

SUSPECT ADVERSE REACTION REPORT										

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY Portugal	2. DATE OF BIRTH			2a. AGE 52 Years	3. SEX Male	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year			Day	Month	Year	
								Feb	2021	
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) Other Seriousness Criteria: Medically Significant #1 statin-induced dermatomyositis/Gottron's papules on the back of the MCFs and PIPs of the hands [Dermatomyositis] Other Seriousness Criteria: Medically Significant #2 asthenia and disabling proximal myalgias of the lower limbs, associated with skin lesions on the hands, eyelids and helices again [Asthenia] Other Seriousness Criteria: Medically Significant #3 asthenia and disabling proximal myalgias of the lower limbs, associated with skin lesions on the hands, eyelids and helices again [Myalgia] Other Seriousness Criteria: Medically Significant /...continued										<input type="checkbox"/> PATIENT DIED <input type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALISATION <input type="checkbox"/> INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY <input type="checkbox"/> LIFE THREATENING <input type="checkbox"/> CONGENITAL ANOMALY <input checked="" type="checkbox"/> OTHER

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name) #1 Rosuvastatin + Ezetimibe Rosuvastatin + Ezetimibe Film-coated tablet Unknown {Lot#: Asked But #2 Atorvastatina Atorvastatin calcium, Atorvastatin calcium Unknown (NOS) Unknown {Lot#: Asked But /...continued		20 DID REACTION ABATE AFTER STOPPING DRUG? #1 <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA #2 <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA
15. DAILY DOSE(S) #1 UNK UNK, QID #2 20 mg, QID	16. ROUTE(S) OF ADMINISTRATION #1 Unknown #2 Unknown	
17. INDICATION(S) FOR USE #1 dyslipidemia [Dyslipidaemia] #2 dyslipidemia [Dyslipidaemia] /...continued		21. DID REACTION REAPPEAR AFTER REINTRODUCTION? #1 <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA #2 <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA
18. THERAPY DATES (from/to) #1 May-2020 to Unknown #2 Aug-2021 to Unknown	19. THERAPY DURATION #1 Unknown #2 Unknown	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY (e.g diagnostics, allergics, pregnancy with last month of period, etc.) Medical History Sub Section: #1 Historical Condition Coronary artery disease [Coronary artery disease] Ongoing #2 Current Condition Dyslipidemia [Dyslipidaemia] Ongoing #3 Historical Condition Smoker [Tobacco user] #4 Historical Condition Thrombocytopenia [Thrombocytopenia] Ongoing #5 Historical Condition Hepatic steatosis [Hepatic steatosis] Ongoing /...continued

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER FERRER INTERNACIONAL, S.A. Diagonal Avenue 549, 08029, Barcelona, Spain Phone: +34936003700,	26. REMARKS Company Comments: ID: 20-25-PRT-FER-0000458 Dermatomyositis, skin lesion, polyarthritis, heliotrope rash, cyanosis, synovitis, sclerodactylia, paronychia, lymphopenia and haemorrhage are unexpected according to the reference safety document of Rosuvastatin+Ezetimibe, while asthenia, myalgia, arthralgia, inflammation, thrombocytopenia and myositis are expected according to the reference safety document of Rosuvastatin+Ezetimibe. These adverse reactions were involved in a serious case due to medically significant was reported. The action taken with the drug was withdrawn and the outcome of the events were recovering. In this particular case, the temporal relationship and the well-known pharmaco-toxicologic profile of the product could enhance the causal relationship. Moreover, the patient was on another suspect treatments at the same time. Further information should be needed to make a clear medical assessment and to investigate other etiologies. Based on the information provided, the Company assessed as Possible the causal relationship between the drug and the events according to the Karch Lasagna modified method.
--	---

	24b. MFR CONTROL NO. 20-25-PRT-FER-0000458	25b. NAME AND ADDRESS OF REPORTER Portugal Physician Physician
24c. DATE RECEIVED BY MANUFACTURER 01-Aug-2025	24d. REPORT SOURCE <input type="checkbox"/> STUDY <input checked="" type="checkbox"/> HEALTH PROFESSIONAL <input type="checkbox"/> LITERATURE <input type="checkbox"/> OTHER:	
DATE OF THIS REPORT 08-Aug-2025	25a. REPORT TYPE <input checked="" type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOWUP:	

