Australian Government
Department of Health
Therapeutic Goods Administration

Compositional guideline for Levomefolate Glucosamine

Name of the ingredient

Levomefolate glucosamine (AAN)

Definition of the ingredient

(6S)-5-methyltetrahydrofolic acid, Glucosamine salt

Molecular formula: $C_{32}H_{51}N_9O_{16}$

Molecular Weight: 817.8019 g/mol

CAS number: 1181972-37-1

Table 1 Ingredient specific requirements

Test	Method reference	Acceptance criteria
Description		
Appearance	Visual	Cream to light brown powder
Characteristics		
Solubility	BP General Notices	Very soluble in water; soluble in dilute acid and dilute alkali; Practically insoluble in most organic solvents.
pH (1% w/v aqueous solution)	Ph Eur method 2.2.3	5.5 – 6.5
Identification		
IR spectroscopy	USP <197A>	Spectrum complies with authenticated reference material.

Test	Method reference	Acceptance criteria
Specific optical rotation (dry, 10% w/v in water)	USP <781>	+53° to +59°
Assay		
Levomefolate glucosamine equivalent to (6S)-5-methyltetrahydro folic acid	HPLC	96.0 to 102.0% on anhydrous basis equivalent to 53.8 to 57.1% on anhydrous basis
Glucosamine	HPLC	42.2 to 44.9% on anhydrous basis

Table 2 Incidental constituents

Test	Method reference	Acceptance criteria
Incidental metals and non-metals		
While ingredient manufacturers are encouraged to include limits for Incidental metals and non-metals, it is the product into which those substances are formulated that contains the ingredient, alone or in combination with other ingredients, must comply with the acceptance criteria set in the United States Pharmacopeia - National Formulary general chapter '<2232> Elemental Contaminants in Dietary Supplements'. When testing is performed at the raw material stage, calculation of the total daily exposure in the finished product should be performed. This calculation is based on the quantity of each ingredient present in the product, the maximum potential contamination given the proposed limits for each raw material and the daily dose of the product.		
Other organic or inorganic impurities or toxins		
Diastereomeric purity	HPLC	Not less than 99.0% w/w
Water	USP <921>	Not more than 8.0% w/w
Total impurities	HPLC	Not more than 2.5% w/w
4-Aminobenzoylglutamic acid (ABGA)	HPLC	Not more than 0.3% w/w

Test	Method reference	Acceptance criteria
4a-Hydroxy-5-methyltetrahydrofolic acid (HOMeTHFA)	HPLC	Not more than 1.0% w/w
(6S)-Pyrazino-s-triazine derivative [(6S)-Mefox]	HPLC	Not more than 0.3% w/w
5-Methyltetra-hydropteroic acid (MeTHPA)	HPLC	Not more than 0.3% w/w
Any other impurity	HPLC	Not more than 0.15% w/w
Microbiology		
While substance manufacturers are encouraged to include limits for objectionable microorganisms, it is the product into which those substances are formulated that is subject to a legally binding set of criteria. The Therapeutic Goods Order No. 77 *'Microbiological Standards for Medicines'* mandates that any finished product that contains the ingredient, alone or in combination with other ingredients, must comply with the microbial acceptance criteria set by Clause 9 of the Order.		

Key to abbreviations:

AAN = Australian Approved Name

BP = British Pharmacopoeia

CAS = Chemical Abstracts Service

HPLC = High Performance Liquid Chromatography

IR = Infrared Spectroscopy

USP = US Pharmacopoeia