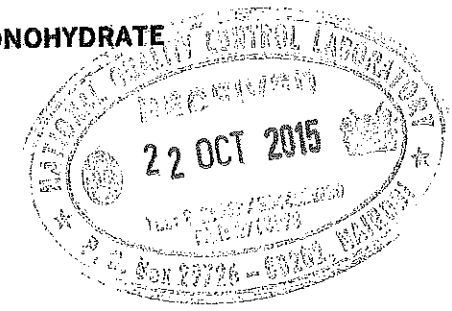
WRS 24-2

NOVARTIS

Novartis Pharma Reference Standards Unit International Service Laboratory

Novartis International Pharmaceutical Ltd. Branch Ireland, Ringaskiddy, Co. Cork, Ireland.

Certificate of Analysis /Reference Standard



Compound name : **ZOLEDRONIC ACID MONOHYDRATE**
Novartis identity number : **3106531**

Reference standard :
Batch number : H3332
Expiry date : March 2016
SAP/QAO number : 089100086487

Origin of material :
Lot number of manufacturer : C0004
Manufacturing date : July 2012
Manufacturing site : Novartis Pharma AG, 4002 Basel Switzerland

Analysis (Testing Monograph: DS_3106531_A_R_4)

Test	Result	Requirement
Identity:		
Appearance by visual examination	white crystalline powder	white, crystalline powder
Infrared spectrum (*)	corresponds	corresponds to the reference
Thin layer chromatography	corresponds	corresponds to the reference
^{1}H-NMR Spectrum (**)	corresponds	corresponds to the reference
Impurities:		
Absorbance of the solution at 420 nm	0.00	max. 0.1
Water (Karl Fischer)	6.44 %	6.0 – 7.5 %
Polymorph content by X-ray powder diffraction trihydrate	< 5 %	max. 15 %
Methane sulfonic acid (CE)	< 0.1 %	max. 0.1 %
Residual solvent – ethanol (GC)	< 0.01 %	max. 0.3 %
Related substances:		
NAP205-02 by IC	0.24 %	max. 0.5 %
NAP501-99 by ^{31}P – NMR spectrum	< 0.05 %	max. 0.1 %
CGP 76892 by HPLC	< 0.05 %	max. 0.1 %
Any unspecified impurity by HPLC	< 0.05 %	max. 0.10 %
Total unspecified impurities by HPLC and IC	< 0.05 %	max. 0.2 %
Total impurities by HPLC, IC and ^{31}P-NMR	0.24 %	max. 0.8 %
Content		
Assay by HPLC (***)	99.1 %	98.0 – 102.0 % (Requirement for Japan: not less than 99.0 %)
Content (****)	93.3 %	

(*) Compared to USP batch no G0L332
(**) According to DS-11_NR_1
(***) Based on anhydrous substance
(****) Content calculation (According to API RS qualification Report for batch H3332): 100.0 % - total impurities (HPLC, IC and ^{31}P-NMR) – water – residual solvent

Conclusion ; released as reference standard for quantitative and qualitative use
Storage condition : do not store above + 30°C

Prepared by: _____ Reviewed by: _____ Approved by: _____
RSU QA Facilitator

Date: 28 Aug 2015 Date: 28 Aug 2015 Date: 28 Aug 2015

Certificate Version 02

NIP.ISL.169