EMSAM®
(selegiline transdermal system)

INDICATION

EMSAM (selegiline transdermal system) is a monoamine oxidase inhibitor (MAOI) indicated for the treatment of adults with major depressive disorder (MDD).

EMSAM – The First and Only Selegiline Patch Indicated for MDD[1]

Not an actual patient. Patch is not drawn to scale and does not reflect an actual image of patch.

Boxed Warning and Important Safety Information

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening and for emergence of suicidal thoughts and behaviors.

EMSAM is contraindicated in patients less than 12 years of age because of an increased risk of hypertensive crisis.

Please see full Important Safety Information on pages 2-4. Click here for full Prescribing Information.

EMSAM® (selegiline transdermal system)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- The EMSAM Transdermal System is contraindicated with selective serotonin reuptake inhibitors (SSRIs); serotonin and norepinephrine reuptake inhibitors (SNRIs); the tricyclic antidepressants clomipramine and imipramine; the opiate analgesics meperidine, tramadol, methadone, pentazocine, and propoxyphene; and the antitussive agent dextromethorphan because of a risk of serotonin syndrome when the EMSAM Transdermal System is used with these agents.

- Carbamazepine is contraindicated with EMSAM because of a possible increased risk of hypertensive crisis.

- Stop the use of these agents 1 week (at least 5 weeks for fluoxetine) before starting therapy with the EMSAM Transdermal System. The EMSAM Transdermal System should be stopped at least 2 weeks before starting therapy with any drug that is contraindicated with EMSAM.

- EMSAM is contraindicated in patients less than 12 years of age because of the potential for a hypertensive crisis.

- EMSAM is contraindicated in patients with pheochromocytoma because MAOIs may precipitate a hypertensive crisis in such patients.

WARNINGS and PRECAUTIONS

- **Suicidal Thoughts and Behaviors in Adolescents and Young Adults:** In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients and over 4,400 pediatric patients, the incidence of suicidal thoughts and behaviors in pediatric and young adult patients was greater in antidepressant-treated patients than in placebo-treated patients. No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about antidepressant drug effect on suicide. Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes.

  Consider changing the therapeutic regimen, including possibly discontinuing EMSAM, in patients whose depression is persistently worse or who are experiencing emergent suicidal thoughts or behaviors.

- **Serotonin Syndrome:** The development of a potentially life-threatening serotonin syndrome has been reported with concomitant use of MAOIs, such as EMSAM, with serotonergic drugs. These reactions have also been reported in patients who have discontinued serotonergic drugs and then subsequently started an MAOI. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS and PRECAUTIONS (Cont'd):

(e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, and hyperthermia), neuromuscular changes (e.g., tremor, rigidity, myoclonus, hyperreflexia, and incoordination), seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, and diarrhea). Patients should be monitored for the emergence of serotonin syndrome. Treatment with EMSAM and any concomitant serotonergic agents should be discontinued immediately and supportive treatment should be initiated.

- **Blood Pressure Elevation:**

  Tyramine-Induced Hypertensive Crisis: EMSAM inhibits the catabolism of dietary amines, such as tyramine, and has the potential to produce a hypertensive crisis following the ingestion of tyramine-rich foods or beverages. Hypertensive crises, which in some cases may be fatal, are characterized by some or all of the following symptoms: occipital headache which may radiate frontally, palpitation, neck stiffness or soreness, nausea, vomiting, sweating (sometimes with fever and sometimes with cold, clammy skin), dilated pupils, and photophobia. Either tachycardia or bradycardia may be present and can be associated with constricting chest pain. Intracranial bleeding has been reported in association with the increase in blood pressure. Patients should be instructed as to the signs and symptoms of severe hypertension and advised to seek immediate medical attention if these signs or symptoms are present. If a hypertensive crisis occurs, EMSAM should be discontinued immediately and therapy to lower blood pressure should be instituted immediately. Fever should be managed by means of external cooling. Patients must be closely monitored until symptoms have stabilized.

  To prevent a hypertensive crisis, foods and beverages high in tyramine must be avoided while on EMSAM 9 mg/24hr or 12 mg/24hr, and for 2 weeks following discontinuation of EMSAM Transdermal System at these doses, or after reducing the dose to 6 mg/24hr.

  Blood Pressure Elevation Related to Concomitant Medication: Carbamazepine is contraindicated with EMSAM because carbamazepine has been shown to significantly elevate selegiline levels, which may increase the risk of a hypertensive crisis. The use of EMSAM with adrenergic drugs or buspirone may produce substantial increases in blood pressure. Therefore, monitor blood pressure if EMSAM is used with any of the following drugs: buspirone, amphetamines, and cold products or weightreducing preparations that contain sympathomimetic amines (e.g., pseudoephedrine, phenylephrine, phenylpropanolamine, and ephedrine).

