Initiating Auvelity® (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 Auvelity and addressing perceived barriers.

Introduction

- Auvelity® – formulated as an extended-release oral tablet containing a fixed dose combination of 45 mg dextromethorphan and 105 mg bupropion – is an N-methyl-D-aspartate (NMDA) receptor antagonist and sigma-1 receptor agonist approved as monotherapy in adults with MDD.[1-6]
- While most antidepressants primarily modulate monoamines, Auvelity 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 Auvelity to their patients was convened to participate in a modified Delphi Panel process.[7-8]

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 Auvelity.

Survey development
The Chair developed draft statements for initiating Auvelity (informed by a literature review), which covered two main categories:
- Overcoming barriers to the initiation and use of Auvelity in the treatment of MDD.
- Approaches to the initiation of Auvelity, 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

1. Tabuteau H, et al. Am J Psychiatry. 2022;179(7):490-499.
2. Iosifescu DV, Jones A, et al J Clin Psychiatry. 2022 May 30;83(4):21m14345. doi: 10.4088/JCP.21m14345.
3. Auvelity® [Prescribing Info]. Axsome Therapeutics, Inc.
4. O'Gorman C, Jones A, et al. ASCP Annual Meeting 2021
5. Chepke C, Iosifescu D, et al. Psych Elevate 2024, Las Vegas NV
6. McIntyre RS, Parikh SV, et al. American Society of Clinical Psychopharmacology (ASCP), 2024, Miami, FL.
7. Dalkey N, Helmer O. Manage Sci. 1963 Apr;9(3):458–67.
8. Fink A, Kosecoff J, et al. Am J Public Health. 1984 Sep;74(9):979

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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, & Sirtsei Pharmaceuticals, Inc., received grants from Daré 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-Ingleheim, 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.
JJM 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.

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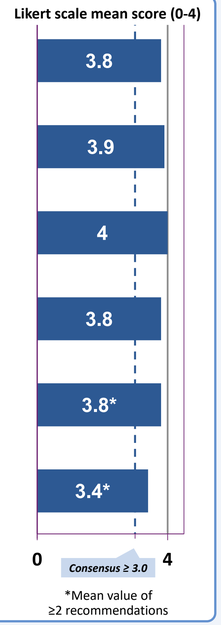
Results

Key Recommendations

1. **Auvelity** 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. **Auvelity 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. **Auvelity** is appropriate for individuals with **MDD with and without symptoms of anxiety.**
5. When **switching from, or adding Auvelity 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



Conclusions

- Panelists reached consensus on 28 recommendation statements, which included:
  - Auvelity 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 Auvelity 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 Auvelity in their patients with MDD.

Normal Titration of Auvelity

QD = Once a day; BID = Twice a day

Recommendations for Initiating Auvelity From Prior SSRI or SNRI Treatment*

Recommendations for Switching from SSRIs or SNRIs to Auvelity**

To **switch** from **SSRIs or SNRIs with low CYP2D6 inhibition** *up titrate* with Auvelity 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 Auvelity (example: duloxetine)

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

Recommendations for Adding Auvelity to SSRIs or SNRIs**

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

To **add Auvelity 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.

SSRI or SNRI alone
SSRI or SNRI and DM-BUP
DM-BUP alone
Washout

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