

RESEARCH MONOGRAPH . COMPOUND PROFILE

MK-677 (Ibutamoren)

A Merck-developed orally bioavailable non-peptide ghrelin receptor agonist that produces sustained GH and IGF-1 elevation with once-daily oral dosing.

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AUTHOR	Kodi <i>ac</i> biolabs Research
COMPOUND CLASS	Orally active non-peptide ghrelin receptor agonist

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ABSTRACT

MK-677 (Ibutamoren; CAS 159752-10-0; molecular formula C₂₇H₃₆N₄O₅S; molecular weight 528.66) is a non-peptide ghrelin receptor agonist developed by Merck in the 1990s. Unlike the peptide GHRPs, MK-677 is orally bioavailable and produces sustained GH and IGF-1 elevation over 24 hours with once-daily dosing. Phase 2 trials in elderly subjects showed sustained increases in GH, IGF-1, and lean body mass over 12 to 24 month treatment periods. The compound did not advance to FDA approval; the program was deprioritized after disappointing Phase 3 results in the GHD elderly population. The compound is sold as a research chemical/dietary supplement in some markets, though FDA has issued warnings against its sale as a supplement. Pharmacokinetics: plasma half-life 4 to 6 hours; high oral bioavailability; hepatic CYP3A4 metabolism. Doses are typically 10 to 25 mg orally once daily, usually at bedtime to align with the natural GH pulse. Adverse events include increased appetite, water retention, and modest insulin resistance with chronic high-dose use.

1. Compound Identification

MK-677 (Ibutamoren) is described as orally active non-peptide ghrelin receptor agonist. A Merck-developed orally bioavailable non-peptide ghrelin receptor agonist that produces sustained GH and IGF-1 elevation with once-daily oral dosing.

1.1 Class summary

Orally active non-peptide ghrelin receptor agonist

1.2 Subtitle

A Merck-developed orally bioavailable non-peptide ghrelin receptor agonist that produces sustained GH and IGF-1 elevation with once-daily oral dosing.

2. Abstract

MK-677 (Ibutamoren; CAS 159752-10-0; molecular formula C₂₇H₃₆N₄O₅S; molecular weight 528.66) is a non-peptide ghrelin receptor agonist developed by Merck in the 1990s. Unlike the peptide GHRPs, MK-677 is orally bioavailable and produces sustained GH and IGF-1 elevation over 24 hours with once-daily dosing. Phase 2 trials in elderly subjects showed sustained increases in GH, IGF-1, and lean body mass over 12 to 24 month treatment periods. The compound did not advance to FDA approval; the program was deprioritized after disappointing Phase 3 results in the GHD elderly population. The compound is sold as a research chemical/dietary supplement in some markets, though FDA has issued warnings against its sale as a supplement. Pharmacokinetics: plasma half-life 4 to 6 hours; high oral bioavailability; hepatic CYP3A4 metabolism. Doses are typically 10 to 25 mg orally once daily, usually at bedtime to align with the natural GH pulse. Adverse events include increased appetite, water retention, and modest insulin resistance with chronic high-dose use.

3. Mechanism of Action

Non-peptide ghrelin receptor agonist; orally bioavailable. Sustained 24-hour GH/IGF-1 elevation.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

10 to 25 mg per day, typically at bedtime.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Patchett AA, et al. Design and biological activities of L-163,191 (MK-0677): a potent, orally active growth hormone secretagogue. PNAS 1995.
2. Nass R, et al. Effects of an oral ghrelin mimetic on body composition and clinical outcomes in healthy older adults. Ann Intern Med 2008.

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