- **Activation of Mania/Hypomania:** In patients with bipolar disorder, treating a depressive episode with EMSAM or another antidepressant may precipitate a mixed/manic episode. Prior to initiating treatment with EMSAM, screen patients for any personal or family history of bipolar disorder, mania, or hypomania.

- **External Heat:** Heat may result in an increase in the amount of selegiline absorbed from EMSAM and produce elevated serum levels of selegiline. Patients should be advised to avoid exposing the EMSAM application site to external sources of direct heat, such as heating pads or electric blankets, heat lamps, saunas, hot tubs, heated water beds, and prolonged direct sunlight.

IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE REACTIONS

- Treatment-emergent adverse events (at ≥2% incidence with EMSAM Transdermal System and greater than placebo, respectively) in short-term clinical trials: application site reactions (24% vs 12%), headache (18% vs 17%), insomnia (12% vs 7%), diarrhea (9% vs 7%), dry mouth (8% vs 6%), dyspepsia (4% vs 3%), rash (4% vs 2%), pharyngitis (3% vs 2%), and sinusitis (3% vs 1%).

DRUG INTERACTIONS

- **Serotonergic Drugs:** Serious, sometimes fatal, central nervous system (CNS) toxicity referred to as the "serotonin syndrome" has been reported with the combination of nonselective MAOIs and serotonergic drugs. Use of EMSAM with these drugs is contraindicated.

- **Tyramine:** EMSAM has the capacity to inhibit intestinal MAO, which is responsible for the catabolism of tyramine in foods and beverages. As a result of this inhibition, large amounts of tyramine may enter the systemic circulation and precipitate a sudden, large rise in blood pressure or hypertensive crisis. To prevent a hypertensive crisis, foods and beverages high in tyramine must be avoided while on EMSAM 9 mg/24 hr, and for 2 weeks following discontinuation of the EMSAM Transdermal System at these doses, or after reducing the dose to 6 mg/24 hr.

- **Sympathomimetic Amines and Buspirone:** The use of EMSAM with sympathomimetic amines or buspirone may produce substantial elevations in blood pressure. Therefore, monitor blood pressure if EMSAM is used with any of the following drugs: buspirone, amphetamines, and cold products or weight-reducing preparations that contain sympathomimetic amines.

- **Effect of Other Drugs on EMSAM:** Carbamazepine is contraindicated with MAOIs, including selegiline.

- **Effect of EMSAM on Other Drugs:** Use of alcohol while taking EMSAM is not recommended, even though EMSAM has not been shown to increase the impairment of mental and motor skills caused by alcohol (0.75 mg per kg). Monitor blood pressure if sympathomimetic agents (e.g., phenylpropanolamine [PPA] or pseudoephedrine) are used with EMSAM, even though selegiline does not appear to affect the pharmacokinetics of PPA or pseudoephedrine.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** When treating a pregnant woman with EMSAM, the physician should carefully consider both the potential risks of taking an MAOI, particularly the risk of hypertensive crisis during pregnancy, along with the established benefits of treating depression with an antidepressant.

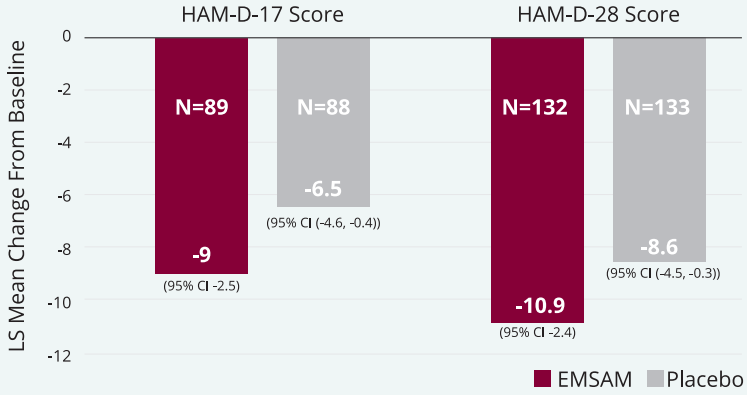
- **Lactation:** Because of the potential for serious adverse reactions in breastfed infants from EMSAM, including the potential for hypertensive crisis, advise a woman that breastfeeding is not recommended during treatment with EMSAM and for 5 days after the final dose.

