



**LIPOIC ACID**

**ALFASIGMA POST-MARKETING SURVEILLANCE  
REPORT**

## Background

On 28 January 2021 EFSA has launched an open consultation on its draft opinion on alpha-lipoic acid to discuss data on the relationship between intake of alpha-lipoic acid and the risk of insulin autoimmune syndrome (IAS) and investigates whether a dose may be set below which ALA added to foods is not expected to cause IAS in the general population or in vulnerable subgroups.

Alfasigma commercializes food supplements containing Alpha-Lipoic Acid (ALA) in many countries, and set up a Post-marketing Surveillance System to collect undesirable effects of food supplements. Objective of this report is to share with EFSA the Alfasigma post-marketing surveillance safety data.

## Alfasigma Food Supplements containing Alpha Lipoic Acid (ALA)

Alfasigma distributes and sells food supplements containing Alpha-Lipoic Acid (ALA) in association to other components such as Omega-3, Superoxide dismutase (SOD), Honokiol (a lignan isolated from the bark, seed cones, and leaves of trees belonging to the genus Magnolia) vitamins E, B1, B2, B5, B6, Selenium and Magnesium. The exact composition of each product is reported in Table 1 (A-B-C-D).

**Table 1. ALA-Line compositions**

<b>A) ALANERV</b>	
<b>INGREDIENTS</b>	<b>DOSAGE 2 caps/d</b>
Lipoic Acid	600 mg
Omega-3	360 mg
Vitamin E	15 mg
Vitamin B5	9 mg
Vitamin B6	2.8 mg
Vitamin B2	2.4 mg
Vitamin B1	2.1 mg
Selenium	50 mcg

<b>B) ALANERV ON</b>	
<b>INGREDIENTS</b>	<b>DOSAGE 2 caps/d</b>
Lipoic Acid	600 mg
Omega-3	360 mg
Honokiol	54 mg
Vitamin E	15 mg
Vitamin B5	9 mg
Vitamin B6	2.8 mg
Vitamin B2	2.4 mg
Vitamin B1	2.1 mg
Selenium	50 mcg

<b>C) ALA SOD 600</b>	
<b>INGREDIENTS</b>	<b>DOSAGE 1 cpr/d</b>
Lipoic Acid	600 mg
SOD	140 UI
Vitamin E	7.5 mg
Selenium	25 mcg

<b>D) ALANERV AGE</b>	
<b>INGREDIENTS</b>	<b>DOSAGE 2 caps/d</b>
Lipoic Acid	600 mg
Omega-3	333.33 mg
Vitamin E	12 mg
Vitamin D	5 mcg
Magnesium	56.25 mg

These products are commercialized in several countries (Italy, Portugal, Poland, Spain, Romania, Malaysia). As reported in the table 2.

**Table 2. ALA-Line (Alfa Lipoic Acid – Line)**

Country	Product	Launch date
ITALY	ALANERV	2006
	ALA SOD 600	2010
	ALANERV AGE	2014
	ALANERV ON	2012
SPAIN	ALANERV	2006
	ALASOD	2012
	ALAON	2014
PORTUGAL	ALANERV	2011
	ALA SOD 600	2013
POLAND	ALANERV	2006
TUNISIA	ALANERV	2010
MALAYSIA	ALANERV	2014
ROMANIA	ALANERV	2009
	ALA SOD 600	2016

The table below (Table 3) shows Alfasigma internal sales data regarding ALA brand family in Volume Packs from MAT December 2017 to MAT December 2019 and the cumulative total of the three years

