

# Initiating Dextromethorphan 45 mg – Bupropion 105 mg in Patients With Major Depressive Disorder (MDD): Expert Panel Consensus Recommendations

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## Key Objective

To establish, for the treatment of major depressive disorder (MDD) in adults, expert consensus recommendations on initiating dextromethorphan-bupropion and addressing perceived barriers.

## Introduction

- Dextromethorphan 45 mg – bupropion 105 mg (Auvelity®; DM-BUP) is an oral N-methyl-D-aspartate (NMDA) receptor antagonist and sigma-1 receptor agonist approved as monotherapy in adults with MDD.<sup>1-6</sup>
- While most antidepressants primarily modulate monoamines, dextromethorphan-bupropion is hypothesized to also modulate glutamate, a mechanism of action (MOA) distinct from other oral MDD treatments.
- Prescribing Information of recently-approved medications often contain limited clinical guidance information on how to initiate treatment for patients who are on prior treatment or otherwise differ from the controlled clinical trial population.
- To address any potential gaps in real-world use, a panel of clinicians with experience prescribing dextromethorphan-bupropion to their patients was convened to participate in a modified Delphi Panel process.<sup>7-8</sup>

## Methods

### Modified Delphi Panel Process



#### Panel selection and characteristics

The panel comprised of 10 U.S.-based healthcare professionals with experience in psychiatry and treating patients with dextromethorphan-bupropion.



#### Survey development

- The Chair developed draft statements for initiating dextromethorphan-bupropion (informed by a literature review), which covered two main categories:
- Overcoming barriers to the initiation and use of dextromethorphan-bupropion in the treatment of MDD.
  - Approaches to the initiation of dextromethorphan-bupropion, including de novo initiation, switching from, or adding to current treatments.



#### Pre-meeting review

Panelists reviewed and anonymously rated each recommendation statement that were compiled and averaged; consensus required a mean score ≥3.0 on a 5-point Likert scale ranging from 0 (do not agree) up to 4 (very much agree).



#### Modified Delphi panel virtual meetings

- Statements were extensively discussed, revised, and anonymously re-rated at two virtual meetings.
- Recommendation statements reaching consensus (mean score ≥3.0) were considered final.

## References

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## QR Code

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## Disclosures

AHC has served as an advisor or consultant to AbbVie, Inc., ACCUMIN, AdhereTech, Axsome Therapeutics, Biogen, Fabre-Kramer, Intra-cellular Therapies, Janssen Research & Development, LLC, Liva-Nova, MycoMedica Life Sciences PBC, Neumora Therapeutics, Neurocrine Therapeutics, PSL Group Services, Seaport Therapeutics (formerly PureTech Health), Reunion Neuroscience, Inc., & Sirsiel Pharmaceuticals, Inc., received grants from Darig Bioscience, Janssen, Neumora Therapeutics, Neurocrine Therapeutics, Otsuka, Relmada Therapeutics, Inc., & Reunion Neuroscience, Inc., received copyright or royalties from Ballantine Books/Random House, Changes in Sexual Functioning Questionnaire, & Guilford Publications, and owns shares or RSUs of Mediflix LLC & S1 Biopharma.

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EC has served as a consultant with Abbvie and as a consultant and promotional speaker for Axsome Therapeutics, Inc., Boehringer-Ingelheim, Otsuka, Lundbeck, Neurocrine, Supernus, Johnson & Johnson, and Intracellular.

BD has served as a consultant for Axsome Therapeutics.

PD is on the advisory boards for Eisai, Idorsia, and Bayer Healthcare; is on the speaker's bureaus of Eisai, Idorsia, AbbVie, and Jazz; and is a stock shareholder in Pfizer and CVS.

BK serves on the advisory board or speaker bureaus of Alkermes, Axsome, BMS, Intracellular, Johnson & Johnson, Janssen, Luye, Teva.

JIM serves on the speaker bureaus of Otsuka/Lundbeck, Abbvie, Teva, Neurocrine, Janssen, Intra-Cellular Therapies, Axsome Therapeutics, & Bristol Myers Squibb and serves on the advisory boards of Axsome Therapeutics & Bristol Myers Squibb.

