nuBioAge
WELLNESS NETWORK

Pharmacy Changes

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Safety Risks Associated with Certain Bulk Drug Substances Nominated for Use in Compounding

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Category 2 of the Bulk Substances Nominated Under Sections 503A or 503B of the Federal Food, Drug, and Cosmetic Act

FDA finalized two guidances clarifying the agency's proposed policies concerning the use of certain bulk drug substances in compounding by state-licensed pharmacies, federal facilities, and licensed physicians (under section 503A), and by outsourcing facilities (under section 503B):

Which Peptides Were Affected?

- AOD 9604
- BPC-157
- LL-37
- CJC-1295
- Dihexa
- DSIP
- Epitalon
- GHK-Cu (Injectable)
- Ibutamoren
- Ipamorelin
- Kisspeptin-10
- KPV
- Melanotan II
- PEG-MGF
- MOTs-C
- Selank
- Semax
- Thymosin Alpha-1
- Thymosin Beta 4, Fragment

Category 1 vs Category 2

Category 1 – These substances may be eligible for inclusion on the list of bulk drug substances that can be used in compounding under section 503A or 503B, **were nominated with sufficient information for FDA to evaluate them and do not appear to present a significant safety risk in compounding at this time.** FDA does not intend to take action against a compounder for compounding drugs using bulk drug substances listed in Category 1 of either 503A or 503B, whichever is applicable, provided that the conditions described in the guidance documents and all other applicable requirements of the FD&C Act are met.

Category 2 – **These are bulk drug substances that were nominated with sufficient supporting information for FDA to evaluate them**, but raise significant safety concerns, and are not eligible for the policy that applies to substances in Category 1. These bulk drug substances cannot be used in compounding unless FDA publishes a final rule (section 503A (b)(1)(A)(i)(III)) or final Federal Register notice (section 503B(a)(2)(A)) authorizing the particular substance's use in compounding. See Safety Risks Associated with Certain Bulk Drug Substances Nominated for Use in Compounding for a list of the substances and a summary of the identified safety risks.

So What Are The Safety Concerns?

- Peptide related impurities and API characterization.
  - Active pharmaceutical ingredient is obtained from FDA registered facilities
  - These same facilities provide the same active ingredient for pharmaceutical companies running human clinical trials
  - These APIs come with certificate of analysis.
- The safety-related information in the nomination is inadequate for the FDA to sufficiently understand the extent of any safety issues.
  - They place peptides on this list that have already been evaluated for safety and have GRAS and orphan drug status by the FDA

Thymosin-alpha 1 (Ta1)	503A	September 29, 2023	Compounded drugs containing thymosin-alpha-1 (Ta1) may pose significant risk for immunogenicity for certain routes of administration and may have complexities with regard to peptide-related impurities and API characterization. The safety-related information in the nomination is inadequate for FDA to sufficiently understand the extent of any safety issues raised by the proposed compounded product.

Thymosin Alpha-1 and Orphan Status

Biotechnol Healthc. 2006 Aug; 3(4): 16, 21.

PMCID: PMC3571076 | PMID: 23424368

Approvals, FDA Actions, Clinical Trials

Bob Carlson, MHA

The FDA approved orphan drug status for SciClone Pharmaceuticals' **thymalfasin injection** (**Zadaxin**) for malignant melanoma

Thymosin-Alpha-1 Safety

Safety in Humans

Since 1979, Zadaxin has been evaluated in more than 3,000 patients in over 70 clinical studies. Administration has been in daily doses ranging from 0.6 to 9.6 mg/m^2 and **1 mg to 16 mg, primarily administered subcutaneously on a biweekly schedule, for treatment periods ranging from 1 day to 18 months. No serious adverse experiences have been observed.** Zadaxin has been shown to be well tolerated even in patients with poor performance status, including those with decompensated liver disease, renal disease requiring hemodialysis, primary immunodeficient individuals, and elderly patients as old as 101 years. The lack of significant side effects with Zadaxin is in sharp contrast to other major immune response modulators such as IFN and IL-2. The side effects and toxicities of the latter drugs make them difficult for most patients to tolerate. For example, IFN results in flu-like side effects (fever, chills, malaise, and headaches) and IL-2 causes significant edema in the lungs and elsewhere.

Substitutions and Alternatives

- Mitochondrial Peptides:
  - MOTS-c = SS-31
- Growth Hormone
  - CJC/IPA➡ Sermorelin, Tesamorelin
- BPC-157
  - Larazotide still available
  - BPC/KPV available as nutraceutical
  - Pain: Pentosan Polysulfate injectable
  - Gut Health: Low dose Oral PPS
- Thymosin Alpha-1
  - Nothing replaces this fully
  - Thymogen, LDN, Larazotide, Methylene Blue
- Selank/Semax
  - FGL Nasal Spray
  - PE22-28
  - Oxytocin
  - Ketone Esters
  - Methylene Blue

Cellular Medicine Compounds:Repurposing

- **SGLT II Inhibitors (empagliflozin)**
  - Delay the aging of endothelial cells. (Atherosclerosis)
  - Powerful exercise mimetic
- **PDE5 inhibitors (Tadalafil)**
  - Exercise and muscle performance
  - Blood pressure
- **Rapamycin**
  - Compounded vs Commercial (Bioavailability)
  - Topical (Skin)
- **Amlexanox**
  - Increased energy expenditure, inflammation, insulin sensitivity

Moving Forward

- To our current knowledge all pharmacies are stopping.
- Stability
  - Building programs, processes that will be around for the long run.
  - We still have many compounds, peptides and supplements that are still available.
- **We will move forward with our trusted network of pharmacies on taking advantage of all the compounds we still have available.**

Thank you

Contact

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