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Datasheet for the decision of 10 June 2026

Case Number: T 0132/25 - 3.3.07

Application Number: 14859589.5

Publication Number: 3065742

IPC: A61K31/485, A61K31/137, A61P25/00

Language of the proceedings: EN

Title of invention:
COMPOSITIONS AND METHODS COMPRISING BUPROPION OR RELATED COMPOUNDS AND DEXTROMETHORPHAN

Applicant:
Antecip Bioventures II LLC

Headword:
Bupropion and dextromethorphan I/ANTECIPP

Relevant legal provisions:
EPC Art. 56, 123(2)

Keyword:
Inventive step - auxiliary request 6 (yes)
Amendments - auxiliary request 6 - added subject-matter (no)

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Boards of Appeal

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Case Number: T 0132/25 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 10 June 2026

Appellant: (Applicant)	Antecip Bioventures II LLC 630 Fifth Avenue, Suite 2000 New York, NY 10111 (US)
Representative:	Murgitroyd & Company 165-169 Scotland Street Glasgow G5 8PL (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted/electronically transmitted on 14 August 2024 refusing European patent application No. 14859589.5 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	A. Jimenez

Summary of Facts and Submissions

I. The appeal was filed by the applicant (appellant) against the decision of the examining division to refuse European patent application EP 14 859 589.5.

II. The appealed decision was based on the claims of the main request and auxiliary requests 1-3 filed on 28 March 2024 and auxiliary request 4 filed during the oral proceedings held on 29 April 2024.

The examining division cited *inter alia* the following documents:

D1: Journal of Clinical Psychopharmacology (2005), 25(3), 226-229
D4: WO2009/006194 A1
D6: WO2012/118562 A1
D10: Clinical Pharmacokinetics (2011), 50(8), 519-530.

The examining division arrived at the following conclusions:

(a) Claim 1 of the main request defined bupropion for use in a method of increasing dextromethorphan plasma levels in a human being who is an extensive metabolizer of dextromethorphan and is in need of treatment with dextromethorphan, wherein the use comprises co-administering bupropion with dextromethorphan at least once a day for at least eight days.

The defined objective of increasing dextromethorphan plasma levels did not qualify as a further specific use within the meaning of Article

54(5) EPC. The subject-matter of claim 1 was therefore not further characterized by the defined specific use and lacked novelty in view of, for instance, document D6.

(b) Claim 1 of auxiliary request 1 defined, with respect to claim 1 of the main request, the additional feature that the plasma levels of dextromethorphan are increased compared to treatment without bupropion. The subject-matter of claim 1 of auxiliary request 1 lacked novelty for the same reasons as outlined for claim 1 of the main request.

(c) Claim 1 of auxiliary request 2 defined bupropion (or hydroxybupropion, erythrohydroxybupropion, or threohydroxybupropion), co-administered with dextromethorphan, for use in the treatment of depression, major depressive disorder, or treatment-resistant depression in a human who is an extensive metabolizer of dextromethorphan.

The distinguishing feature over document D4 was the use of bupropion instead of quinidine.

The comparison between the 60-fold increase of dextromethorphan plasma levels (AUC) observed with bupropion in Figures 5 and 6 of the application and the 43-fold increase by quinidine derivable from Table III of document D4 did not establish any improvement resulting from the substitution of quinidine by bupropion due to the difference in the doses used, the difference in the baseline levels, and the error margins reported in document D4. Moreover, the therapeutically beneficial effect depended on the absolute plasma levels of

dextromethorphan, rather than on its fold increase. The objective technical problem was therefore the provision of an alternative treatment.

Documents D1 and D10 described bupropion as an alternative CYP2D6 inhibitor suitable to increase dextromethorphan plasma levels. Document D10 indicated, in Figure 3, generally similar fold increases in plasma levels of victim drugs in the presence of quinidine and bupropion. The higher increase in plasma levels of dextromethorphan from quinidine than from bupropion predicted in Figure 3 of document D10 was speculative and did not teach the skilled person away from using bupropion instead of quinidine to increase dextromethorphan plasma levels. As bupropion was itself already known for the treatment of depression from document D6, it was obvious to combine bupropion with dextromethorphan as a solution to the problem of providing an alternative treatment. Auxiliary request 2 therefore did not comply with the requirement of inventive step.

