

RESEARCH MONOGRAPH . COMPOUND PROFILE

Buspirone

An azapirone 5-HT_{1A} partial agonist; a non-benzodiazepine anxiolytic without dependence or sedation.

DOCUMENT	KDC-MN-248
ISSUED	2026-05-09
REVISION	1.0
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COMPOUND CLASS	5-HT _{1A} partial agonist anxiolytic

RESEARCH USE ONLY

ABSTRACT

Buspirone (8-[4-(4-pyrimidin-2-yl-1-piperazinyl)butyl]-8-azaspiro[4.5]decane-7,9-dione; CAS 36505-84-7; molecular formula C₂₁H₃₁N₅O₂; molecular weight 385.50) is an azapirone 5-HT_{1A} partial agonist developed at Bristol-Myers Squibb and approved by the FDA in 1986 under the trade name BuSpar. The compound is the first clinically approved non-benzodiazepine anxiolytic, distinguished by mechanism (5-HT_{1A} partial agonism rather than GABA-A potentiation), tolerance/dependence profile (none), and absence of sedation. 5-HT_{1A} affinity is approximately 21 nM (intrinsic activity approximately 35 percent); secondary D₂ antagonism (K_i approximately 100 nM) is of unclear clinical significance. The active metabolite 1-(2-pyrimidinyl)piperazine (1-PP) is an alpha-2 adrenergic antagonist contributing to noradrenergic effects. Onset of anxiolytic effect is delayed (2 to 4 weeks), reflecting the time course of 5-HT_{1A} autoreceptor desensitization. Plasma half-life is 2 to 3 hours; metabolism is extensive via CYP3A4 with significant first-pass effect (oral bioavailability approximately 4 percent). Approved for generalized anxiety disorder. Used as the canonical 5-HT_{1A} partial agonist in mechanism studies.

1. Compound Identification

Buspirone is described as 5-HT_{1A} partial agonist anxiolytic. An azapirone 5-HT_{1A} partial agonist; a non-benzodiazepine anxiolytic without dependence or sedation.

1.1 Class summary

5-HT_{1A} partial agonist anxiolytic

1.2 Subtitle

An azapirone 5-HT_{1A} partial agonist; a non-benzodiazepine anxiolytic without dependence or sedation.

2. Abstract

Buspirone (8-[4-(4-pyrimidin-2-yl-1-piperazinyl)butyl]-8-azaspiro[4.5]decane-7,9-dione; CAS 36505-84-7; molecular formula C₂₁H₃₁N₅O₂; molecular weight 385.50) is an azapirone 5-HT_{1A} partial agonist developed at Bristol-Myers Squibb and approved by the FDA in 1986 under the trade name BuSpar. The compound is the first clinically approved non-benzodiazepine anxiolytic, distinguished by mechanism (5-HT_{1A} partial agonism rather than GABA-A potentiation), tolerance/dependence profile (none), and absence of sedation. 5-HT_{1A} affinity is approximately 21 nM (intrinsic activity approximately 35 percent); secondary D₂ antagonism (K_i approximately 100 nM) is of unclear clinical significance. The active metabolite 1-(2-pyrimidinyl)piperazine (1-PP) is an alpha-2 adrenergic antagonist contributing to noradrenergic effects. Onset of anxiolytic effect is delayed (2 to 4 weeks), reflecting the time course of 5-HT_{1A} autoreceptor desensitization. Plasma half-life is 2 to 3 hours; metabolism is extensive via CYP3A4 with significant first-pass effect (oral bioavailability approximately 4 percent). Approved for generalized anxiety disorder. Used as the canonical 5-HT_{1A} partial agonist in mechanism studies.

3. Mechanism of Action

5-HT_{1A} partial agonism (intrinsic activity ~35 percent); secondary D₂ antagonism. No GABA-A activity. Active metabolite 1-PP is an alpha-2 antagonist.

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 15 to 60 mg per oral administration daily, in divided doses. Rodent studies 1 to 30 mg/kg/day.

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. Goa KL, Ward A. Buspirone. A preliminary review of its pharmacological properties and therapeutic efficacy as an anxiolytic. *Drugs* 1986.
2. Eison MS, Temple DL. Buspirone: review of its pharmacology and current perspectives on its mechanism of action. *Am J Med* 1986.
3. Loane C, Politis M. Buspirone: what is it all about? *Brain Res* 2012.

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.