Classification of Unscheduled Peptides

Submission to the Medicines Classification Committee

Medsafe

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Background

The Investigation & Enforcement Team at Medsafe have been recording data on a wide variety of unscheduled peptides that have been intercepted at the border. From 1 April 2025 to 19 May 2025, 56 parcels have been intercepted containing peptides or selective androgen receptor modulators (SARMs). Whilst SARMs are classified as prescription medicines (as a group entry) in New Zealand, many peptides are not scheduled.

Peptides first came to the attention of Medsafe in 2013 after an Australian Crime Commission investigation into the use of peptides in professional sports. At that time, peptides were sourced by individuals primarily for performance and image enhancement purposes. However, in recent years, a variety of peptides have been developed for a range of therapeutic purposes, including (but not limited to) cognitive enhancement, hair growth, libido enhancers, sexual dysfunction, immune enhancers, and cancer treatment.

There are many websites overseas selling these products 'for research purposes only'. However, these products are being purchased by individuals who are importing with the intention to administer them for a therapeutic purpose.

With this recent proliferation of new/novel peptides, many are not scheduled. When substances that are not scheduled as a prescription medicine are intercepted at the border, the product is released to the individual with a high-risk medicine letter (**Appendix A**) as Medsafe does not have the grounds, pursuant to the Medicines Act 1981, to seize them. This is posing a risk to health, as the product's quality, efficacy and interactions with other medicines is unknown.

Medsafe has investigated how group entries may be used to schedule some of these peptides as prescription medicines. Group entries have been used previously to encompass groups of substances that frequently see new variations. Examples include:

- Vaccines
- Racetams
- SARMs
- GLP-1 agonists (group entry recommended at the 73rd Medicines Classification Committee meeting, held on 26 February 2025)

This submission provides recommendations to the Medicines Classification Committee (MCC) regarding the potential for classifying many of these peptides through group entries. A summary of the proposed entries is provided in **Appendix B**. A brief description of the compounds of interest, their proposed mechanism of action, and potential clinical significance is provided, where possible. The current regulatory status of the substances in New Zealand and Australia is also provided.

Thymic peptide hormones and their analogues (naturally occurring & synthetic)

The thymus gland is a major lymphoid organ that regulates the immune and endocrine systems through modulation of hormone and cytokine levels. Thymic peptide hormones are a group of polypeptides synthesised in the thymus gland, including those that are synthetically derived and mimic naturally synthesised thymic peptide hormones. Thymic hormones and their analogues have been used to treat a range of inflammatory diseases, including multiple sclerosis, sepsis, HIV, viral hepatitis, and cancer.

There are four categories of thymic peptide hormones:

1. Alpha-thymosin (e.g. thymosin alpha-1)

Thymosin alpha-1 (and its synthetic form, thymalfasin) is known to be immune enhancing, immune-modulating, and immune-restoring. It exerts its immune system function through activation of toll-like receptor signalling pathways, stimulation of pro-inflammatory cytokines, and activation of immune cells.

Thymosin alpha-1 is currently used in many countries for the treatment of hepatitis B and C, and early clinical trials appear to aim to gather evidence showing that it may be useful in the treatment of cystic fibrosis, septic shock, SARS, and cancer. However, thymosin alpha-1 is also being sold 'for research purposes only' to personal importers who intend to administer it for a therapeutic purpose.

There are known risks associated with thymosin alpha-1 that have become apparent during clinical trials, including fever, fatigue, nausea, vomiting, and neutropenia. It is contraindicated in patients with hypersensitivity to thymosin alpha-1 and immuno-suppressed patients.

Thymosin alpha-1/thymalfasin is not currently scheduled in New Zealand or Australia.