ADDITIONAL INFORMATION**7+13 DESCRIBE REACTION(S) continued**

#4| asthenia and disabling proximal myalgias of the lower limbs, associated with skin lesions on the hands, eyelids and helices again [Skin lesion] |

Other Seriousness Criteria: Medically Significant

#5| symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands [Polyarthrits] |

Other Seriousness Criteria: Medically Significant

#6| symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands [Arthralgia] |

Other Seriousness Criteria: Medically Significant

#7| heliotropic rash on the eyelids and helices [Heliotrope rash] |

Other Seriousness Criteria: Medically Significant

#8| symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands [Cyanosis] |

Other Seriousness Criteria: Medically Significant

#9| symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands [Inflammation] |

Other Seriousness Criteria: Medically Significant

#10| synovitis of several PIPs (especially 2nd and 3rd) [Synovitis] |

Other Seriousness Criteria: Medically Significant

#11| sclerodactyly in the intermediate phalanges and perionychia on all the fingers [Acrosclerosis] |

Other Seriousness Criteria: Medically Significant

#12| sclerodactyly in the intermediate phalanges and perionychia on all the fingers [Paronychia] |

Other Seriousness Criteria: Medically Significant

#13| lymphopenia [Lymphopenia] |

Other Seriousness Criteria: Medically Significant

#14| thrombocytopenia [Thrombocytopenia] |

Other Seriousness Criteria: Medically Significant

#15| myositis/myopathy [Myositis] |

Other Seriousness Criteria: Medically Significant

#16| megacapillaries and hemorrhages in all fingers [Haemorrhage] |

This case has been downloaded from the EudraVigilance database without narrative (L2A). (PT-EMA-DD-20250728-7482701-120330).

Patient details: 52 years-old, adult, male.

Medical history (if applicable)

- Historical Condition: Coronary artery disease (LLT: Coronary artery disease) // asymptomatic coronary artery disease (traced by the existence of a family history at a young age)
- Current Condition: Dyslipidemia (LLT: Dyslipidemia)
- Historical Condition: Smoker (LLT: Smoker) // past smoking
- Historical Condition: Thrombocytopenia (LLT: Thrombocytopenia) // thrombocytopenia minor
- Historical Condition: Hepatic steatosis (LLT: Hepatic steatosis)
- Historical Condition: Hepatic hemangioma rupture (LLT: Hepatic hemangioma rupture) // hepatic hemangiomas

- Historical Condition: Dyslipidemia (LLT: Dyslipidemia)

Suspect:

- EZETIMIBE/ROSUVASTATIN ; Action taken: Withdrawn
- ATORVASTATIN ; Action taken: Unknown
- EZETIMIBE ; Action taken: Unknown
- SIMVASTATIN ; Action taken: Not Applicable

Events:

- statin-induced dermatomyositis/Gottron's papules on the back of the MCFs and PIPs of the hands (LLT: Dermatomyositis) / Outcome: Unknown
- asthenia and disabling proximal myalgias of the lower limbs, associated with skin lesions on the hands, eyelids and helices again (LLT: Asthenia) / Outcome: Unknown
- asthenia and disabling proximal myalgias of the lower limbs, associated with skin lesions on the hands, eyelids and helices again (LLT: Myalgia of lower extremities) / Outcome: recovering/resolving
- asthenia and disabling proximal myalgias of the lower limbs, associated with skin lesions on the hands, eyelids and helices again (LLT: Skin lesion) / Outcome: recovering/resolving
- symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands (LLT: Inflammatory polyarthritis) / Outcome: recovering/resolving
- symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands (LLT: Polyarthralgia) / Outcome: recovering/resolving
- heliotropic rash on the eyelids and helices (LLT: Heliotrope rash) / Outcome: recovering/resolving
- symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands (LLT: Acrocyanosis) / Outcome: recovering/resolving
- symmetrical polyarthralgias of inflammatory rhythm, involving the metacarpophalangeal (MCFs) and proximal interphalangeal (PIPs) joints of the hands, and acrocyanosis of the hands (LLT: Inflammation) / Outcome: recovering/resolving
- synovitis of several PIPs (especially 2nd and 3rd) (LLT: Synovitis) / Outcome: recovering/resolving
- sclerodactyly in the intermediate phalanges and perionychia on all the fingers (LLT: Sclerodactylia) / Outcome: recovering/resolving
- sclerodactyly in the intermediate phalanges and perionychia on all the fingers (LLT: Perionychitis) / Outcome: recovering/resolving
- lymphopenia (LLT: Lymphopenia) / Outcome: recovering/resolving
- thrombocytopenia (LLT: Thrombocytopenia) / Outcome: recovering/resolving
- myositis/myopathy (LLT: Myositis) / Outcome: recovering/resolving
- megacapillaries and hemorrhages in all fingers (LLT: Hemorrhage) / Outcome: recovering/resolving

