BRING THIS TO YOUR DOCTOR · GREY PEPTIDES

Endomorphin-2 (EM-2)

Also called: Endomorphin-2; Endomorphin 2; EM-2; Tyr-Pro-Phe-Phe-NH2; YPFF-amide

What it is

Endomorphin-2 (EM-2) is the amidated tetrapeptide Tyr-Pro-Phe-Phe-NH2 and, with endomorphin-1, one of the two most selective endogenous agonists of the mu-opioid receptor (PMID 9617760). It produces potent antinociception in animals (PMID 12184724), differing from endomorphin-1 by recruiting dynorphin and Met-enkephalin and by a non-opioid effect on reward-circuit dopamine (PMID 16034447). Its precursor gene has never been firmly identified. It is a research peptide and analgesic lead, not an approved medicine, and has never been given to people as a treatment.

Approval status

Research Chemical. Not a drug: Drugs@FDA and the openFDA label endpoint hold no record, and FDA GSRS and ChEMBL hold no drug record for endomorphin-2 (searched November 7, 2026). It is an endogenous opioid peptide; there is no therapeutic development of endomorphin-2 itself and no registered interventional trial of giving it to people. It is studied as a selective endogenous mu-opioid agonist and an analgesic lead, largely through stabilised analogs, which remain preclinical.

Dosing, as printed in the page's Recommended Dosing box

No established human dose

Endomorphin-2 is an endogenous peptide that has never been given to people as a treatment. The work is in animals and cells, where it is given directly into the brain or spinal fluid, or as engineered analogs, at experimental amounts that do not carry over to people.

Educational information, not medical advice. None is a recommendation for you. An unapproved compound has no established safe or effective human dose, and products sold for "research use only" are not made or tested for people. Talk to a doctor before acting on anything on this site, including before you start, stop or change any medicine or dose.

Key human evidence

No human study is carded on the page; its 6 study cards are reviews, animal or cell work. The first 2:

• **Endomorphin-2 is a partial agonist at the human mu-opioid receptor** (In Vitro, 1998). In human mu-opioid-receptor-transfected cells, endomorphin-1 and endomorphin-2 stimulated G-protein activation (35S-GTPgammaS binding) as partial agonists, with efficacy similar to morphine. This confirmed the endomorphins act on the human mu receptor with morphine-like activity — a receptor-pharmacology result. **PMID 9617760**

• **Endomorphin-2 activates mu receptors in guinea-pig gut neurons** (Animal, 1998). In guinea-pig ileum preparations, endomorphin-2 (and endomorphin-1) inhibited electrically evoked contractions as full agonists; the effect was shifted by a mu-selective antagonist but not by delta- or kappa-selective antagonists, showing endomorphin-2 acts selectively through mu-opioid receptors on excitatory myenteric neurons (an ex-vivo tissue result). **PMID 9879730**

Interactions

A PubMed search for interaction studies of this compound with any drug (November 7, 2026, 28 records) found none in people. That is not evidence that it is safe to combine with anything.

Side effects and cautions

Reported side effects	Contraindications and cautions
• No human adverse-event data exist: no published study has administered endomorphin-2 to people • As a mu-opioid-receptor agonist it is in the same pharmacological class as morphine, so opioid-type effects (sedation, respiratory depression, tolerance, dependence) would be the expected risks of any mu agonist — a class inference, not human data for this peptide • In animals it produces antinociception and affects gut, reward and cardiovascular (nitric-oxide) pathways (PMIDs 11337033, 16034447) — preclinical signals, not a human safety profile • Material sold online as 'endomorphin-2' is an unregulated research chemical of unverified content	• Not a medicine: no FDA application or label, and no approval anywhere • No human dosing, interaction, pregnancy or long-term safety data exist for administered endomorphin-2 • It is a laboratory research peptide, not a treatment • Its mu-opioid class warrants caution about the known risks of opioids in any use

Five questions to ask

1. Endomorphin-2 (EM-2) is listed here as "Research Chemical". What does the evidence on this sheet mean for someone in my situation, and is there an approved treatment I should consider instead?
2. Here are the medicines and supplements I take. Do any of them interact with Endomorphin-2 (EM-2)? This sheet records none published, which does not mean none exist.
3. Which side effects should make me stop and call you, for example no human adverse-event data exist: no published study has administered endomorphin-2 to people?
4. Do any of the cautions on this sheet apply to me, such as: Not a medicine: no FDA application or label, and no approval anywhere?
5. What should we check before I start and while I am on it (blood tests, blood pressure, weight), and how often?

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