ALCAR-Omitted Agmatine, PEA and Citicoline State-Regulation Systems, PEA and Citicoline Compositions, Single-Unit Enteric/HPMC Dosage Forms, Sachets, Kits, Release Profiles and Use Embodiments

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Relationship to earlier publication: This document adds explicit embodiments to the defensive publication titled "Agmatine-Containing and Agmatine-Adjacent State-Regulation Systems," published by Offmap Ltd on May 13th, 2026. The earlier publication remains incorporated by reference for all definitions, ingredient classes, dose ranges, routes, release profiles, phenotypes, outcome measures, kit architectures, product systems and disclosure rules that are technically compatible with this additions document.

Earlier publication: https://offmap.co.uk/research/agmatine-state-regulation-defensive-publication/

This additions document: https://offmap.co.uk/research/agmatine-state-regulation-defensive-publication-additions-2026-05-13/

Abstract

This additions document expressly discloses state-regulation compositions, dosage forms, kits, sachets, protocols and product systems that include palmitoylethanolamide, citicoline and, in selected embodiments, agmatine, while omitting acetyl-L-carnitine, L-acetylcarnitine, L-carnitine and related acylcarnitines.

The principal disclosed system is a single oral dosage unit comprising agmatine sulfate, palmitoylethanolamide and citicoline sodium with a hydrophilic gel-forming polymer such as hydroxypropyl methylcellulose. The unit may be an enteric-coated tablet, an enteric capsule, a multiparticulate capsule, a sachet containing enteric-coated granules, a mini-tablet system, a MUPS tablet or another oral dosage form that provides gastric resistance and intestinal release.

This additions document also discloses palmitoylethanolamide plus citicoline compositions without agmatine and without acetyl-L-carnitine, as well as agmatine plus palmitoylethanolamide plus citicoline compositions without acetyl-L-carnitine. These compositions are disclosed for state-regulation applications including action initiation, executive state-transition difficulty, autistic inertia, sensory overload, reduced sensory tolerance, shutdown vulnerability, post-demand recovery, social fatigue, cognitive rigidity, burnout-associated adaptive loss and related neurodevelopmental, psychiatric, autonomic, sensory, cognitive and fatigue-associated presentations.

The express omission of acetyl-L-carnitine, L-acetylcarnitine, L-carnitine and related acylcarnitines is part of the disclosed technical architecture. The omission may be selected for freedom-to-operate reasons, simplicity, cost, stability, dose volume, sensory tolerability, trimethylamine or trimethylamine

N-oxide control, regulatory positioning, microbiome considerations, or because citicoline provides the preferred choline-cytidine and frontal bioenergetic support in the disclosed state-regulation system.

All embodiments in this additions document are disclosed as compositions comprising, consisting essentially of and consisting of the listed components. All embodiments are disclosed with and without enteric protection, with and without HPMC or another hydrophilic polymer, with and without physical separation between active components, and with tablet, capsule, sachet, multiparticulate, mini-tablet, MUPS, powder, liquid and kit formats where technically feasible.

Keywords: agmatine; agmatine sulfate; palmitoylethanolamide; PEA; citicoline; CDP-choline; HPMC; hydroxypropyl methylcellulose; enteric tablet; enteric capsule; enteric granules; state regulation; action initiation; autistic inertia; executive dysfunction; sensory overload; shutdown; burnout; ALCAR omitted; LAC omitted; defensive publication; prior art.

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1. Incorporation and Disclosure Rules

The earlier Offmap defensive publication dated May 13th, 2026 is incorporated by reference. All definitions, ingredient forms, salt forms, release profiles, dosage formats, excipients, phenotypes, indications, populations, outcome measures, diagnostic measures, clinical service models, kit architectures, dose ranges and interpretation rules in the earlier publication apply to this additions document unless this document expressly states otherwise.

This additions document provides direct and individual disclosure of ALCAR-omitted and LAC-omitted systems. Each embodiment is disclosed as a standalone embodiment and also in combination with any compatible disclosure in the earlier publication.

