

RESEARCH MONOGRAPH . COMPOUND PROFILE

Darbepoetin alfa

A hyperglycosylated EPO analog with two additional N-linked glycan chains; extended plasma half-life for less frequent dosing.

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COMPOUND CLASS	Long-acting EPO analog

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ABSTRACT

Darbepoetin alfa (CAS 209810-58-2; modified EPO with two additional N-linked glycosylation sites at amino acid positions 30 and 88; molecular weight approximately 37 kDa) is a hyperglycosylated EPO analog developed at Amgen and approved by the FDA in 2001 (Aranesp). The compound has the same EPO receptor binding mechanism as native EPO but with substantially extended plasma half-life (approximately 25 hours subcutaneous, versus 6 to 13 hours for native EPO) owing to the additional carbohydrate chains slowing renal and hepatic clearance. The receptor binding affinity is approximately 4-fold lower than native EPO at equimolar doses, but the longer half-life produces greater erythropoietic effect per dose. Approved indications match native EPO (CKD anemia, chemotherapy-induced anemia). Used as the canonical long-acting EPO analog in research.

1. Compound Identification

Darbepoetin alfa is described as long-acting epo analog. A hyperglycosylated EPO analog with two additional N-linked glycan chains; extended plasma half-life for less frequent dosing.

1.1 Class summary

Long-acting EPO analog

1.2 Subtitle

A hyperglycosylated EPO analog with two additional N-linked glycan chains; extended plasma half-life for less frequent dosing.

2. Abstract

Darbepoetin alfa (CAS 209810-58-2; modified EPO with two additional N-linked glycosylation sites at amino acid positions 30 and 88; molecular weight approximately 37 kDa) is a hyperglycosylated EPO analog developed at Amgen and approved by the FDA in 2001 (Aranesp). The compound has the same EPO receptor binding mechanism as native EPO but with substantially extended plasma half-life (approximately 25 hours subcutaneous, versus 6 to 13 hours for native EPO) owing to the additional carbohydrate chains slowing renal and hepatic clearance. The receptor binding affinity is approximately 4-fold lower than native EPO at equimolar doses, but the longer half-life produces greater erythropoietic effect per dose. Approved indications match native EPO (CKD anemia, chemotherapy-induced anemia). Used as the canonical long-acting EPO analog in research.

3. Mechanism of Action

Hyperglycosylated EPO analog (2 extra N-linked glycans); same receptor mechanism as EPO with extended plasma half-life.

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

Clinical 0.45 mcg/kg subcutaneous weekly or 0.75 mcg/kg every 2 weeks.

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. Egrie JC, Browne JK. Development and characterization of novel erythropoiesis stimulating protein (NESP). Br J Cancer 2001.
2. Macdougall IC. Optimizing the use of erythropoietic agents - pharmacokinetic and pharmacodynamic considerations. Nephrol Dial Transplant 2002.
3. Heatherington AC, et al. Pharmacokinetics of novel erythropoiesis stimulating protein (NESP) in cancer patients. Br J Cancer 2001.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.