2. Beta-thymosin (e.g. thymosin beta-4)

Thymosin beta-4 (and its synthetic form, TB-500) has a broad range of biological functions, including supporting tissue regeneration and wound healing, increasing angiogenesis, and reducing inflammatory reactions. It is thought to exert its biological activity through several mechanisms, including downregulation of NF-kB pathways, promoting cell migration (including keratinocytes and endothelial cells), enhancing endothelial cell differentiation, and possibly increasing ferroptosis.

Thymosin beta-4 has been studied in several clinical trials, including trials for pressure ulcers, dry eye, and neurotrophic keratopathy. It is considered a performance enhancing substance and is banned in sports by the World Anti-Doping Agency due to its potential effects in aiding soft tissue recovery.

Thymosin beta-4 and TB-500 are classified as prescription medicines in both New Zealand and Australia.

3. Thymulin

Thymulin is a metallopeptide produced by thymic epithelial cells that requires conjugation with zinc to permit its biological activities. Thymulin secretion is influenced by prolactin, growth hormone, interleukin (IL)-1 alpha and IL-1 beta. It is thought to stimulate the production of luteinising hormone, promote T-cell differentiation, activate NK cells, and have anti-inflammatory effects.

However, it appears that these functions have only been studied in animal models, as thymulin does not appear to have yet entered clinical trials. As such, whilst thymulin is currently being investigated for hormonal and reproductive abnormalities, its clinical risks are unknown.

Thymulin is not currently scheduled in New Zealand or Australia.

4. Thymopoietin

Thymopoietin (and its derivatives, including thymopentin) is a polypeptide produced by thymic epithelial cells with a wide range of biological effects, including modulation of the neuromuscular junction through the nicotinic acetylcholine receptor, T lymphocyte precursor differentiation, and inhibition of NF-kB pathways.

Animal studies are reported to have shown that thymopoietin may increase resistance to infection. In humans, thymopoietin pentapeptide has previously been investigated for use in rheumatoid arthritis.

Thymopoietin is not currently scheduled in New Zealand or Australia.

Recommended Group Entry

Medsafe recommends that thymic peptide hormones and their analogues, both naturally occurring and synthetically derived, are classified as a group entry (and individually, when new substances arise) as prescription medicines. These peptide hormones have related biological functions and synthesis pathways, warranting a group entry.

This entry will encompass thymosins, thymulin, thymopoietin, their synthetic versions, and future analogues of these hormones.

Body Protective Compound (BPC)-157 and its analogues (naturally occurring & synthetic)

BPC-157 is a naturally occurring peptide found in gastric juices that is reported to have cytoprotective, neuroprotective, and anti-inflammatory properties. Synthetic versions have been produced for athletic performance enhancement. As such, BPC-157 was classified as a prohibited substance by the World Anti-Doping Agency in 2022. BPC-157 was classified at the 70th MCC meeting held on 25 May 2023 as a prescription medicine, following several instances of importation for personal use. It is classified as a prescription medicine in Australia.

BPC-157 has been sold with claims regarding bone/joint healing, stomach ulcers, organ damage, nervous system regeneration, and athletic performance. The safety and efficacy of BPC-157 in humans remains to be fully elucidated.

Since 2023, derivatives of BPC-157 have been intercepted, including NL-BPC-157 Hexadecapeptide. Such derivatives are not currently captured by the BPC-157 classification.

Recommended Group Entry

Medsafe recommends that Body Protective Compound (BPC)-157 and its analogues (both naturally occurring and synthetic) are classified as a group entry (and individually, when new substances arise) as prescription medicines.

This will encompass BPC-157 and future chemically related analogues of these peptides.

Adrenocorticotropic hormone analogues (naturally occurring & synthetic)

Adrenocorticotropic hormone (ACTH) is a pituitary gland hormone already classified under the 'pituitary hormones' class as a prescription medicine in New Zealand. Several ACTH analogues have appeared on the market, with individuals importing them into New Zealand. These analogues tend to make nootropic claims through promoting neurogenesis and increasing brain-derived neurotrophic factor levels. Their mechanism of action is often unknown.