AM serves as a consultant for Otsuka Pharmaceuticals and Neurocrine Biosciences.

JS is a speaker for AbbVie, Alkermes, Janssen, Otsuka, Neurocrine, and Teva. D.M. is a consultant/speaker for Neurocrine, AbbVie, Intracellular Therapeutics, and Alkermes.

## Results

### Key Recommendations

1

**Dextromethorphan-bupropion** is indicated as a **monotherapy for adults with MDD** and should be considered as first-line treatment in appropriate patients across target clinical populations.

2

HCPs should individualize treatment decisions that **prioritize safety considerations** noted in the Prescribing Information.

3

**Dextromethorphan-bupropion is also recommended for those with inadequate response** (e.g. residual symptoms) **and/or intolerable side effects to traditional monoaminergic treatments**, who may benefit from a pharmacologically distinct treatment option in MDD.

4

**Dextromethorphan-bupropion** is appropriate for individuals with **MDD with and without symptoms of anxiety**.

5

When **switching from, or adding dextromethorphan-bupropion to**, TCAs, SSRI/SNRIs, atypical antidepressants, or adjunctive antipsychotics prescribed for MDD, **the level of CYP2D6 inhibition** of the current treatment **must be considered**.

6

When **switching from, or adding to, other NMDA modulators** (e.g. ketamine or esketamine) for MDD, it may be possible to **start in close temporal proximity** but should be done **with caution**.

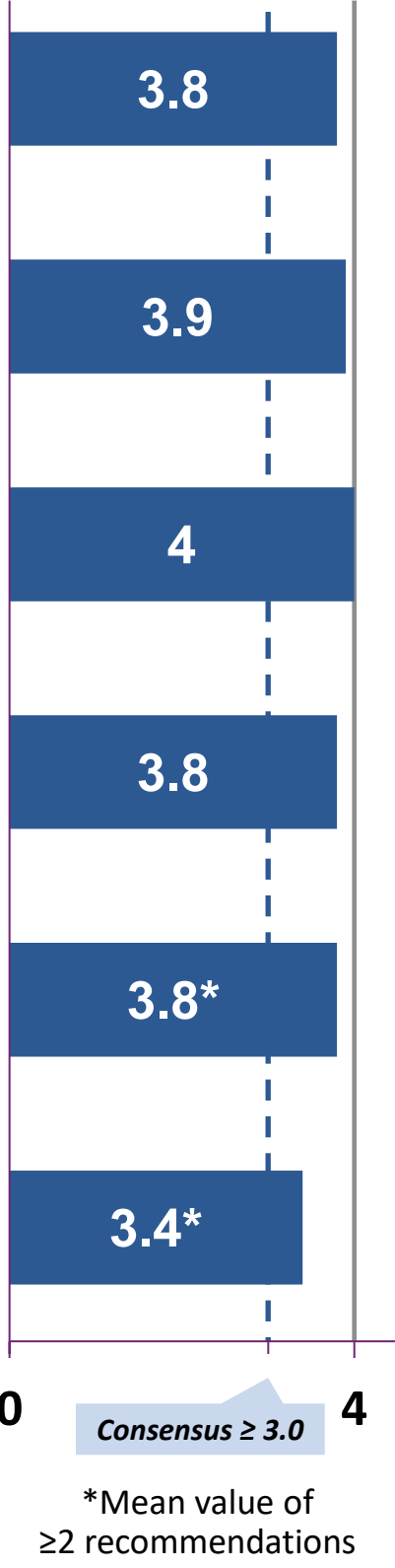


Scan QR code for the full list of Consensus Panel Recommendation Statements



To review all safety considerations, please see the Auvelity® Prescribing Information

