



## CERTIFICATE OF ANALYSIS

**Product** TRETINOIN-USP /EP Current edition **Code N°** 2610460 **Batch N°** 1910002550

**Manufacturing date** Dec 2019 **Retesting date (where applicable)** Dec 2022 **Expiration date (where applicable)**

| Analysis Number                                 |                                                                                                                                                                                                                                                                                                                             | 040000016041 |                            | Limits         |  |
|-------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|----------------------------|----------------|--|
| Test                                            | Results                                                                                                                                                                                                                                                                                                                     | M.U.         | Min                        | Max            |  |
| Description                                     | Light yellow, crystalline powder                                                                                                                                                                                                                                                                                            |              | Yellow, crystalline powder | Light orange   |  |
| Identification                                  |                                                                                                                                                                                                                                                                                                                             |              |                            |                |  |
| - IR                                            | Conforms to Standard                                                                                                                                                                                                                                                                                                        |              | Conforms to Standard       |                |  |
| - UV                                            | Conforms to Standard                                                                                                                                                                                                                                                                                                        |              | Conforms to Standard       |                |  |
| Loss on drying                                  | 0,0                                                                                                                                                                                                                                                                                                                         | %            |                            | 0,5            |  |
| Residue on ignition                             | 0,0                                                                                                                                                                                                                                                                                                                         | %            |                            | 0,1            |  |
| Heavy metals                                    | < 20                                                                                                                                                                                                                                                                                                                        | ppm          |                            | 20             |  |
| Assay (TBAH)                                    | 99,0                                                                                                                                                                                                                                                                                                                        | %dried       | 98,0                       | 102,0          |  |
| Related Substances HPLC :                       |                                                                                                                                                                                                                                                                                                                             |              |                            |                |  |
| - Isotretinoin                                  | < 0,01                                                                                                                                                                                                                                                                                                                      | %            |                            | 0,50           |  |
| - Epoxy derivative                              | 0,02                                                                                                                                                                                                                                                                                                                        | %            |                            | Less than 0,15 |  |
| - Impurity a (4-metoxo retinoic acid)           | < 0,02                                                                                                                                                                                                                                                                                                                      | %            |                            | Less than 0,15 |  |
| - Largest unknown impurity                      | 0,06                                                                                                                                                                                                                                                                                                                        | %            |                            | 0,10           |  |
| - Total Impurities(apart from Isotretinoin)     | 0,12                                                                                                                                                                                                                                                                                                                        | %            |                            | 0,50           |  |
| Residual Solvents (GC) :                        |                                                                                                                                                                                                                                                                                                                             |              |                            |                |  |
| - ICH Class 1 solvents : Not used               | Not tested                                                                                                                                                                                                                                                                                                                  |              | Not tested                 |                |  |
| - ICH Class 2 solvents :                        | In specific                                                                                                                                                                                                                                                                                                                 |              | In specific                |                |  |
| Chloroform                                      | < 25                                                                                                                                                                                                                                                                                                                        | ppm          |                            | 50             |  |
| Methanol                                        | < 26                                                                                                                                                                                                                                                                                                                        | ppm          |                            | 100            |  |
| - ICH Class 3 solvents :                        |                                                                                                                                                                                                                                                                                                                             |              |                            |                |  |
| Ethyl Acetate                                   | < 20                                                                                                                                                                                                                                                                                                                        | ppm          |                            | 100            |  |
| Isopropanol                                     | 414                                                                                                                                                                                                                                                                                                                         | ppm          |                            | 2000           |  |
| Related Substances (HPLC) EP :                  |                                                                                                                                                                                                                                                                                                                             |              |                            |                |  |
| - Isotretinoin                                  | < 0,05                                                                                                                                                                                                                                                                                                                      | %            |                            | 0,50           |  |
| - 4-Methoxyretinoic acid (Impurity a)           | < 0,05                                                                                                                                                                                                                                                                                                                      | %            |                            | Less than 0,15 |  |
| - (all-trans)-5,6-epoxy-5,6dihydroretinoic acid | < 0,05                                                                                                                                                                                                                                                                                                                      | %            |                            | Less than 0,15 |  |
| - Largest unknown impurity                      | < 0,05                                                                                                                                                                                                                                                                                                                      | %            |                            | 0,10           |  |
| - Total impurities (apart from isotretinoin)    | < 0,05                                                                                                                                                                                                                                                                                                                      | %            |                            | 0,50           |  |
| Clarity of solution 2%                          |                                                                                                                                                                                                                                                                                                                             |              |                            |                |  |
| - in chloroform (NTU)                           | 0,5                                                                                                                                                                                                                                                                                                                         | NTU          |                            | 3,0            |  |
| - in THF                                        | Clear                                                                                                                                                                                                                                                                                                                       |              | Clear                      |                |  |
| Paricle size (laser) :                          |                                                                                                                                                                                                                                                                                                                             |              |                            |                |  |
| - d(90) :                                       | 317                                                                                                                                                                                                                                                                                                                         | µm           | 300                        |                |  |
| - d(50) :                                       | 120                                                                                                                                                                                                                                                                                                                         | µm           |                            | 150            |  |
| - d(10) :                                       | 27                                                                                                                                                                                                                                                                                                                          | µm           | 15                         |                |  |
| Packaging and Storage                           | Store in airtight containers, in a dry place, protected from light, heat and moisture, at a mean temperature of 25°C (allowed excursions 15-30°C). It is recommended that the contents of an opened container be used as soon as possible and any unused part be protected under vacuum or under atmosphere of an inert gas |              |                            |                |  |

This batch has been manufactured, packaged and tested in accordance with EU GMP Guideline Volume 4 Part II (ICH Q7A) .  
Manufacturing site of the Active Pharmaceutical Ingredient : OLON S.P.A. - GARBAGNATE MIL.se

Date

Jan 17, 2020

Ed01

Reissued on  
Dec 10, 2021

Q.C. Manager

Reviewed by Qualified Person

Reissued for: Retest extension