

**Dossier zur Nutzenbewertung
gemäß § 35a SGB V**

Selumetinib (Koselugo®)

Alexion Pharma Germany GmbH

Anhang 4-G1

Studie SPRINKLE

*1. Datenschnitt vom 08. April 2024 –
weitere Auswertungen*

Stand: 04.02.2026

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Anhang 4-G1 Studie SPRINKLE 1. Datenschnitt vom 08. April 2024 – weitere Auswertungen

1 Endpunktkategorie Sicherheit

1.1 Endpunkt Unerwünschte Ereignisse (UE)

1.1.1 Gesamtraten UE und nach Schweregrad inkl. Subgruppenanalysen

Study Code: D1346C00004 Phase I/II

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Table 1: Overall summary of adverse events - by age category and sex (Safety analysis set)

	Age Category		Sex		Study Total
	>=1 to <3 years	>=3 to <7 years	Female	Male	Total
	(N=13) n (%)	(N=23) n (%)	(N=14) n (%)	(N=22) n (%)	(N=36) n (%)
Any adverse event (AE)	13 (100)	23 (100)	14 (100)	22 (100)	36 (100)
Any AE of CTCAE Grade 3 or higher	2 (15.4)	2 (8.7)	1 (7.1)	3 (13.6)	4 (11.1)
Any AE of CTCAE Grade 3	2 (15.4)	2 (8.7)	1 (7.1)	3 (13.6)	4 (11.1)
Any AE of CTCAE Grade 4	0	0	0	0	0
Any AE of CTCAE Grade 5	0	0	0	0	0
Any serious adverse event (SAE)	1 (7.7)	1 (4.3)	0	2 (9.1)	2 (5.6)
Any AE leading to discontinuation of selumetinib	0	0	0	0	0
Any AE leading to interruption of selumetinib	5 (38.5)	6 (26.1)	6 (42.9)	5 (22.7)	11 (30.6)
Any AE leading to dose reduction of selumetinib	0	0	0	0	0

Includes AEs with an onset or worsening date on or after the date of first selumetinib dose up to and including 30 days after the date of last selumetinib dose.

Subjects with multiple occurrences in the same category are counted once per category regardless of the number of occurrences.

CTCAE Common Terminology Criteria for Adverse Events version 5.0.

N=Number of subjects per subgroup factor; n=Number of subjects per category.

Program: t_overall_ae.sas

Date of output generation: 24OCT2025:16:59:02

1.1.2 UE nach System Organ Class (SOC) und Preferred Terms (PT) bei ≥ 10 % der Patienten inkl. Subgruppenanalysen

Study Code: D1346C00004 Phase I/II

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Table 2: Adverse Events by System Organ Class and Preferred Term occurring at least 10% in a study arm (Safety Analysis Set)

System Organ Class Preferred Term	Age Category		Sex		Study Total
	≥ 1 to < 3 years (N=13) n (%)	≥ 3 to < 7 years (N=23) n (%)	Female (N=14) n (%)	Male (N=22) n (%)	Total (N=36) n (%)
Subjects with any AE	13 (100.0)	23 (100.0)	14 (100.0)	22 (100.0)	36 (100.0)
INFECTIONS AND INFESTATIONS	11 (84.6)	20 (87.0)	12 (85.7)	19 (86.4)	31 (86.1)
Folliculitis	3 (23.1)	6 (26.1)	4 (28.6)	5 (22.7)	9 (25.0)
Gastroenteritis	2 (15.4)	3 (13.0)	1 (7.1)	4 (18.2)	5 (13.9)
Nasopharyngitis	2 (15.4)	4 (17.4)	5 (35.7)	1 (4.5)	6 (16.7)
Paronychia	6 (46.2)	10 (43.5)	6 (42.9)	10 (45.5)	16 (44.4)
Rhinitis	3 (23.1)	3 (13.0)	2 (14.3)	4 (18.2)	6 (16.7)
Upper respiratory tract infection	5 (38.5)	9 (39.1)	7 (50.0)	7 (31.8)	14 (38.9)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	4 (30.8)	5 (21.7)	1 (7.1)	8 (36.4)	9 (25.0)
Anaemia	3 (23.1)	5 (21.7)	1 (7.1)	7 (31.8)	8 (22.2)
METABOLISM AND NUTRITION DISORDERS	5 (38.5)	5 (21.7)	5 (35.7)	5 (22.7)	10 (27.8)
PSYCHIATRIC DISORDERS	1 (7.7)	3 (13.0)	2 (14.3)	2 (9.1)	4 (11.1)
NERVOUS SYSTEM DISORDERS	2 (15.4)	2 (8.7)	1 (7.1)	3 (13.6)	4 (11.1)