For each composition in this additions document, the following forms are expressly disclosed:

1. a composition comprising the listed active components;
2. a composition consisting essentially of the listed active components and pharmaceutically or nutritionally acceptable excipients;
3. a composition consisting of the listed active components and pharmaceutically or nutritionally acceptable excipients;
4. a daily regimen containing the listed active components in one dosage unit;
5. a daily regimen containing the listed active components in two or more physically separate dosage units;
6. a kit containing the listed active components in one package;
7. a blister, strip, sachet, carton, pouch or refill system containing the listed active components;
8. a method of manufacturing any listed dosage form;
9. a method of using any listed dosage form for state-regulation support or related measurement; and
10. a method of monitoring response using the outcome measures disclosed in the earlier publication.

For avoidance of doubt, any embodiment that says "without ALCAR" also means without acetyl-L-carnitine, without L-acetylcarnitine, without LAC, without L-carnitine, without L-carnitine tartrate, without propionyl-L-carnitine, without glycine propionyl-L-carnitine and without another acylcarnitine unless a specific acylcarnitine is expressly reintroduced.

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2. Pinpoint Embodiments

2.1 PEA plus citicoline without ALCAR

A composition is disclosed comprising palmitoylethanolamide and citicoline, wherein the composition does not comprise acetyl-L-carnitine, L-acetylcarnitine, L-carnitine or another acylcarnitine.

In specific embodiments, the composition comprises 50-2400 mg/day palmitoylethanolamide and 50-2000 mg/day citicoline. More specific embodiments comprise 100-1200 mg/day palmitoylethanolamide and 100-1000 mg/day citicoline. Further specific embodiments comprise about 300-600 mg/day palmitoylethanolamide and about 250 mg/day citicoline.

The palmitoylethanolamide may be non-micronized PEA, micronized PEA, ultra-micronized PEA, co-micronized PEA, a PEA complex, a PEA dispersion, a PEA salt, a PEA derivative, a PEA prodrug, a PEA-class N-acylethanolamide or another palmitoylethanolamide-class component. The citicoline may be citicoline sodium, CDP-choline, cytidine diphosphate choline, a citicoline salt, a citicoline hydrate, a choline-cytidine donor or another membrane-support donor disclosed in the earlier publication.

The PEA plus citicoline composition may be provided as an immediate-release capsule, tablet, sachet, powder, drink mix, chewable, orally disintegrating tablet, liquid, multiparticulate dosage form, enteric-coated dosage form or kit.

The composition is disclosed for state-regulation applications including executive dysfunction, action initiation, autistic inertia, cognitive rigidity, impaired task switching, sustained-attention impairment, working-memory impairment, reduced sensory tolerance, sensory overload, post-demand cognitive recovery, social fatigue, burnout-associated cognitive depletion, mast-cell-associated dysregulation, histamine-intolerance-associated dysregulation and neuroimmune-associated state-regulation difficulty.

2.2 Agmatine plus PEA plus citicoline without ALCAR

A composition is disclosed comprising an agmatine-pathway component, a palmitoylethanolamide-class component and a citicoline or choline-cytidine donor component, wherein the composition does not comprise acetyl-L-carnitine, L-acetylcarnitine, L-carnitine or another acylcarnitine.

In specific embodiments, the composition comprises 50-3000 mg/day agmatine sulfate or another agmatine salt, 50-2400 mg/day palmitoylethanolamide and 50-2000 mg/day citicoline. More specific embodiments comprise 250-1500 mg/day agmatine sulfate, 300-1200 mg/day palmitoylethanolamide and 100-1000 mg/day citicoline. Further specific embodiments comprise about 1000 mg/day agmatine sulfate, about 600 mg/day palmitoylethanolamide and about 250 mg/day citicoline.

The agmatine-pathway component may be agmatine sulfate, agmatine dihydrochloride, agmatine hydrochloride, agmatine free base, an agmatine salt, an agmatine hydrate, an agmatine prodrug, an agmatine derivative, an arginine decarboxylase pathway component or another agmatine-pathway component disclosed in the earlier publication.

The composition may further comprise HPMC, methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, sodium carboxymethyl cellulose, polyethylene oxide, carbomer, alginate, pectin, xanthan gum, gellan gum or another hydrophilic gel-forming polymer.

