

### ***What is treatment resistant depression (TRD)?***

When 2+ treatments of adequate dose and duration do not produce response or remission, a person may be considered to have treatment-resistant depression.

Practically, we would suggest prior trial of, *at an absolute minimum*:

- 2 different antidepressant classes (with adequate dose/duration of each)
- regularly recurring psychotherapy/counseling
  - o 6+ appointments with the same psychotherapy provider
  - o Appointments occurring at least as frequent as every 2 weeks

### **TMS** (Transcranial magnetic stimulation)

An electromagnetic coil is used to generate a targeted magnetic field in areas of the brain known to be underactive in people with depression.

*Details:* Treatment sessions 5 days a week for 4-6 weeks, then the frequency tapers down on a set schedule. Sessions last 30-60 minutes, patients can drive themselves. There is no anesthesia involved.

*Notable adverse effects:* Headache

*Who might be a good fit?* Somebody with TRD who is able to participate in a treatment that requires 5 day a week regular involvement for a set period of time.

*Limitations:* Often limited to metropolitan areas. Covered by insurance, but insurance providers may expect more treatment trials before covering TMS.

*How to get started:* Patients can refer themselves or ask for a provider referral. Most TMS clinics will evaluate the patient to see whether the treatment is a reasonable option.

### **Ketamine**

A medication that blocks NMDA receptors (among others), can be added along with other antidepressant medication treatments. IV ketamine and nasal esketamine rely on essentially the same medication, but the different routes result in some differences between the two.

*Notable adverse effects (common to both):* Nausea, altered taste, dizziness, anxiety, sedation, dissociation

#### *IV ketamine infusion:*

*Details:* 4 to 6 initial treatments, booster treatment every 4-6 weeks sometimes recommended

*Who might be a good fit?* Somebody with severe symptoms who is able to try a treatment that may require a full day multiple times, and

*Limitations:* Generally not covered by insurance, with advertised cash prices per treatment ranging \$400-500 as of 2021. Typically only available in large cities.

*How to get started:* Patients may look for private clinics offering the treatment. Some IV ketamine clinics may require referral from a mental health provider.

*Intranasal esketamine (Spravato):* FDA approved March 2019, as adjunctive treatment for TRD and also now for depression in patients with acute suicidal ideation or behavior.

*Details:* 2 times per week for 4 weeks, sometimes continued once per week for an additional 4 weeks. 2 hours of supervision in a medical setting required after each dose.

*Notable adverse effects:* Nausea, altered taste, dizziness, anxiety, sedation, dissociation

*Who might be a good fit?* Somebody with severe symptoms who is able to use a treatment that may require a half day several times per week.

*Limitations:* There is a national REMS program that registers and tracks providers, pharmacies, and patients involved in esketamine usage.

*How to get started:* Patients may self-refer to an identified prescribing provider, who will evaluate for whether the treatment is a reasonable option.

### **Other Psychedelics** (eg psilocybin, MDMA)

Not currently a treatment option that can be recommended by medical providers. Psilocybin-assisted therapy has been made legal in Oregon as of November 2020 with plans for a 2-year implementation period with anticipated legal psilocybin therapy available starting January 2023. This is an area of active research.

*Who might be a good fit?* No patients at this time

### **ECT** (electroconvulsive therapy)

Electrically conductive paddles are used to incite a 40-60 seconds long seizure in a patient who has received anesthesia.

*Details:* 2-3 times per week for up to 12 sessions. Some patients received maintenance treatment every 4-8 weeks after that

*Notable adverse effects:* Sedation, confusion for 12-36 hours after treatment. Forgetting events that occurred earlier in life – a common concern for patients after reading about the procedure – is exceptionally rare.

*Who might be a good fit?* Somebody with severe symptoms who is able to use a treatment that may be incapacitating several times per week for the first several weeks.

*Limitations:* Must be performed in a medical setting with anesthesiology and psychiatry both participating.

*How to get started:* Refer for evaluation by an ECT program/a psychiatrist who performs ECT.

### **?Other things to include here?**

Lithium augmentation (for MDD)

Liothyronine

Antipsychotic augmentation