Therapeutic response shortened (PT: 10078575)	38	4.99	3.63	4.98	120.46	2.31	1.71	4.96	3.61
Drug effect less than expected (PT: 10083365)	22	7.56	4.97	7.55	124.31	2.91	1.95	7.51	4.94
Therapeutic response delayed (PT: 10053181)	11	33.55	18.45	33.52	338.94	5.03	2.32	32.76	18.01
Others									
Unevaluable event (PT: 10062355)	67	5.53	4.35	5.50	245.99	2.45	2.01	5.48	4.31
Therapeutic response unexpected (PT: 10043417)	22	3.35	2.20	3.34	36.09	1.74	1.00	3.34	2.20
Inhibitory drug interaction (PT: 10068071)	3	14.05	4.51	14.05	35.99	3.80	0.27	13.92	4.46

The colors of the individual table cells represent the values of each index.

Supplementary Table S7. Case number and signal strength of 24 rimegepant-related signals at the PT level.

PT	Case Number	ROR	Lower limit of 95% CI	PRR	χ^2	IC	IC025	EBGM	EBGM05
Gastrointestinal disorders (SOC: 10017947)									
Nausea (PT: 10028813)	598	5.58	5.13	5.31	2105.75	2.40	2.27	5.29	4.87
Abdominal pain upper (PT: 10000087)	133	4.47	3.77	4.43	353.00	2.14	1.86	4.42	3.72
Abdominal discomfort (PT: 10000059)	96	3.21	2.62	3.19	144.33	1.67	1.34	3.18	2.60
Dyspepsia (PT: 10013946)	70	5.14	4.06	5.12	231.25	2.35	1.93	5.10	4.03
Paraesthesia oral (PT: 10057372)	16	7.89	4.83	7.88	95.60	2.97	1.78	7.84	4.80
Swollen tongue (PT: 10042727)	16	4.41	2.70	4.41	42.02	2.14	1.17	4.40	2.69
Hypoaesthesia oral (PT: 10057371)	14	7.22	4.27	7.21	74.53	2.84	1.60	7.18	4.24
Retching (PT: 10038776)	11	3.96	2.19	3.96	24.26	1.98	0.83	3.95	2.19
Tongue discomfort (PT: 10077855)	10	10.92	5.86	10.91	89.37	3.44	1.64	10.84	5.82
Eructation (PT: 10015137) *	9	3.98	2.07	3.97	19.97	1.99	0.70	3.96	2.06
Oral discomfort (PT: 10030973)	8	4.32	2.16	4.32	20.37	2.11	0.69	4.31	2.15
Vomiting projectile (PT: 10047708) *	3	8.84	2.84	8.83	20.71	3.14	0.13	8.79	2.82
General disorders and administration site conditions (SOC: 10018065)									
Feeling abnormal (PT: 10016322)	164	4.62	3.96	4.56	456.55	2.19	1.93	4.55	3.90
Hangover (PT: 10019133) *	11	24.67	13.59	24.64	245.23	4.60	2.20	24.24	13.35
Performance status decreased (PT: 10048919) *	9	17.92	9.28	17.91	141.86	4.15	1.81	17.69	9.17
Feeling drunk (PT: 10016330) *	7	8.99	4.28	8.99	49.38	3.16	1.14	8.94	4.25
Nervous system disorders (SOC: 10029205)									
Somnolence (PT: 10041349)	123	4.36	3.65	4.32	314.26	2.11	1.81	4.31	3.61
Head discomfort (PT: 10019194)	22	7.22	4.74	7.20	116.93	2.84	1.89	7.17	4.71
Immune system disorders (SOC: 10021428)									
Hypersensitivity (PT: 10020751)	114	3.76	3.12	3.73	227.53	1.90	1.59	3.72	3.09
Reaction to excipient (PT: 10079925) *	9	16.52	8.56	16.50	129.57	4.03	1.77	16.32	8.46
Allergic reaction to excipient (PT: 10078853) *	6	12.60	5.64	12.60	63.50	3.64	1.14	12.49	5.59
Reaction to food additive (PT: 10037977) *	6	337.32	138.35	337.12	1621.59	8.09	1.57	272.07	111.59
Respiratory, thoracic and mediastinal disorders (SOC: 10038738)									
Pharyngeal swelling (PT: 10082270)	11	3.63	2.01	3.63	20.87	1.86	0.74	3.62	2.00
Ear and labyrinth disorders (SOC: 10013993)									
Motion sickness (PT: 10027990) *	4	15.36	5.73	15.35	53.09	3.93	0.68	15.20	5.67

*Emerging findings of rimegepant-induced adverse events. The colors of the individual table cells represent the values of each index.