The composition is disclosed for state-regulation applications including action initiation, executive state-transition difficulty, autistic inertia, task paralysis, sensory overload, reduced sensory tolerance, shutdown vulnerability, meltdown vulnerability, autonomic dysregulation, chronic hyperarousal, cognitive rigidity, perseverative state-locking, social fatigue, impaired recovery after social demand, impaired recovery after sensory or cognitive demand, stress-recovery failure and burnout-associated adaptive loss.

2.3 Single enteric/HPMC dosage unit containing agmatine, PEA and citicoline

A single oral dosage unit is disclosed comprising agmatine sulfate, palmitoylethanolamide, citicoline sodium and HPMC, wherein the dosage unit does not comprise acetyl-L-carnitine, L-acetylcarnitine, L-carnitine or another acylcarnitine.

In one specific embodiment, a daily serving comprises four enteric-coated tablets. Each tablet comprises about 250 mg agmatine sulfate, about 150 mg palmitoylethanolamide and about 62.5 mg citicoline sodium, plus HPMC and standard excipients. The four-tablet daily serving provides about 1000 mg agmatine sulfate, about 600 mg palmitoylethanolamide and about 250 mg citicoline sodium.

In another specific embodiment, a daily serving comprises two enteric-coated tablets. Each tablet comprises about 500 mg agmatine sulfate, about 300 mg palmitoylethanolamide and about 125 mg citicoline sodium, plus HPMC and standard excipients. The two-tablet daily serving provides about 1000 mg agmatine sulfate, about 600 mg palmitoylethanolamide and about 250 mg citicoline sodium.

In another specific embodiment, a daily serving comprises one enteric-coated tablet, caplet or sachet unit comprising about 1000 mg agmatine sulfate, about 600 mg palmitoylethanolamide and about 250 mg citicoline sodium, plus HPMC and standard excipients, provided the final dosage form is acceptable for swallowability, compressibility, stability, disintegration, dissolution and sensory tolerability.

The enteric coating may target release at pH 5.5, pH 6.0, pH 6.5 or pH 6.8. Suitable enteric materials include Eudragit L 100-55, Eudragit L 30 D-55, HPMCP HP-55, cellulose acetate phthalate, polyvinyl acetate phthalate, shellac or another enteric polymer compatible with the intended regulatory category.

The HPMC or other hydrophilic polymer hydrates after enteric opening and moderates local intestinal exposure to agmatine while co-localizing PEA and citicoline in the released dosage mass. This architecture may reduce gastric exposure, moderate intestinal bolus effects, improve gastrointestinal tolerability, support local mast-cell or histamine tolerance and provide a single-unit daily product architecture.

2.4 Single sachet containing enteric granules of agmatine, PEA and citicoline

A sachet dosage form is disclosed comprising enteric-coated granules, microgranules, pellets, beads or mini-tablets containing agmatine sulfate, palmitoylethanolamide, citicoline sodium and HPMC, wherein the sachet does not comprise acetyl-L-carnitine, L-acetylcarnitine, L-carnitine or another acylcarnitine.

The sachet may be opened and sprinkled onto yogurt, apple sauce or another soft food. The granules, pellets, beads or mini-tablets are swallowed without chewing so that enteric performance is preserved.

In specific embodiments, one daily sachet provides about 1000 mg agmatine sulfate, about 600 mg palmitoylethanolamide and about 250 mg citicoline sodium. In other embodiments, two daily sachets each provide about 500 mg agmatine sulfate, about 300 mg palmitoylethanolamide and about 125 mg citicoline sodium.

The sachet format is disclosed for users who cannot swallow tablets or capsules, for sensory-sensitive users, for supervised use, for travel use, for sample packs, for titration packs, for paediatric or adolescent supervised formats and for accessibility-oriented product systems.

2.5 Blister and carton systems for a single-unit product

A blister-packaged product system is disclosed comprising a plurality of enteric-coated tablets, caplets, mini-tablets or capsules, each comprising agmatine, PEA and citicoline and omitting ALCAR and related acylcarnitines.

