Esketamine: Novel Nasal Spray for Treatment Resistant Depression or Major Depressive Disorder with Acute Suicidal Ideation or Behavior

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April 24th, 2022

Images: ChemSpider and Janssen Pharmaceuticals.
Conflict of Interest Disclosure

Emily Beskar, PharmD, faculty for this CE activity, has no relevant relationships with commercial nor non-profit organizations.
Learning Objective

1. Recall eligible populations for esketamine treatment and risks and benefits associated with it.
Pre-Assessment Question

1. **True or False**: Esketamine may be considered as first line therapy for treatment of depression in patients who haven’t trialed other medication therapies.
What is Esketamine?

- Noncompetitive NMDA receptor antagonist that blocks glutamate - similar to ketamine, though only S(+)-enantiomer\textsuperscript{4,5}
Concerns Surrounding Esketamine

- Sedation, dissociation, abuse, misuse (CIII)

- CI in ICH, aneurysmal vascular disease, arteriovenous malformation

- Suicidal thoughts and behaviors

  - REMS program
    - Administered under direct observation of physician
    - Patient monitored for 2 hours after administration
Literature to Support Esketamine Use

- Canuso et al., N = 68
  - Esketamine + standard of care treatment (> 1 noninvestigational antidepressant) versus placebo + standard of care treatment
  - Greater reduction of MADRS in esketamine patients only 4 hours after - not 24 hours nor 25 days after
  - Greater resolution of suicide risk seen w/esketamine as well
  - 94.3% in esketamine group in double blind phase reported adverse effects
    - Nausea, vomiting, dizziness, headache
    - Dissociation, paresthesia, dysgeusia
Literature to Support Esketamine Use (continued)

- Wajs et al., N = 802, but only N = 136 for 12 months of therapy
  - Twice weekly administration in induction phase, then one time weekly every other week for up to 48 weeks for optimization/maintenance phase in conjunction with oral antidepressant therapy
  - MADRS < 12 in 58.2% of patients after optimization/maintenance phase
  - 6.9% experienced serious adverse effects, 3 related to suicide
- Unfortunately, no trials comparing ketamine vs. esketamine vs. arketamine at this time
- Long term trials still needed to reinforce long term safety and efficacy
Guideline Recommendations

● CANMAT Task Force\textsuperscript{10}
  ○ LOE 1 based on large sample RCTs
  ○ No direct comparison to ketamine, uncertain where these fall in treatment algorithm if they are both available

● International Expert Opinion\textsuperscript{11}
  ○ “Intranasal esketamine demonstrates efficacy, safety, and tolerability for up to 1 year in adults with TRD.”
Where are patients receiving these medications?

- Challenging to coordinate administration between multiple facilities
- Becoming more readily available at outpatient treatment facilities
- Insurance coverage may vary
Post-Assessment Question

1. True or False: Esketamine may be considered as first line therapy for treatment of depression in patients who haven’t trialed other medication therapies

FALSE
What questions do you have for me?
References