EMSAM – Significantly Improved MDD Symptoms vs Placebo

EMSAM transdermal patch was more effective than placebo on the Hamilton Depression Rating Scale (HAM-D).[1]

- The efficacy, safety, and tolerability of the selegiline transdermal system (EMSAM) were evaluated using 2 separate randomized, placebo-controlled, double-blind studies. The efficacy, safety, and tolerability of the selegiline transdermal system (EMSAM) were evaluated in outpatients aged 18 to 70 meeting DSM-IV criteria for Major Depressive Disorder using 2 separate randomized, placebo-controlled, double-blind studies. For study 1 (n = 89 for EMSAM and n = 88 for placebo), a 20 cm^2 EMSAM patch (20 mg applied once daily) was evaluated over 6 weeks in adults with MDD. For study 2 (n = 132 for EMSAM and n = 133 for placebo), the dose range of 6 mg to 12 mg/24 hours was evaluated over 8 weeks. Primary efficacy outcomes used for evaluation were HAM-D Scale-17 for study 1 and HAM-D Scale-28 for study 2.
- In both studies, the EMSAM group showed significant improvement in the HAM-D total score (LS mean change from baseline of -9 for EMSAM vs -6.5 for placebo in Study 1 and -10.9 for EMSAM vs -8.6 for placebo in Study 2).

Greater LS Mean Change From Baseline With EMSAM



HAM-D-17: 17-item Hamilton Depression Rating Scale; HAM-D-28: 28-item Hamilton Depression Rating Scale; LS mean: least squares mean.

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- **Suicidal Thoughts and Behaviors in Adolescents and Young Adults:** In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients and over 4,400 pediatric patients, the incidence of suicidal thoughts and behaviors in pediatric and young adult patients was greater in antidepressant-treated patients than in placebo-treated patients. No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about antidepressant drug effect on suicide. Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes.

  Consider changing the therapeutic regimen, including possibly discontinuing EMSAM, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

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EMSAM
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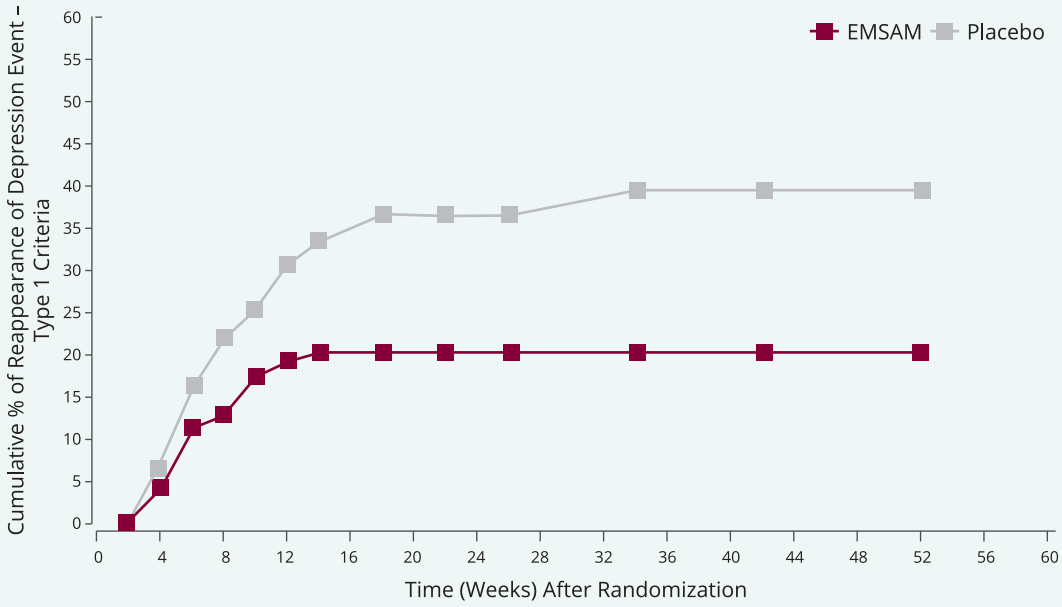
Significantly Longer Time to Relapse With EMSAM Compared to Placebo[1]

- In another trial (study 3), the efficacy and safety of EMSAM (6 mg/24 h) were studied in a randomized, double-blind, placebo-controlled study in adult outpatients with MDD. In this 52-week study, 322 patients who responded with a 17-item HAM-D Scale score of 10 or less were randomly assigned at the same dose to EMSAM (n=159) or placebo (n=163).
  - Discontinuation rates for each were at 52% for the EMSAM and placebo groups by week 12 of the double-blind phase.
- Patients who continued receiving EMSAM experienced significantly longer time to relapse compared to the placebo group patients.*

Longer Time to Relapse With EMSAM Compared to Placebo



*Relapse during the double-blind phase was defined as: (1) a 17-item HAM-D score of 14 or greater; (2) a CGI-S† score of 3 or greater (with at least a 2-point increase from double-blind baseline); and (3) meeting DSM-IV criteria for MDD on two consecutive visits at least 11 days apart.
†CGI-S = Clinical Global Impression-Severity Scale.