There seems to be limited clinical research on the benefits of ACTH analogues, and little is known about their side effects or long-term effects.

Recommended Group Entry

Medsafe recommends that adrenocorticotropic hormone analogues, including those that are synthetically derived and mimic the naturally synthesised adrenocorticotropic hormones, are classified as a group entry (and individually, when new substances arise) as prescription medicines.

This class would encompass any analogues of ACTH, such as Adamax and Semax (two peptide products currently marketed as cognitive enhancers). It would capture any new/novel products with a similar chemical structure.

Pineal gland peptides and their analogues (naturally occurring & synthetic)

Key pineal gland peptides (and their analogues) include epitalon and epithalamin. Both epitalon and epithalamin have been reported to increase telomere lengths, with claims that they could be effective anti-aging substances. In addition, it is reported that they may restore melatonin secretion by the pineal gland in older adults, suggesting they can improve circadian rhythm.

These substances are often marketed as anti-aging and/or hair growth promotion products. In some cases, they are marketed as a cancer preventative. These therapeutic claims appear to be unsubstantiated.

Epitalon and epithalamin are not currently scheduled in New Zealand or Australia.

Recommended Group Entry

Medsafe recommends that pineal gland peptides and their analogues, both naturally occurring and synthetically derived, are classified as a group entry (and individually, when new substances arise) as prescription medicines.

This class would encompass any pineal gland peptides and their analogues (naturally occurring and synthetic) such as epithalamin and epitalon. It would capture any new/novel products with a similar mode of action and/or chemical structure. It would not include melatonin, as melatonin is not a peptide hormone.

Anti-microbial peptides and their precursors

Antimicrobial peptides (AMPs) are a class of small peptides that are reported to have a range of inhibitory effects against bacteria, fungi, parasites, and viruses in a wide range of organisms. Mammalian AMPs are broadly classified as either cathelicidins or defensins:

1. Cathelicidins

Cathelicidins are cationic, amphipathic peptides that are a component of the innate immune system. They exert anti-microbial effects in response to many pathogens through binding to negatively charged cell membranes, leading to cell death. In addition, they induce upregulation of inflammatory cytokines and chemokines, increase phagocytosis, and are chemotactic for mast cells.

Due to these activities, peptides belonging to the cathelicidin family (such as LL-37) are being marketed as immune modulators for use in wound healing, tissue regeneration, and infection. Cathelicidin precursors (e.g. CAP-18) have also been imported into New Zealand, with such products suggesting potential therapeutic use in HIV and sepsis.

2. Defensins

Defensins are cationic peptides that are a component of the innate immune system. Like cathelicidins, they have anti-microbial and immune-modulation effects, and are also suggested to play a role in tumorigenesis.

Recommended Group Entry

Medsafe recommends that anti-microbial peptides and their precursors are classified as a group entry (and individually, when new substances arise) as prescription medicines.

This class would encompass any anti-microbial peptide and their precursors, such as LL-37 and CAP-18, and will account for future AMP products that may arise.

Myostatin modulator peptides

Myostatin is a myokine that is produced and released by myocytes. It acts on myocytes to inhibit muscle growth. As such, inhibitors of myostatin are of interest to those in the body building community, for the treatment of muscular dystrophy, and in the treatment of muscle wasting associated with cancer.

Clinical trials for muscular dystrophy are reported to have not proven successful thus far due to a lack of efficacy, despite promising results from animal studies. Adverse side effects from various clinical trials include nosebleeds, gum bleeding, erythema, tendon injury, and potentially an increased risk of thromboembolism.

Myostatin inhibitors are banned by the World Anti-Doping Agency, and are not scheduled in New Zealand or Australia.

Recommended Group Entry

Medsafe recommends that myostatin modulator peptides are classified as a group entry (and individually, when new substances arise) as prescription medicines.

This class would encompass any myostatin modulator peptides (such as GDF-8, ACE-031, and myostatin pro-peptide) and will account for future peptides that may arise.