(d) Claim 1 of auxiliary request 3 defined, with respect to claim 1 of auxiliary request 2, the additional feature that the plasma levels of dextromethorphan are increased compared to treatment without bupropion. Auxiliary request 3 did not comply with Article 123(2) EPC due to this additional feature.

Moreover, the subject-matter of claim 1 of auxiliary request 3 did not involve an inventive step in view of document D4.

(e) Claim 1 of auxiliary request 4 defined bupropion for use in treating a human being who is in need of treatment with dextromethorphan, wherein the human being is an extensive metabolizer of dextromethorphan, wherein the use comprises co-administering bupropion with dextromethorphan at least once a day for at least eight days and wherein the plasma levels of dextromethorphan are increased compared to treatment with dextromethorphan without bupropion.

Auxiliary request 4 did not comply with Article 123(2) EPC, because the combination of features defined in claim 1 of this request had not been originally disclosed.

III. With the statement of grounds of appeal, the appellant filed a main request and auxiliary requests 1-5.

The main request and auxiliary requests 1, 2, 4 and 5 correspond, respectively, to the main request and auxiliary requests 1, 4, 2 and 3 on which the decision under appeal was based.

Auxiliary request 3 was filed for the first time during the appeal proceedings. Claim 1 of this request defines:

"A combination of bupropion and dextromethorphan, for use in treatment of a human being in need of treatment with dextromethorphan, wherein bupropion is administered to the human being at least daily for at least 8 days, wherein dextromethorphan is administered to the human being at least daily for at least 8 days, wherein the human being is an extensive metabolizer of dextromethorphan, and wherein, on the sixth day, the

dextromethorphan plasma level is higher than the dextromethorphan plasma level that would have been achieved by administering the same amount of dextromethorphan administered without bupropion for six consecutive days."

The appellant cited the following additional documents in its statement of grounds of appeal:

D11: "Consolidated Financial Results for the Third Quarter of the Fiscal Year Ending December 31, 2016" issued by Otsuka Holdings Company Limited
D12: "Consolidated Financial Results FY2016 Q3 (Nine Months Ended September 30, 2016)"
D13: "Otsuka Group Pipeline Information" (as of 30 September 2016)
D14: Wellbutrin - Bupropion HCI product information
D15: Nuedexta - Patient Information Leaflet
D16: Extended data set for trials disclosed in the application as filed
D17: Declaration of Michael Chen, PhD
D17a: Bioavailability Studies Submitted in NDAs or IND
D17b: Cicali et al 2020
D18: Psychiatric News: https://psychnews.psychiatryonline.org/doi/10.1176/appi.pn.2022.11.11.13
D19: WO2016/081027 A1.

IV. In the communication pursuant to Article 15(1) RPBA the Board expressed *inter alia* the preliminary opinion that:

- the subject-matter of the main request and auxiliary requests 1-2 lacks an inventive step in view of document D4 as closest prior art,

- the admittance of auxiliary request 3 into the appeal proceedings is not justified; its subject-matter also lacks an inventive step,

- the dependent claims of auxiliary requests 4 and 5 do not comply with Article 123(2) EPC, and

- the efficacy of bupropion in co-administration with dextromethorphan in the treatment of major depressive disorder as defined in auxiliary requests 4 and 5 was unexpected; its efficacy in the treatment of treatment-resistant depression was not confirmed in document D18.

V. With its submission of 8 May 2026, the appellant filed a new auxiliary request 6 comprising a single claim and an adapted description. The claim of this request defines:

"Bupropion, hydroxybupropion, erythrohydroxybupropion, or threohydroxybupropion for use in the treatment of major depressive disorder in a human being who is an extensive metabolizer of dextromethorphan, wherein the bupropion, hydroxybupropion, erythrohydroxybupropion, or threohydroxybupropion is co-administered with dextromethorphan at least once a day for at least eight consecutive days."

This claim is based on claim 1 of auxiliary request 4 in which the therapeutic indication is limited to major depressive disorder.

VI. The appellant's arguments can be summarized as follows:

Auxiliary request 6 was filed in response to the observations in the Board's communication under Article

15(1) RPBA, in which the Board expressed a partially positive assessment of the allowability of the subject-matter of auxiliary request 4. Auxiliary request 6 rendered the remaining objections raised in the communication moot.

VII. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the single claim and the amended description of auxiliary request 6. The main request and auxiliary requests 1-5 were withdrawn on the condition that the Board allow auxiliary request 6.