In one embodiment, the product system comprises 120 tablets arranged as a 30-day supply, with four tablets per day. In another embodiment, the product system comprises 60 tablets arranged as a 30-day supply, with two tablets per day. In another embodiment, the product system comprises 30 unit-dose sachets arranged as a 30-day supply.

The carton may include a product information leaflet, batch number, expiry or best-before date, barcode, tamper-evident seal, Braille product name, printed blister lidding foil, responsible operator details, adverse-event contact route, DataMatrix code, QR batch-verification code, certificate-of-analysis link, large-print leaflet link and screen-reader accessible leaflet link.

The single-unit blister or sachet architecture does not require separate cavities for an ALCAR-containing unit because no ALCAR-containing unit is present.

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3. Mechanistic Rationale for ALCAR-Omitted Systems

ALCAR is not required for the disclosed state-regulation architecture. ALCAR provides acylcarnitine support, acetyl-group donation and mitochondrial fatty-acid transport through the carnitine shuttle. Those mechanisms may be useful in some fatigue, metabolic or deficiency-associated contexts, and the earlier publication discloses them. This additions document expressly discloses systems in which those mechanisms are omitted.

The omission is technically meaningful because neurons primarily rely on glucose-derived pyruvate, oxidative phosphorylation and lactate support rather than long-chain fatty-acid beta-oxidation. Ketone bodies can support brain energy during fasting or carbohydrate restriction, but ketone utilization does not require the carnitine shuttle. Brain fatty-acid oxidation is more relevant to astrocytes and supporting cells than to direct neuronal energy supply.

The disclosed ALCAR-omitted architecture targets state regulation through three remaining axes:

1. agmatine-pathway modulation of NMDA, imidazoline, nitric-oxide, polyamine and stress-response signalling;
2. PEA-class neuroimmune, mast-cell, histamine and PPAR-alpha support; and

3. citicoline or choline-cytidine support for acetylcholine availability, membrane phospholipid metabolism and frontal bioenergetic function.

Citicoline provides the preferred cognitive and membrane-support component in the ALCAR-omitted system. Citicoline may support acetylcholine synthesis through choline donation and may support phospholipid and frontal-lobe bioenergetic mechanisms. In selected embodiments, citicoline replaces the practical need for ALCAR as the cognitive-support component of the stack.

The omission of ALCAR may also reduce formulation bulk, sour taste, hygroscopicity, sensory burden, lower-intestinal microbial carnitine substrate exposure, trimethylamine formation, trimethylamine N-oxide formation and manufacturing complexity.

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4. Dose Ranges and Ratios

The following dose ranges are expressly disclosed for ALCAR-omitted systems:

Component	Broad daily range	Preferred daily range	Specific daily embodiments
Agmatine sulfate or equivalent agmatine form	50-3000 mg	250-1500 mg	500 mg, 750 mg, 1000 mg, 1500 mg
PEA or PEA-class component	50-2400 mg	300-1200 mg	300 mg, 600 mg, 900 mg, 1200 mg
Citicoline sodium or equivalent choline-cytidine donor	50-2000 mg	100-1000 mg	100 mg, 250 mg, 500 mg, 1000 mg
HPMC or equivalent hydrophilic gel former	10-1000 mg	25-400 mg	50 mg, 100 mg, 150 mg, 250 mg

Specific ratio embodiments include:

1. agmatine sulfate to PEA at about 5:3 by mass;
2. agmatine sulfate to citicoline sodium at about 4:1 by mass;
3. PEA to citicoline sodium at about 12:5 by mass;
4. agmatine sulfate, PEA and citicoline sodium at about 1000:600:250 per daily serving;
5. agmatine sulfate, PEA and citicoline sodium at about 250:150:62.5 per tablet in a four-tablet daily serving;
6. agmatine sulfate, PEA and citicoline sodium at about 500:300:125 per tablet in a two-tablet daily serving.

All ranges include their endpoints and all intermediate values. All dose ranges may be adjusted for salt form, free-base equivalent, hydrate state, assay potency, age, body mass, tolerability, regulatory category, serving size, release profile and unit count.