Mitochondria-derived peptides and their analogues (naturally occurring & synthetic)

Mitochondria-derived peptides are small peptides encoded by mitochondrial DNA that have biological activity outside of the mitochondria. These include humanin, MOTS-c, and SHLP peptides 1-6.

Several of these peptides have been imported into New Zealand for personal use. They are marketed as having a range of broad functions, including reducing cell stress, inflammation modulation, lifespan extension, and combating obesity and diabetes. Some are also reported to have protective effects against Alzheimer's disease and Huntington's disease. Whilst this is reported to have been observed *in vitro,* these findings have not been substantiated in humans.

None of these peptides are scheduled in New Zealand or Australia.

Recommended Group Entry

Medsafe recommends that mitochondria-derived peptides and their analogues (both naturally occurring and synthetic) are classified as a group entry (and individually, when new substances arise) as prescription medicines. Peptides originating from the mitochondria appear to be attracting increasing attention for their performance enhancement potential, warranting a group class for these substances.

This class would encompass any mitochondria-derived peptides (including humanin, MOTS-c and SHLP peptides) and will account for future peptides that may arise.

Erythropoietin and its analogues (naturally occurring & synthetic)

Erythropoietin is a hormone that stimulates the production of red blood cells in the bone marrow. It is a well-known performance-enhancing drug, and there are an increasing number of erythropoietin derivatives being produced (for example, ARA-290) that are being marketed as treatments for neuropathic pain. ARA-290 is reported to function by reducing inflammation and stimulating nerve fibre regrowth. These peptides are still in development, and their efficacy and potential clinical risk have not been assessed.

Recommended Group Entry

Medsafe recommends that erythropoietin and its analogues, both naturally occurring and synthetically derived, are classified as a group entry (and individually, when new substances arise) as prescription medicines.

Erythropoietin is already classified as a prescription medicine in both New Zealand and Australia. This class would encompass any analogues of erythropoietin (such as ARA-290) and will account for future substances that may arise. It would capture any new/novel products with a similar mode of action and/or chemical structure.

Tuftsin and its analogues (naturally occurring & synthetic)

Tuftsin is a peptide derived from the Fc-domain of immunoglobulin G (IgG). It is an immunomodulator involved in activation of phagocytic cells, cell motility, and antigen augmentation. It is also reported to have anti-bacterial and anti-cancer effects.

Tuftsin has been investigated in several clinical trials, mainly relating to auto-immune conditions, and a range of studies into its potential therapeutic uses are ongoing.

Selank, an elongated analogue of tuftsin, has been imported into New Zealand with claims of anti-anxiety and nootropic effects, as well as the claimed potential to improve depression, learning, memory, and cognition. These claims are unsubstantiated.

Recommended Group Entry

Medsafe recommends that tuftsin and its analogues, both naturally occurring and synthetically derived, are classified as a group entry (and individually, when new substances arise) as prescription medicines.

This class would encompass tuftsin and any structurally related analogues (such as Selank) that may arise.

Kisspeptins (naturally occurring & synthetic)

Kisspeptins are a family of peptides important in the regulation of reproduction, puberty, fertility, and hormone secretion. Kisspeptin neurons in the hypothalamus stimulate Gonadotropin-releasing hormone (GnRH) secretion, leading to LH (luteinising hormone) and FSH (follicle-stimulating hormone) release.

Kisspeptin products marketed as improving sexual and reproductive health and treating sexual dysfunction have been imported into New Zealand for personal use. These products are reported to cause side effects such as flushing, nausea, headaches, increased blood pressure, mood swings, menstrual cycle changes, and libido changes.

Whilst kisspeptin has been reported to show potential as a therapeutic for sexual dysfunction, more research is required to understand its efficacy and associated clinical risks.

Recommended Group Entry

Medsafe recommends that kisspeptins, both naturally occurring and synthetically derived, are classified as a group entry (and individually, when new substances arise) as prescription medicines.