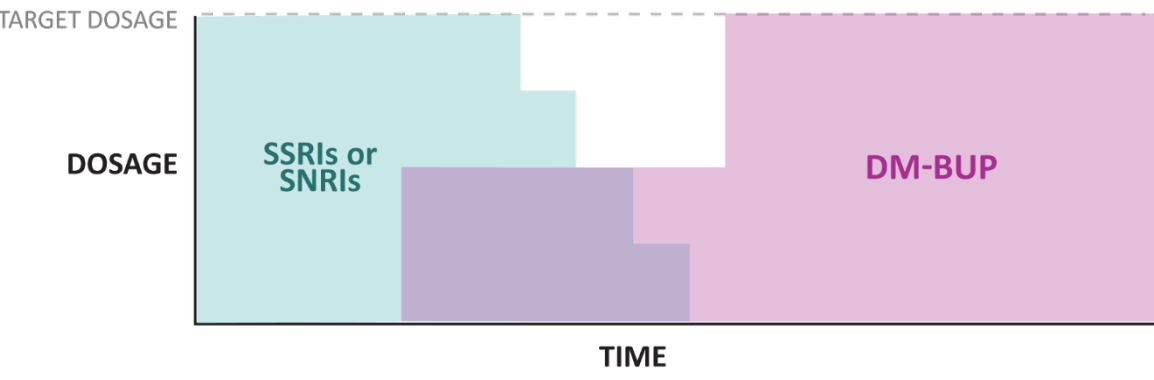
Likert scale mean score (0-4)



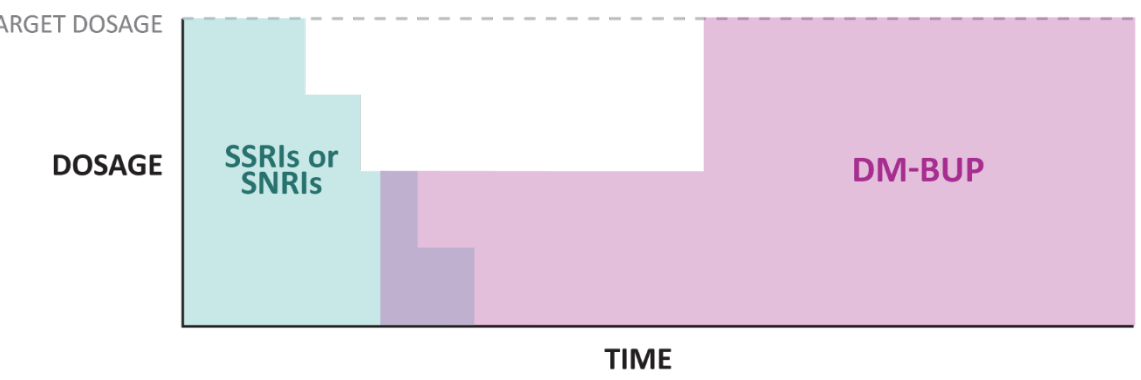
### Recommendations for Initiating Dextromethorphan-Bupropion From Prior SSRI or SNRI Treatment\*

#### Recommendations for Switching from SSRIs or SNRIs to DM-BUP\*\*

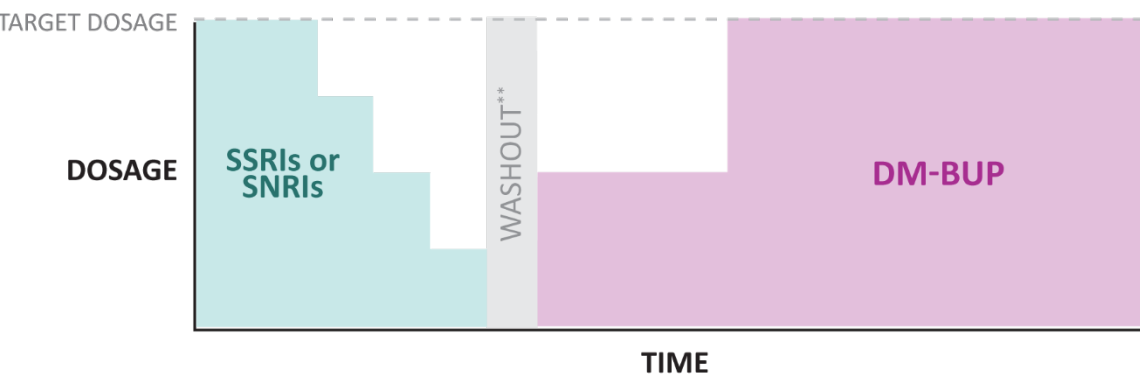
To switch from **SSRIs or SNRIs with low CYP2D6 inhibition up titrate** with DM-BUP and cross-taper SSRI or SNRI (examples: escitalopram, citalopram, sertraline)



