Dossier zur Nutzenbewertung gemäß § 35a SGB V

Selumetinib (Koselugo®)

Alexion Pharma Germany GmbH

Anhang 4-G4

Studie D1346C00015
2. Datenschnitt vom 24. April 2023 –
weitere Auswertungen

Stand: 14.11.2025

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1 Endpunktkategorie Sicherheit

1.1 Endpunkt Unerwünschte Ereignisse

1.1.1 Adverse Events of Special Interest (AESI)

1.1.1.1 Operationalisierung Adverse Events of Special Interest (AESI) in der Studie D1346C00015

Tabelle 1: Operationalisierung Adverse Events of Special Interest (AESI) in der Studie **D1346C00015**

Medical concept	AE of special interest	Approach to delineating PTs
Skin and mucous membrane events	Acneiform rash	HLT Acnes HLT Pustular conditions
	Non acneiform rash	HLT Rashes, eruptions and exanthema NEC HLT Pruritus NEC
	Nail disorder events	HLT Nail and nail bed conditions PT Paronychia
	Oral mucositis	HLT Oral soft tissue disorders NEC HLT Stomatitis and ulceration
Bone marrow effects	Leukopenic events	SMQ Haematopoietic leukopenia
	Thrombocytopenic events	SMQ Haematopoietic thrombocytopenias
	Erythropenic event	SMQ Haematopoietic erythropenia
Retinal events	RPED/CSR events RVO events Other retinal disorders	SMQ Retinal disorders
Cardiac events	Ejection fraction decreased Other cardiac events	SMQ Cardiac failure
Muscle events	Muscle events CK increased	SMQ Rhabdomyolysis/myopathy
Physeal dysplasia	Physeal dysplasia	HLT Epiphyseal disorders

AE: adverse event; CK: creatine kinase; CSR: central serous retinopathy; HLT: high level term; MedDRA: Medical Dictionary for Regulatory Activities; NEC: not elsewhere classified; PT: preferred term; RPED: retinal pigment epithelial detachment; RVO: retinal vein occlusion; SMQ: standardised MedDRA query.

Both broad and narrow SMQs will be used.

Quelle: AstraZeneca. Clinical Study Protocol – D1346C00015: A Phase I, Single-Arm, Sequential Study to Evaluate the Effect of Food on the Gastrointestinal Tolerability and Pharmacokinetics of Selumetinib after Multiple Doses in Adolescent Children with Neurofibromatosis Type 1 (NF1) Related Plexiform Neurofibromas (PN). Version 4.0. Data on File. Stand: 07.04.2025. 2025.

1.1.1.2 Gesamtraten Adverse Events of Special Interest (AESI)

Tabelle 2: Ergebnisse für den Endpunkt „Gesamtraten unerwünschter Ereignisse von besonderem Interesse“ aus der Studie **D1346C00015**

Studie	**Selumetinib 25 mg/m² BID**
D1346C00015 **Datenschnitt: 24. April 2023**	***Safety*-Population** **N = 24**
Gesamtraten AESI	**Anzahl Patienten, n/N (%)**
Jegliches AESI	24/24 (100)
AESI – Ausschlag akneiform	21/24 (87,5)
AESI – Hautausschlag nicht-akneiforme	6/24 (25,0)
AESI – Nagelerkrankungen / Nagelveränderungen	9/24 (37,5)
AESI – Mukositis oral	3/24 (12,5)
AESI – Leukopenie-Ereignisse (Hämatopoetische Leukopenie)	1/24 (4,2)
AESI – Erythropenie-Ereignis (Hämatopoetische Erythropenie)	1/24 (4,2)
AESI – Auswurffraktion verkleinert	3/24 (12,5)
AESI – Muskelerkrankungen / Muskuloskelettale Ereignisse	1/24 (4,2)
AESI – Kreatinkinase erhöht	6/24 (25,0)

AESI: Unerwünschte Ereignisse von besonderem Interesse (engl. Adverse Events of Special Interest); BID: Zweimal täglich.

Quelle: AstraZeneca. Clinical Study Report – D1346C00015: A Phase I, Single-Arm, Sequential Study to Evaluate the Effect of Food on the Gastrointestinal Tolerability and Pharmacokinetics of Selumetinib after Multiple Doses in Adolescent Children with Neurofibromatosis Type 1 (NF1) Related Plexiform Neurofibromas (PN). Clinical Study Report Addendum. Data on File. Stand: 28.11.2023. 2023.