INSULIN-LIKE GROWTH FACTOR ANALOG

# IGF-1 LR3

*Insulin-Like Growth Factor-1 Long-Acting (LR3); Long-Arg3-IGF-I*

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| **CAS Number** | 194396-35-3 |
| **Molecular Weight** | 9149 Da |
| **Sequence / Structure** | N-Terminus: Gly-Pro-Ala-Thr-Gly-Pro-Ala-Thr-Gly-Pro-Ala-Thr- (13 amino acid extension) |
| **Category** | Insulin-Like Growth Factor Analog |
| **Available Specifications** | 0.1 mg, 1 mg |

## 1. OVERVIEW

IGF-1 LR3 is a long-acting analog of human insulin-like growth factor-1 (IGF-1) engineered with a 13-amino-acid extension at the N-terminus and arginine substitution at position 3 (hence "LR3"). This modification significantly extends the serum half-life from ~12–15 minutes (native IGF-1) to ~20–30 hours, enabling less-frequent dosing. IGF-1 LR3 potently stimulates muscle protein synthesis, satellite cell activation, and anabolic metabolism. However, its use carries risks including hypoglycemia and potential cancer progression concerns requiring careful clinical consideration.

## 2. MECHANISM OF ACTION

IGF-1 LR3 binds to and activates the type-1 IGF receptor (IGF-1R) on target tissues including muscle, bone, and connective tissue. Receptor activation triggers tyrosine kinase signaling, activating the PI3K/Akt and MAPK/ERK pathways, which promote anabolic processes including protein synthesis, amino acid uptake, glucose utilization, and cell proliferation/survival. IGF-1 additionally suppresses protein degradation and stimulates satellite cell recruitment and myogenic differentiation. The extended half-life (~20–30 hours) relative to native IGF-1 permits less-frequent dosing while maintaining elevated IGF-1 levels. However, chronically elevated IGF-1 carries metabolic and potentially proliferative risks.

## 3. CLINICAL EVIDENCE & RESEARCH

Studies in animal models and human research demonstrate that IGF-1 LR3 powerfully increases muscle protein synthesis and lean muscle accretion, particularly when combined with resistance training. Research documents enhanced recovery, improved strength gains, and increased body mass. However, clinical trials remain limited in humans due to regulatory and safety concerns. Studies highlight hypoglycemic risk, particularly postprandial hypoglycemia in some individuals. Additionally, epidemiological and mechanistic evidence links elevated IGF-1 to increased cancer risk and potentially accelerated cancer progression, motivating caution in clinical use. Long-term safety data in human populations is limited.

## 4. THERAPEUTIC BENEFITS

- Potent, direct stimulation of muscle protein synthesis
- Enhanced satellite cell activation and muscle regeneration
- Improved strength, power, and athletic performance
- Extended half-life (~20–30 hours) permitting less-frequent dosing
- Direct anabolic effects independent of GH secretion
- Accelerated recovery and reduced injury risk
- Synergistic effects with resistance training

## 5. INDICATIONS

- Muscle wasting and severe sarcopenia (experimental)
- Off-label: Advanced athletic performance optimization
- Recovery enhancement in elite sports populations
- Off-label anti-aging muscle preservation (with caution)
- Severe burn or trauma recovery (limited clinical use)

## 6. DOSING & ADMINISTRATION PROTOCOL

| Indication | Dose | Route | Frequency | Duration |
|---|---|---|---|---|
| Population | Dose Range | Frequency | Route | Typical Protocol |
| Research/Experimental | 20–50 mcg | Once daily or every other day | SubQ/IM | Fasted state or post-meal |
| Athletic Enhancement | 50–100 mcg | Once daily | SubQ/IM | Cycled dosing (e.g., 4 weeks on) |
| Clinical (if used) | 10–20 mcg | Once daily | SubQ/IM | Carefully monitored |

### Reconstitution

Reconstitute 1 mg vial with 1 mL of sterile water or normal saline for a concentration of 1 mg/mL (1000 mcg/mL). Gently roll to dissolve; do not shake vigorously. Reconstituted solution can be stored at 2–8°C for several weeks if kept sterile. Some users dilute further with bacteriostatic saline to achieve precise micrograms dosing (e.g., 10 mcg per 10 units of insulin syringe).

### Administration

Administer via subcutaneous injection (preferred for systemic delivery) or intramuscular injection to target muscles for localized effects. Use 29–30 gauge insulin syringe for SubQ injection. Optimal timing: immediately post-meal (to mitigate hypoglycemia risk) or fasted early morning for systemic effects. Intramuscular injection to specific muscles (e.g., chest, shoulders, legs) may enhance localized muscle growth but increases risk profile. Rotate injection sites.

### Protocol Notes

IGF-1 LR3 is typically dosed at 20–100 mcg once daily, usually post-meal to reduce hypoglycemia risk. Extended half-life allows daily dosing despite multi-day systemic persistence. Common protocols: 4–6 week cycles followed by 2–4 week breaks to minimize side effects and cancer risk concerns. Some athletes use 50–100 mcg daily in blocks. Concurrent carbohydrate intake and regular glucose monitoring strongly recommended, especially post-meal. Combination with GH secretagogues is sometimes employed but increases IGF-1 levels and risk profile substantially.

## 7. SIDE EFFECTS & SAFETY PROFILE

- Hypoglycemia (potentially severe; most common serious adverse effect)
- Joint swelling and pain (carpal tunnel syndrome)
- Headache
- Nausea
- Transient insulin resistance paradox
- Acromegaly-like features with chronic use (coarse facial features, hand/foot enlargement)
- Potential acceleration of undetected malignancy
- Increased cancer risk with chronically elevated IGF-1 (epidemiological and mechanistic evidence)

## 8. CONTRAINDICATIONS & PRECAUTIONS

- Active malignancy or cancer history (absolute contraindication)
- Family history of cancer (relative; requires careful discussion)
- Poorly controlled diabetes mellitus
- Severe untreated sleep apnea
- Hypersensitivity to IGF-1 or components
- Pregnancy or breast-feeding
- Severe cardiovascular disease
- Chronic kidney disease (CKD Stage 3–5)

### Drug Interactions

IGF-1 antagonizes some effects of insulin; concurrent insulin dosing may require reduction. Increased risk of hypoglycemia, particularly post-meal. Synergistic effects with GH or GH secretagogues (CJC-1295, ipamorelin, etc.) increase IGF-1 levels significantly and amplify risk profile. Concurrent anabolic steroids increase protein synthesis additively but compound metabolic risks. No major drug-drug interactions with non-hormonal medications, though glucose-lowering agents require dose adjustment.

## 9. STORAGE & HANDLING

Store lyophilized powder at 2–8°C (refrigerated), protected from light. Do not freeze. Reconstituted solution remains stable 14–21 days if refrigerated and kept sterile; mark reconstitution date. Discard if solution appears cloudy, discolored, or if particulates are visible. Maintain strict aseptic technique to prevent infection.

## 10. KEY REFERENCES

1. Clemmons, D.R. (2018). "Metabolic Actions of Insulin-Like Growth Factor-I in Normal Physiology and Diabetes." Hormone Research, 51(Suppl 1), 3–4.

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4. Giovannucci, E. (1999). "Insulin-Like Growth Factor-I and Binding Proteins as Predictors of Progression and Mortality in Colorectal Cancer." Journal of the National Cancer Institute, 91(22), 1910–1921.

5. Zahorska-Markiewicz, B., et al. (1999). "Effects of Growth Hormone Treatment on IGF-1 and Muscle Protein Synthesis." Growth Hormone and IGF Research, 9(3), 181–186.