To switch from **SSRIs or SNRIs with moderate CYP2D6 inhibition** consider reducing SNRI to mid-range dose then cross-taper DM-BUP (example: duloxetine)

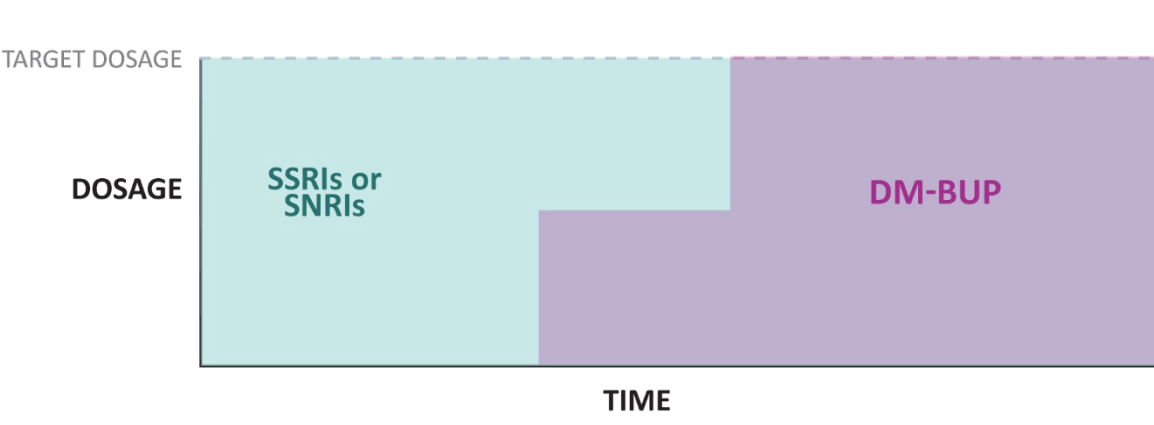


To switch from **SSRIs or SNRIs with high CYP2D6 inhibition** consider discontinuation and washout prior to initiating DM-BUP (examples: fluoxetine, paroxetine)