Individual Peptides

Whilst the above group classes encompass many peptides, not all peptides being imported into New Zealand can be captured in this way. As such, Medsafe have identified several peptides that would benefit from being classified individually, as prescription medicines:

1. Larazotide:

   Larazotide is a synthetic peptide that is reported to act as a tight junction regulator. Larazotide has been investigated in clinical trials for the treatment of coeliac disease, but such trials appear to have been discontinued due to patient recruitment and efficacy issues.

2. PTD-DBM:

   Protein Transduction Domain-fused Dishevelled Binding Motif (PTD-DBM) is a synthetic peptide reported to treat hair loss through negative regulation of the Wnt/beta-catenin signalling pathway. Early studies in animals appear to identify PTD-DBM as a promising potential treatment for alopecia, however no clinical trials in humans have been conducted.

3. AICAR:

   5-aminoimidazole-4-carboxamide-ribonucleoside (AICAR) is an analogue of adenosine monophosphate (AMP) that stimulates AMP-dependent protein kinase (AMPK) activity. It is reported to have performance-enhancing effects, and the World Anti-Doping Agency declared AICAR a banned substance in 2011. There appears to be clinical concerns regarding neurodegeneration and metabolic disorders.

4. B7-33:

   B7-33 is a single-chain peptide that is reported to be a selective agonist of the relaxin receptor 1. Relaxin is a hormone known for its role in childbirth, however it also appears to have potential cardiovascular effects. B7-33 is reported to be cardioprotective in animal models of myocardial infarction, and is being sold by websites overseas as a product to

reduce fibrosis and promote heart health. B7-33 does not appear to have been studied in human clinical trials.

5. PNC-27:

   PNC-27 is reported as being an anti-cancer peptide that induces tumour cell necrosis *in vitro*. It is being sold by websites overseas as a potential cure for a range of cancers, however these claims are unsubstantiated. The Food and Drug Administration in the United States have previously issued warnings to the public regarding PNC-27 use, and concerns appear to have been raised regarding the safety of this substance.

