Australian Government
Department of Health
Therapeutic Goods Administration

Compositional guideline for alpha-casozepine enriched hydrolysed milk protein

Name of the ingredient

alpha (α)-casozepine enriched hydrolysed milk protein (AAN)

Definition of the ingredient

The above named substance is a low-lactose, spray dried powder form of a protein hydrolysate of bovine (*Bos taurus*) skim milk. Alpha-casozepine is a decapeptide from αS1-casein.

Specific condition

The milk used in the manufacture of the substance must be sourced either from Australian herds or herds from countries which are considered BSE-free, and which are registered for milk production for human consumption. The milk shall comply with the maximum residue limits for agricultural and veterinary chemicals established for milk in Standard 1.4.2 of the Australia New Zealand Food Standards Code.

Animal origin information would need to be provided with all new applications to list medicines containing α-casozepine enriched hydrolysed milk protein. In some instances further information may be required for evaluation by the TGA in relation to products containing this substance (see Supplementary information on Transmissible Spongiform Encephalopathies (TSEs) regulation).

Table 1. Ingredient specific requirements

Test	Method reference	Acceptance criteria
Description		
Appearance	Visual	White/cream free flowing powder
Characteristics		
Loss on drying	IDF 26A (102°C for 2 h)	Not more than 5.5%

Test	Method reference	Acceptance criteria
pH of solution	IDF 115A (pH meter)	5.0–7.5
Ash	IDF 27 (550°C, furnace)	Not more than 20% (as is)
Identification		
Chromatographic profile	HPLC[1]	Profile consistent with that of authenticated reference material
Assay		
Content of alpha (α)-casozepine	HPLC[1]	Not less than 1.8%
Protein (as N x 6.38)	IDF 20B (Kjeldahl method)	Not less than 73% (as is)
Lactose	Enzymatic	Not more than 1.0%
Notes		
1. A company method involving solution in water/acetonitrile/trifluoroacetic acid and analysed by HPLC with ultraviolet detection		

Table 2. Incidental constituents

Test	Method reference	Acceptance criteria
Incidental metals and non-metals		
Lead	AAS	Not more than 1 ppm
Arsenic	AAS	Not more than 3 ppm
Cadmium	AAS	Not more than 0.05 ppm
Mercury	AAS	Not more than 0.1 ppm
Sodium	Flame spectrometric	Not more than 6%
Potassium	Flame spectrometric	Not more than 0.2%

Test	Method reference	Acceptance criteria
Calcium	AAS	Not more than 0.5%
Magnesium	AAS	Not more than 0.1%
Phosphorus	Spectrometric	Not more than 1%
Other organic or inorganic impurities or toxins		
Aflatoxins	ISO 14501	Complies
Lysinoalanine[2]	HPLC	Not detected
Nitrite/nitrosamines[2]	Chromatography	Not detected
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.		
Notes		
2. Lysinoalanine is an amino acid sometimes found in alkali treated proteins. Nitrite/nitrosamines originate from the drying gases used in some spray-drying procedures. These tests may be omitted subject to TGA approval.		

Key to abbreviations:

AAS = atomic absorption spectroscopy

BP = British Pharmacopoeia

HPLC = High-pressure liquid chromatography

IDF = International Dairy Federation

ISO = International Standards Organisation

Ph Eur = European Pharmacopoeia