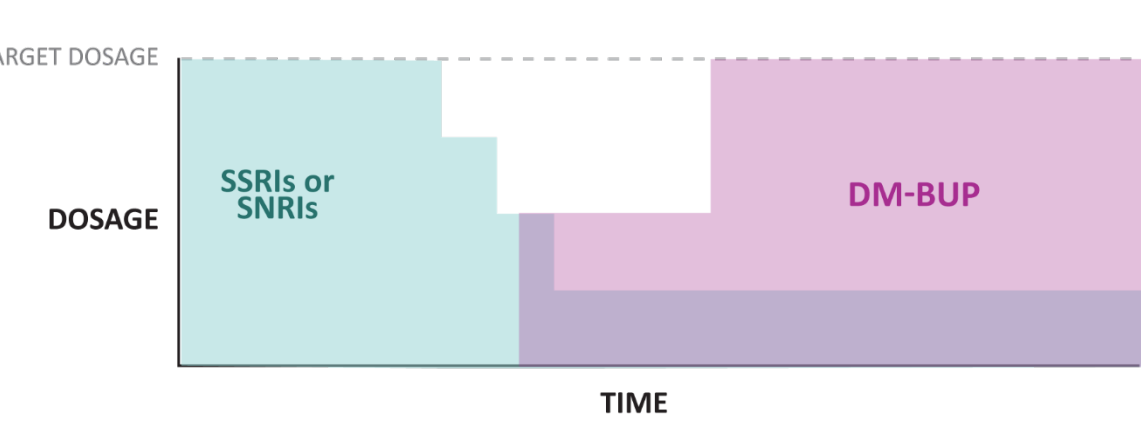


#### Recommendations for Adding DM-BUP to SSRIs or SNRIs\*\*

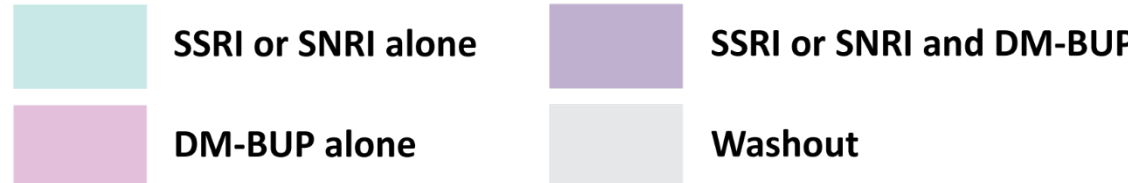
To add DM-BUP to **SSRIs or SNRIs with low CYP2D6 inhibition** add DM-BUP at standard SSRI or SNRI doses (examples: escitalopram, citalopram, sertraline)



To add DM-BUP to **SSRIs or SNRIs with moderate CYP2D6 inhibition** decrease SNRI or SSRI to low or midrange doses† (examples: duloxetine)



It was not considered appropriate to add DM-BUP to **SSRIs or SNRIs with high CYP2D6 inhibition** (examples: fluoxetine, paroxetine), or to bupropion, at their therapeutic doses. It was advised to taper SSRIs or SNRIs with high CYP2D6 inhibition to discontinuation prior to initiating DM-BUP, or to the lowest possible dose and use caution when adding DM-BUP.



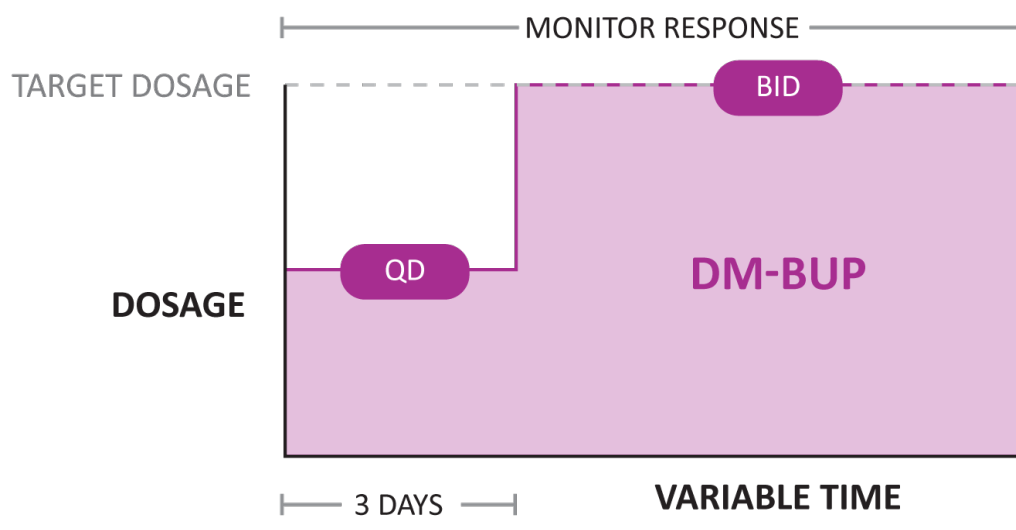
\*Representative approaches; timing and doses vary.  
\*\*Refer to individual medication Prescribing Information.  
†Option 2: give only 1 tablet of DM-BUP  
DM-BUP = dextromethorphan-bupropion; SNRI = Serotonin–Norepinephrine Reuptake Inhibitors; SSRI = Selective Serotonin Reuptake Inhibitors.

## Conclusions

- Panelists reached consensus on 28 recommendation statements, which included:
  - Dextromethorphan-bupropion is a safe, well-tolerated, and effective monotherapy for the treatment of MDD
  - HCPs should be informed that primary safety concerns are noted in the prescribing information
  - Guidance on how to initiate dextromethorphan-bupropion when switching from, or adding to, other classes of MDD treatments
- The experts' recommendations provide clinicians with real-world guidance to optimize care when initiating treatment with DM-BUP in their patients with MDD.

### Normal Titration of Dextromethorphan-Bupropion

#### Titration per Prescribing Information



QD = Once a day; BID = Twice a day