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5. Release Profiles and Manufacturing Embodiments

An ALCAR-omitted agmatine, PEA and citicoline dosage unit may use any of the following release profiles:

1. immediate release of all three actives;
2. delayed intestinal release of all three actives;
3. enteric release followed by HPMC-mediated gel moderation;
4. enteric-coated granules in a sachet;
5. multiparticulate release with agmatine, PEA and citicoline in the same granules;
6. multiparticulate release with agmatine, PEA and citicoline in separate granules within one dosage unit;
7. layered tablet release with one or more active layers;
8. bilayer or multilayer tablet release;
9. mini-tablet or MUPS release; and
10. capsule-in-capsule or compartmentalized release, provided no ALCAR-containing component is present.

A method of manufacturing an enteric tablet is disclosed comprising:

1. blending agmatine sulfate, PEA, citicoline sodium, HPMC and standard excipients;
2. granulating the blend if needed for flow, compressibility or content uniformity;
3. compressing tablets, caplets or mini-tablets;
4. applying an enteric coating;
5. testing acid-stage resistance;
6. testing intestinal-stage release of agmatine, PEA and citicoline;
7. blister-packing the dosage units; and
8. packing the blisters into cartons with product information and batch-verification features.

A method of manufacturing an enteric sachet is disclosed comprising:

1. blending agmatine sulfate, PEA, citicoline sodium, HPMC and standard excipients;
2. producing granules, microgranules, beads, pellets or mini-tablets;
3. applying an enteric coating to the particles;
4. testing particle acid resistance;
5. testing intestinal-stage release of agmatine, PEA and citicoline;
6. filling one or more daily sachets; and
7. packing sachets into cartons, pouches, strips or accessibility-oriented kits.

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6. Explicit Exclusions

The following excluded compositions are expressly disclosed as optional negative limitations for any embodiment in this additions document:

1. the composition does not comprise acetyl-L-carnitine;
2. the composition does not comprise L-acetylcarnitine;
3. the composition does not comprise LAC;
4. the composition does not comprise L-carnitine;
5. the composition does not comprise L-carnitine tartrate;
6. the composition does not comprise propionyl-L-carnitine;
7. the composition does not comprise glycine propionyl-L-carnitine;
8. the composition does not comprise an acylcarnitine;
9. the composition does not comprise a carnitine shuttle substrate; and
10. the composition does not comprise a lower-intestinal carnitine substrate intended to generate trimethylamine or trimethylamine N-oxide.

These exclusions may be used individually or in any combination.

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7. Claim-Territory Crosswalk

Potential later claim target	**Express disclosure in this additions document**
PEA plus citicoline composition	Section 2.1
PEA plus citicoline without ALCAR	Sections 2.1 and 6
Agmatine plus PEA plus citicoline composition	Section 2.2
Agmatine plus PEA plus citicoline without ALCAR	Sections 2.2 and 6
Single enteric tablet containing agmatine, PEA and citicoline	Section 2.3
HPMC-moderated enteric agmatine, PEA and citicoline	Sections 2.3 and 5
Sachet containing enteric granules of agmatine, PEA and citicoline	Section 2.4
Blister or carton system for the single-unit product	Section 2.5
Dose of about 1000 mg agmatine sulfate, 600 mg PEA and 250 mg citicoline	Sections 2.2, 2.3 and 4
Four-tablet daily serving with 250 mg agmatine sulfate, 150 mg PEA and 62.5 mg citicoline per tablet	Sections 2.3 and 4
Two-tablet daily serving with 500 mg agmatine sulfate, 300 mg PEA and 125 mg citicoline per tablet	Sections 2.3 and 4
Omission of LAC, ALCAR or acylcarnitines	Sections 1, 2, 3 and 6

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8. Statement of Defensive Intent

This additions document is published to create public prior art for ALCAR-omitted and LAC-omitted PEA, citicoline and agmatine state-regulation systems. The document discloses the specific combinations, omissions, dose ranges, release profiles, formats, kits, packaging architectures, manufacturing steps and use contexts described above so that later patent applicants cannot credibly present those combinations or omissions as new.

The disclosure is intentionally redundant. The same technical territory is stated in composition language, dosage-form language, kit language, method language, release-profile language, dose-range language, exclusion language and claim-crosswalk language. The redundancy is intended to make the publication searchable, citable and difficult to miss.