Includes AEs with an onset or worsening date on or after the date of first selumetinib dose up to and including 30 days after the date of last selumetinib dose.

A subject can have one or more preferred terms reported under a given system organ class.

N= Number of subjects per subgroup factor; n=Number of subjects with AE; Percentages are based on total number of subjects in the subgroup factor(N).

Sorted by international order for the system organ class and alphabetically for preferred term.

Program: t_ae_soc_pt.sas

Date of output generation: 03NOV2025:16:53:47

Study Code: D1346C00004 Phase I/II

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Table 2: Adverse Events by System Organ Class and Preferred Term occurring at least 10% in a study arm (Safety Analysis Set)

System Organ Class Preferred Term	Age Category		Sex		Study Total
	>=1 to < 3 years (N=13) n (%)	>=3 to < 7 years (N=23) n (%)	Female (N=14) n (%)	Male (N=22) n (%)	Total (N=36) n (%)
EYE DISORDERS	1 (7.7)	3 (13.0)	2 (14.3)	2 (9.1)	4 (11.1)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	6 (46.2)	6 (26.1)	4 (28.6)	8 (36.4)	12 (33.3)
Rhinorrhoea	2 (15.4)	2 (8.7)	2 (14.3)	2 (9.1)	4 (11.1)
GASTROINTESTINAL DISORDERS	11 (84.6)	18 (78.3)	9 (64.3)	20 (90.9)	29 (80.6)
Abdominal pain	1 (7.7)	4 (17.4)	2 (14.3)	3 (13.6)	5 (13.9)
Diarrhoea	6 (46.2)	8 (34.8)	3 (21.4)	11 (50.0)	14 (38.9)
Stomatitis	1 (7.7)	4 (17.4)	2 (14.3)	3 (13.6)	5 (13.9)
Vomiting	6 (46.2)	8 (34.8)	6 (42.9)	8 (36.4)	14 (38.9)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	12 (92.3)	21 (91.3)	14 (100.0)	19 (86.4)	33 (91.7)
Alopecia	3 (23.1)	5 (21.7)	4 (28.6)	4 (18.2)	8 (22.2)
Dry skin	4 (30.8)	13 (56.5)	6 (42.9)	11 (50.0)	17 (47.2)
Eczema	5 (38.5)	9 (39.1)	7 (50.0)	7 (31.8)	14 (38.9)
Hair colour changes	1 (7.7)	5 (21.7)	1 (7.1)	5 (22.7)	6 (16.7)

Includes AEs with an onset or worsening date on or after the date of first selumetinib dose up to and including 30 days after the date of last selumetinib dose.

A subject can have one or more preferred terms reported under a given system organ class.

N= Number of subjects per subgroup factor; n=Number of subjects with AE; Percentages are based on total number of subjects in the subgroup factor(N).

Sorted by international order for the system organ class and alphabetically for preferred term.

