

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

Selumetinib (Koselugo®)

Alexion Pharma Germany GmbH

Anhang 4-G3

Studie D1346C00011

*Finaler Datenschnitt vom 15. August 2023 –
weitere Auswertungen*

Stand: 14.11.2025

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Tabelle 1: Operationalisierung Adverse Events of Special Interest (AESI) in der Studie D1346C00011

AESI	MedDRA Preferred Terms (PT) Defining the AESIs
Ocular toxicity	Chorioretinopathy (central serous retinopathy [CSR]); Retinal detachment; Retinal tear; Vision blurred; Visual impairment; Vitreous floaters; Photopsia; Eye disorder; Photophobia; Retinal vein occlusion (RVO); Detachment of retinal pigment epithelium (Retinal pigment epithelial detachment [RPED]).
Hepatotoxicity	Drug-induced liver injury; ALT increased; AST increased.
Muscular toxicity	Blood creatine phosphokinase increased; Musculoskeletal pain; Muscular weakness; Myalgia; Rhabdomyolysis; Myoglobin blood increased; Myoglobin urine present; Acute kidney injury; Myopathy.
Cardiac toxicity	Ejection fraction decreased; Oedema peripheral; Peripheral swelling; Oedema; Left ventricular dysfunction; Ventricular dysfunction.
For Paediatric population only	
Physeal dysplasia	Metaphyseal dysplasia, Multiple epiphyseal dysplasia, Arthralgia, Joint stiffness, Joint hyperextension, Gait disturbance, Short stature.
Choking on the capsule	Choking, Retching.
<p>AESI: adverse event of special interest; ALT: alanine transaminase; AST: aspartate transaminase.</p> <p>Quelle: AstraZeneca. Clinical Study Protocol – D1346C00011: A Phase 1 Open Label Study to Assess the Safety, Tolerability, Pharmacokinetics and Clinical Efficacy of Selumetinib, a Selective Mitogen Activated Protein Kinase Kinase (MEK) 1 Inhibitor, in Chinese Paediatric and Adult Subjects with Neurofibromatosis Type 1 (NF1) and Inoperable Plexiform Neurofibromas (PN). Version 3.0. Data on File: Stand: 30.09.2021. 2021.</p>	

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 **D1346C00011**

Studie	Selumetinib 25 mg/m ² BID
D1346C00011 Datenschnitt: 15. August 2023	Safety-Population N = 16
Gesamtraten AESI	Anzahl Patienten, n/N (%)
Jegliches AESI	7/16 (43,8)
Nicht-schweres AESI (CTCAE ≤ 2)	7/16 (43,8)
Schweres AESI (CTCAE ≥ 3)	0/16 (0,0)
Schwerwiegendes AESI	0/16 (0,0)
AESI – Lebertoxizität	
Gesamtrate	4/16 (25,0)
Nicht-schwer (CTCAE Grad < 3)	4/16 (25,0)
Schwer (CTCAE Grad ≥ 3)	0/16 (0,0)
SUE	0/16 (0,0)
AESI – Muskeltoxizität	
Gesamtrate	5/16 (31,3)
Nicht-schwer (CTCAE Grad < 3)	5/16 (31,3)
Schwer (CTCAE Grad ≥ 3)	0/16 (0,0)
SUE	0/16 (0,0)
<p>AESI: Unerwünschte Ereignisse von besonderem Interesse (engl. Adverse Events of Special Interest); BID: Zweimal täglich; CTCAE: Common Terminology Criteria for Adverse Events; SUE: Schwerwiegendes unerwünschtes Ereignis.</p> <p>Quelle: Clinical Study Report – D1346C00011: A Phase 1 Open Label Study to Assess the Safety, Tolerability, Pharmacokinetics and Clinical Efficacy of Selumetinib (a Selective Mitogen Activated Protein Kinase Kinase [MEK] 1 Inhibitor) in Chinese Paediatric and Adult Patients with Neurofibromatosis Type 1 (NF1) and Inoperable Plexiform Neurofibromas (PN). Clinical Study Report Addendum. Data on File. Stand: 13.12.2023. 2023.</p>	