Reasons for the Decision

1. Admittance of documents D11-D19

In the grounds of appeal, the appellant relied on additional documents D11–D19 to support its case. These submissions directly address the issues underlying the appealed decision without giving rise to complications. The introduction of this new evidence can therefore be regarded as a justified response to the appealed decision. Accordingly, the Board admits documents D11–D19 into the appeal proceedings under Article 12(4) RPBA.

2. Auxiliary request 6

2.1 Admittance of auxiliary request 6

In its communication pursuant to Article 15(1) RPBA, the Board questioned whether the dependent claims of auxiliary requests 4 and 5 had a basis in the original disclosure and whether the combination of bupropion and

dextromethorphan shows efficacy in treating treatment-resistant depression as defined in those requests. Auxiliary request 6 addresses these new issues raised in the Board's communication by deleting the dependent claims and limiting the therapeutic indication to major depressive disorder. In the exercise of its discretion under Article 13(2) RPBA, the Board admits auxiliary request 6 into the appeal proceedings, as it clearly overcomes the issues raised by the Board and does not give rise to new objections. Auxiliary request 6 is therefore prima facie allowable, which constitutes exceptional circumstances for admitting it at this late stage of the appeal proceedings.

2.2 Allowability of auxiliary request 6

2.2.1 The application as originally filed and published as WO 2015/069809 discloses in claims 1 and 2 the treatment of depression by administering an antidepressant compound together with dextromethorphan to a patient who is an extensive metaboliser of dextromethorphan. It further discloses, in the context of this teaching, bupropion and its metabolites as defined in auxiliary request 6 as suitable antidepressant compounds (claims 105 to 109). In addition, paragraph [0093] expressly identifies “major depression” as an example of an affective disorder treatable with such a combination. The skilled person would understand this reference to “major depression” as corresponding to the clinical indication of major depressive disorder, which is the therapeutic indication specified in auxiliary request 6. The application thus provides a direct and unambiguous basis for the combination of features defining auxiliary request 6. Consequently, the subject-matter of auxiliary request 6 is derivable from

the application as originally filed. Accordingly, auxiliary request 6 complies with Article 123(2) EPC.

2.2.2 The subject-matter of auxiliary request 6 concerns the use of bupropion, or its metabolites hydroxybupropion, erythrohydroxybupropion or threohydroxybupropion, in the treatment of major depressive disorder when co-administered with dextromethorphan. Document D4 and document D6 each represent suitable starting points for the assessment of inventive step. Document D4 discloses the co-administration of dextromethorphan with the CYP2D6 inhibitor quinidine for treating various disorders, including depression (see D4, page 48). The distinguishing feature over document D4 lies in the replacement of quinidine by bupropion or one of the defined metabolites thereof. Document D6 describes the therapeutic utility of bupropion in the treatment of depression. The distinguishing feature over document D6 lies in the co-administration with dextromethorphan.

The development of the quinidine/dextromethorphan combination for the treatment of major depressive disorder was discontinued for lack of sufficient evidence of efficacy (see D11, page 7; D12, page 19; D13, page 4). By contrast, document D18 reports that the bupropion/dextromethorphan combination was developed for the treatment of major depressive disorder and, in particular, was more effective than bupropion alone, as reflected by greater reductions in MADRS scores (see D18, page 2, ASCEND trial).

In view of the level of efficacy demonstrated in document D18 for the bupropion/dextromethorphan combination, the objective technical problem may be formulated as the provision of an improved treatment of major depressive disorder. Starting from either

document D4 or document D6, the skilled person had no reason to expect that replacing quinidine with bupropion (or the defined metabolites thereof), or adding dextromethorphan to bupropion therapy, would result in the observed improvement. The subject-matter of auxiliary request 6 is therefore not obvious and involves an inventive step.

2.2.3 The description, as amended according to auxiliary request 6, is adapted to the subject-matter claimed.

3. The Board concludes that the patent application as amended according to auxiliary request 6 meets the requirements of the EPC. In accordance with the appellant's request, no decision on the main request and auxiliary requests 1-5 is therefore required.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Examining Division with the order to grant a patent in the following version:

   Description: pages 1-47 as filed on 8 May 2026

   Claim: claim 1 of auxiliary request 6 as filed on 8 May 2026

   Drawings: Sheets 1/11-11/11 as originally filed.

The Registrar: The Chairman:

A. Vottner A. Usuelli

Decision electronically authenticated