Program: t_ae_soc_pt.sas

Date of output generation: 03NOV2025:16:53:47

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Table 2: Adverse Events by System Organ Class and Preferred Term occurring at least 10% in a study arm (Safety Analysis Set)

System Organ Class Preferred Term	Age Category		Sex		Study Total
	>=1 to < 3 years (N=13) n (%)	>=3 to < 7 years (N=23) n (%)	Female (N=14) n (%)	Male (N=22) n (%)	Total (N=36) n (%)
GENERAL DISORDERS AND ADMINISTRATION	9 (69.2)	12 (52.2)	6 (42.9)	15 (68.2)	21 (58.3)
SITE CONDITIONS					
Fatigue	1 (7.7)	5 (21.7)	1 (7.1)	5 (22.7)	6 (16.7)
Pyrexia	8 (61.5)	9 (39.1)	5 (35.7)	12 (54.5)	17 (47.2)
INVESTIGATIONS	2 (15.4)	10 (43.5)	3 (21.4)	9 (40.9)	12 (33.3)
Aspartate aminotransferase increased	1 (7.7)	3 (13.0)	0	4 (18.2)	4 (11.1)
Blood creatine phosphokinase increased	2 (15.4)	9 (39.1)	3 (21.4)	8 (36.4)	11 (30.6)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0	4 (17.4)	1 (7.1)	3 (13.6)	4 (11.1)

Includes AEs with an onset or worsening date on or after the date of first selumetinib dose up to and including 30 days after the date of last selumetinib dose.

A subject can have one or more preferred terms reported under a given system organ class.

N= Number of subjects per subgroup factor; n=Number of subjects with AE; Percentages are based on total number of subjects in the subgroup factor(N).

Sorted by international order for the system organ class and alphabetically for preferred term.

Program: t_ae_soc_pt.sas

Date of output generation: 03NOV2025:16:53:47

1.1.3 Schwere UE (CTCAE Grad ≥ 3) nach SOC und PT bei ≥ 5 % der Patienten inkl. Subgruppenanalysen

Study Code: D1346C00004 Phase I/II

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Table 3: Adverse Events CTCAE Grade 3 or higher by System Organ Class and Preferred Term occurring at least 5% in a study arm (Safety Analysis Set)

	Age Category		Sex		Study Total
	≥ 1 to < 3 years (N=13) n (%)	≥ 3 to < 7 years (N=23) n (%)	Female (N=14) n (%)	Male (N=22) n (%)	Total (N=36) n (%)
Subjects with any AE of CTCAE Grade 3 or higher	2 (15.4)	2 (8.7)	1 (7.1)	3 (13.6)	4 (11.1)
INFECTIONS AND INFESTATIONS	1 (7.7)	1 (4.3)	0	2 (9.1)	2 (5.6)

Includes AEs with an onset or worsening date on or after the date of first selumetinib dose up to and including 30 days after the date of last selumetinib dose.

A subject can have one or more preferred terms reported under a given system organ class.

N= Number of subjects per subgroup factor; n=Number of subjects with AE; Percentages are based on total number of subjects in the subgroup factor(N).

Sorted by international order for the system organ class and alphabetically for preferred term.

Program: t_ae_soc_pt.sas

Date of output generation: 03NOV2025:16:53:49

1.1.4 Schwerwiegende unerwünschte Ereignisse (SUE) nach SOC und PT bei $\geq 5\%$ der Patienten

Study Code: D1346C00004 Phase I/II

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Table 4: Serious Adverse Events by System Organ Class and Preferred Term occurring at least 5% in a study arm (Safety Analysis Set)

No data to report as there are no SOC or PT for serious adverse events with at least 5% frequency in study arm.

Program: t_ae_soc_pt.sas

Date of output generation: 03NOV2025:16:53:49

1.1.5 Abbruch der Studienmedikation aufgrund von UE nach SOC und PT

Study Code: D1346C00004 Phase I/II

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Table 5: Adverse Events leading to discontinuation of selumetinib by System Organ Class and Preferred Term

No data to report as there are no adverse events leading to discontinuation of selumetinib.

Program: t_ae_soc_pt_disc.sas

Date of output generation: 24OCT2025:17:01:30

2 Ergänzende Analysen

2.1 Folgetherapien

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Table 14.1.17 Post discontinuation of investigational product medication by ATC classification and generic drug name (Safety analysis set)

There are no observations for this output