**Table 3. Internal sales data**

Volume in PACKS [Absolute]					
Brand Name	Market/CTY	2017	2018	2019	Total 3YRS
<b>Total ALA Line ROMANIA+ITALY+SPAIN+POLAND+PORTUGAL+TUNISIA</b>		<b>949.241</b>	<b>1.104.819</b>	<b>1.136.306</b>	<b>3.190.366</b>
<b>Total ALA Line ROMANIA</b>		<b>360.626</b>	<b>455.252</b>	<b>507.604</b>	<b>1.323.482</b>
ALANERV 920 MG 20 CPS AWI RUM	Romania	330.686	404.117	230.444	965.247
ALANERV 920 MG 20 CPS RUM	Romania			214.653	214.653
ALA600- SOD 20CPR AW RO	Romania	29.940	51.135	62.507	143.582
<b>Total ALA Line ITALY</b>		<b>243.536</b>	<b>234.427</b>	<b>213.212</b>	<b>691.175</b>
ALANERV 20 Cps	Italy	94.322	92.439	85.064	271.825
ALA 600-SOD 20 CPR	Italy	72.944	68.716	57.627	199.287
ALANERV AGE 20 CPS	Italy	47.206	45.919	49.763	142.888
ALANERV ON 20 CPS	Italy	29.064	27.353	20.758	77.175
<b>Total ALA Line SPAIN</b>		<b>199.225</b>	<b>215.528</b>	<b>212.248</b>	<b>627.001</b>
ALAON 30 soft cap.	Spain	65.219	79.968	85.673	230.860
ALASOD 20 tab.	Spain	64.905	72.713	72.366	209.984
ALANERV 30 soft cap.	Spain	59.879	55.066	47.677	162.622
ALANERV 20 soft cap.	Spain	9.222	7.781	6.532	23.535
<b>Total ALA Line POLAND</b>		<b>100.850</b>	<b>147.659</b>	<b>147.850</b>	<b>396.359</b>
ALANERV 30 CAPS	Poland	100.850	99.755	83.150	283.755
ALANERV ON 30 CPS	Poland		47.904	64.700	112.604
<b>Total ALA Line PORTUGAL</b>		<b>32.008</b>	<b>34.278</b>	<b>35.392</b>	<b>101.678</b>
MR_PT_Alanerv 30 caps	Portugal		10.521	26.806	37.327
MR_PT_ALA600SOD	Portugal		3.455	8.586	12.041
ALANERV 30 CAPS	Portugal	23.342	14.793		38.135
ALA600SOD	Portugal	8.666	5.509		14.175
<b>Total ALA Line TUNISIA</b>		<b>12.996</b>	<b>17.675</b>	<b>20.000</b>	<b>50.671</b>
ALANERV 920 MG 20 CPS TN	Tunisia	12.996	17.675	20.000	50.671

## Data source

In order to monitor the safety of these products, Alfasigma set up a Post-marketing Surveillance System to collect undesirable effects of food supplements.

The surveillance system consists in the collection in the Safety Database of spontaneous reports of suspected undesirable effects that occurred after taking food supplements and their evaluation. Reports can be sent from anybody observing a suspected undesirable effects associated with these products (physicians, pharmacists or consumers), by email and phone call. Each incoming report is analyzed taking into consideration type of event<sup>1</sup>, medical history, laboratory tests, concomitant medications or food, temporal plausibility and all other available information useful to evaluate the causal relationship<sup>2</sup> between the event and the product.

## Data analysis

From January 2010 to September 2020 a total of 100 reports concerning Alpha-Lipoic Acid, including 213 adverse effects, were collected in the safety database, 92 from European countries (34 Italy, 18 Portugal, 6 Poland, 33 Spain and 1 Romania) and 8 from extra-EU country (Malaysia).

These reports were mostly received from physicians (39%), pharmacists (18%) and other health professionals.

**Table 4. Safety reports received for each ALA-Line product**

<b>Product</b>	<b>n° of safety reports (%)</b>
Alanerv	44 (44%)
Ala SOD 600	41 (41%)
Alanerv ON	11 (11%)
Alanerv AGE	1 (1%)
<b>TOTAL</b>	<b>100 (100%)</b>

Up to September 2020 **no case Insulin autoimmune syndrome (IAS) or Hirata disease were received** after taking one of our food supplements containing ALA.

<sup>1</sup> Codified according to WHO-UMC system

<sup>2</sup> Codified according to Medical Dictionary for Regulatory Activities (MedDRA)