6. SS-31:

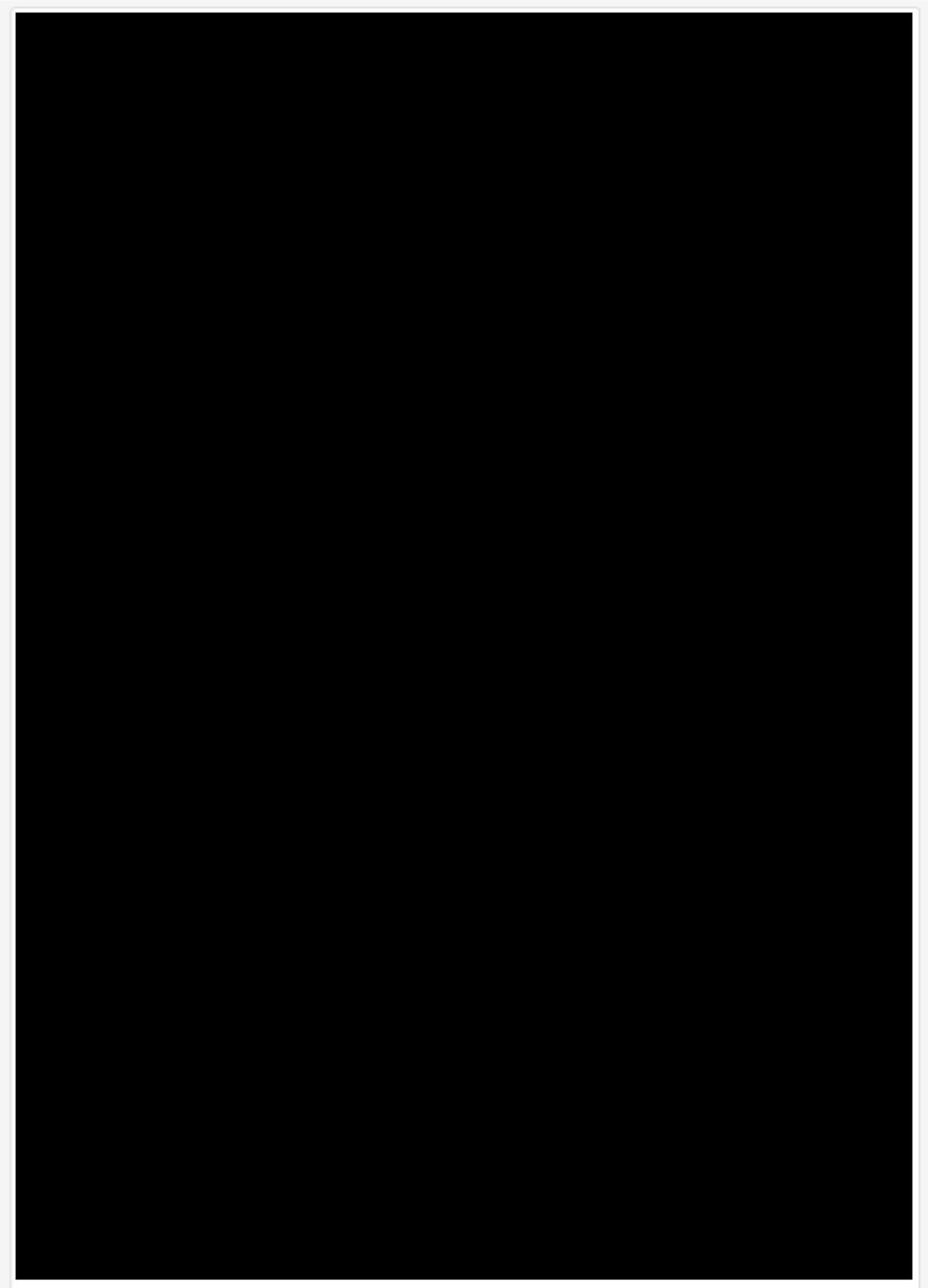
   SS-31, also known as elamipretide, bendavia, and MTP-131, is a small peptide that is reported to be a therapeutic of interest in the treatment of mitochondrial dysfunction disorders including Barth syndrome, as well as in heart failure. Studies in animal models have reported SS-31 as having cardioprotective effects, however SS-31 does not appear to have been studied in human clinical trials.

Conclusion

Based on the increase in unscheduled peptides being imported into New Zealand for personal use, it is proposed that the aforementioned group entries are introduced, as well as classification of the listed individual peptides. In classifying these substances as prescription medicines, the importation of these products into New Zealand without a prescription will not be permitted, mitigating both the known and unknown clinical risks associated with them.

Appendices

Appendix A – High-risk medicine letter



Appendix B – Summary of proposed group entries

Proposed Group Entry	Examples	Intercepted in the last 6 months?
Thymic peptide hormones and their analogues (naturally occurring & synthetic)	Thymosin alpha-1 Thymalfasin Thymosin beta-4 TB-500 Thymulin Thymopoietin	Yes
BCP-157 and its analogues (naturally occurring & synthetic)	BCP-157 NL-BCP-157 Hexadecapeptide	Yes
ACTH analogues (naturally occurring & synthetic)	Adamax Semax	Yes
Pineal gland peptides and their analogues (naturally occurring & synthetic)	Epitalon Epithalamin	Yes
AMPs and their precursors	LL-37 CAP-18	Yes
Myostatin modulator peptides	Myostatin pro-peptide GDF-8 ACE-031	Yes
Erythropoietin and its analogues (naturally occurring & synthetic)	Erythropoietin ARA-290	No
Tuftsin and its analogues (naturally occurring & synthetic)	Selank	Yes
Kisspeptins (naturally occurring & synthetic)	Kisspeptin-10	Yes

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