IMPORTANT SAFETY INFORMATION

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Adverse Events

Adverse reactions which occurred at an incidence of 2% or more among EMSAM-treated patients.[1]

Table 1. The Most Common Adverse Events Reported With EMSAM in Comparison to Placebo[1*]

Body System	EMSAM (n = 817)	Placebo (n = 668)
Body as a whole		
Headache	18	17
Digestive		
Diarrhea	9	7
Dyspepsia	4	3
Nervous		
Insomnia	12	7
Dry mouth	8	6
Respiratory		
Pharyngitis	3	2
Sinusitis	3	1
Skin		
Application site reaction	24	12
Rash	4	2

*Excludes the following reactions, which had an incidence on placebo treatment greater or equal to EMSAM: infection, nausea, dizziness, pain, abdominal pain, nervousness, back pain, asthenia, anxiety, flu syndrome, accidental injury, somnolence, rhinitis, and palpitations.

- Includes doses of EMSAM from 3 mg to 12 mg per 24 hours in placebo-controlled trials of up to 8 weeks in duration.
- Other post-approval adverse reactions were identified [e.g., convulsion and hypoesthesia, disorientation, hallucination (visual), and tension].

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- **Blood Pressure Elevation:**

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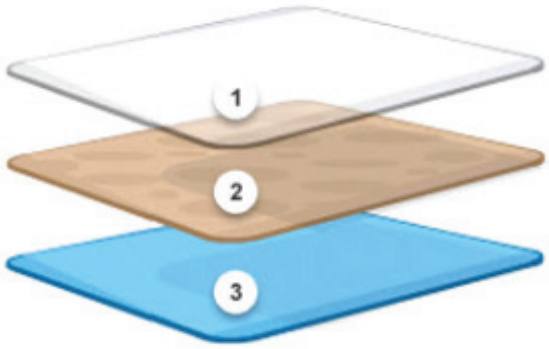
Transdermal Drug-Delivery System

Transdermal delivery system that delivers selegiline over 24 hours.

EMSAM is a matrix-type transdermal system composed of 3 layers:



1. **Backing film:** Provides occlusivity, physical integrity, and protects the adhesive/drug layer
2. **Adhesive:** An adhesive layer that incorporates the active ingredient
3. **Release liner:** Removable coated film or polymer-based protective layer that is peeled off by patient before applying EMSAM

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Flexible Dosage Options

6 mg/24 h	**Recommended starting dose and target dose.**	**No dietary restrictions.**
9 mg or 12 mg/24 h	**Based on clinical judgment, dose can be increased in increments of 3 mg/24 h at intervals of no less than 2 weeks up to a maximum dose of 12 mg/24 h.**	**For 9 mg/24 h and 12 mg/24 h doses, advise patients that right from the first dose of treatment, they must avoid high-tyramine foods and beverages. Continue avoiding up to a period of 2 weeks after a dose reduction to 6 mg/24 h or following the discontinuation of 9 mg or 12 mg/24 h dose.**

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EMSAM (selegiline transdermal system)

Your Eligible, Commercially Insured Patients May Save on Their Out-of-Pocket Costs With the EMSAM Savings Card

Your patients may pay as little as $20 for EMSAM prescriptions.

Eligible, commercially insured patients may have their commercial co-pay amount for EMSAM® reduced up to a maximum of $600 per month after the patient pays the first $20.00 per 30-day prescription, up to a maximum of $7,200.00 per calendar year.

*Eligibility restrictions apply. See full Terms and Conditions at https://www.activatethecard.com/viatrisadvocate/emsam/welcome.html. This program is not valid for patients enrolled in federal or state healthcare programs, such as Medicare (Part D or otherwise), Medicaid, Medigap, VA or DOD, or TRICARE, and not valid for uninsured patients (except for commercially insured patients without coverage for EMSAM). This offer is void where prohibited or restricted by law. Mylan Specialty L.P., a Viatris Company, reserves the right to amend or end this program at any time without notice.

IMPORTANT SAFETY INFORMATION

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- **External Heat:** Heat may result in an increase in the amount of selegiline absorbed from EMSAM and produce elevated serum levels of selegiline. Patients should be advised to avoid exposing the EMSAM application site to external sources of direct heat, such as heating pads or electric blankets, heat lamps, saunas, hot tubs, heated water beds and prolonged direct sunlight.

ADVERSE REACTIONS

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Reference:

1. EMSAM [prescribing information]. Morgantown, WV: Somerset Pharmaceuticals Inc.; 2020.

EMSAM – Selegiline Patch Indicated for Treatment of Adults With MDD

No dietary restrictions for 6 mg dosing option

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US-EMS-2024-00002