This case has been assessed as Serious

Lab Data:

- #1| 2022 | renal function [Renal function test] | Unknown(L) | Unknown(H) | normal
- #2| 2022 | antinuclear antibodies (ANA) [Antinuclear antibody] | Unknown(L) | Unknown(H)
- #3| 2022 | C-reactive protein (CRP) [C-reactive protein] | Unknown(L) | Unknown(H) | normal
- #4| 2022 | liver tests [Liver function test] | Unknown(L) | Unknown(H) | mild liver cytolysis and increased muscle damage markers
- #5| 2022 | Physical examination [Physical examination] | Unknown(L) | Unknown(H) | showed synovitis of several PIPs (especially 2nd and 3rd), Gottron's papules on the back of the MCFs and PIPs of the hands, heliotropic rash on the eyelids and helices, sclerodactyly in the intermediate phalanges and perionychia on all the fingers. , with conserved muscle strength
- #6| May-2022 | muscle biopsy [Biopsy muscle] | Unknown(L) | Unknown(H) | a muscle biopsy of the rectus femoris was performed and therapy with methotrexate (12.5mg per os, weekly) was initiated
- #7| Mar-2022 | magnetic resonance imaging of the thighs [Magnetic resonance imaging] | Unknown(L) | Unknown(H) | was performed, which was compatible with myositis/myopathy
- #8| Mar-2022 | videocapillaroscopy [Angioscopy] | Unknown(L) | Unknown(H) | of the nail bed, which revealed the presence of megacapillaries and hemorrhages in all fingers, compatible with the clinical diagnosis of dermatomyositis.

14-21. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION	20 DID REACTION ABATE AFTER STOPPING DRUG? 21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
#1 Rosuvastatin + Ezetimibe Rosuvastatin + Ezetimibe Film-	UNK UNK, QID; Unknown	dyslipidemia [Dyslipidaemia]	May-2020 to Unknown;	;

coated tablet Unknown {Lot#: Asked But Unknown} Regimen #1		Unknown	
#2 Atorvastatina Atorvastatin calcium, Atorvastatin calcium Unknown (NOS) Unknown {Lot#: Asked But Unknown} Regimen #1	20 mg, QID; Unknown	dyslipidemia [Dyslipidaemia]	Aug-2021 to Unknown; Unknown
#3 Ezetimibe Ezetimibe Unknown (NOS) Unknown {Lot#: Asked But Unknown} Regimen #1	10 mg, QID; Unknown	dyslipidemia [Dyslipidaemia]	Aug-2021 to Unknown; Unknown
#4 Simvastatin Simvastatin Unknown (NOS) Unknown {Lot#: Asked But Unknown} Regimen #1	20 mg, QID; Unknown	dyslipidemia [Dyslipidaemia]	Oct-2019 to 2020; Unknown

23. OTHER RELEVANT HISTORY continued
Medical History Sub Section:

- #6| Historical Condition | Hepatic hemangioma rupture [Hepatic haemangioma rupture] | Ongoing
- #7| Historical Condition | dyslipidemia [Dyslipidaemia] |