

FAST FACTS AND CONCEPTS #372
NON-ORAL PHARMACOTHERAPY OPTIONS FOR DEPRESSION
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Background: While psychological counseling remains the mainstay of depression management, treatment with pharmacotherapy can achieve better outcomes for many patients (1). Palliative care clinicians may encounter depressed patients who are nothing by mouth (NPO) for prolonged periods of time due to swallowing problems or GI abnormalities (e.g. small bowel transplant, a complicated abdominal wound, or severe pancreatitis). This *Fast Fact* reviews the best evidence to identify a care approach for the non-oral pharmacologic management of depression.

Is non-oral anti-depressant treatment necessary? The first question to consider is whether a seriously ill patient who lost the ability to tolerate oral medications requires non-oral antidepressant pharmacotherapy. For many patients with a new diagnosis of depression and a markedly decreased quality of life, prompt initiation of psychological counseling and pharmacotherapy is often necessary, even if that means a non-oral route. Alternatively, patients who are not actively depressed but rather are on anti-depressants for a history of depression, may do better if their antidepressant pharmacotherapy is held until they were able to tolerate medications by mouth. Prognosis and co-morbidities are important considerations. Most antidepressants require several weeks to exhibit therapeutic benefit. Hence, patients with a short life expectancy are unlikely to benefit from their initiation. Initiating anti-depressants is not appropriate for acutely delirious patients.

Can the anti-depressant be given via an enteric tube? Most antidepressants and psychostimulants can be crushed or given as an elixir via an enteric tube. Citalopram, escitalopram, fluoxetine, paroxetine, sertraline, nortriptyline, doxepin, and methylphenidate are all available as solutions or concentrate. In general, short-acting formulations are safe to crush and give via an enteric tube, while long-acting formulations are not. If an enteric tube is not available and the patient is on an anti-depressant with a short half-life (e.g. paroxetine or immediate release venlafaxine), then withdrawal phenomenon could ensue. Initiation of a less standard non-oral anti-depressant (see below) may be warranted. Clinical pharmacists and consult liaison psychiatrists can be vital resources in guiding these decisions

FDA-approved non-oral anti-depressants:

- **Mirtazapine** is available as an oral dissolving tablet (ODT). The ODT is placed under the tongue and dissolves upon contact with a patient's saliva. Still, much of the absorption occurs in the stomach and intestines. Therefore, it may not be appropriate for strict NPO patients, especially those with proximal GI abnormalities. See *Fast Fact #314* for more information on mirtazapine.
- **Selegiline** is a monoamine oxidase inhibitor (MAOI). It is available as an ODT and as a transdermal (TD) patch. These formulations experience less first-pass metabolism compared with the regular oral tablet of selegiline (4). This means there is a decreased risk of tyramine-induced adverse events such as a hypertensive crisis, as there is no significant inhibition of gastrointestinal monoamine oxidase activity (5). Regardless, a psychiatrist should be involved if one wants to use this medication given its numerous drug and food interactions via oral and non-oral administration (6,7). Non-oral formulations of selegiline are relatively costly: a 30-day supply of the selegiline TD patch costs about \$1700 and a 30-day supply of the ODT formulation typically costs > \$4000.

Non-oral formulations that have NOT been FDA-approved for depression management:

- **Tricyclic antidepressants (TCAs):** *Doxepin* is available in a topical cream to treat pruritus. While there have been case reports regarding its use topically and rectally to treat depression (4), it has not been evaluated in any controlled way nor has a reasonable dose been identified. *Amitriptyline* is available intravenously (IV) outside the United States and there are case reports of its compounded use as buccal, topical, and rectal formulations (4,5).
- **Selective serotonin reuptake inhibitors:** *Fluoxetine*: a case report describes its effective use when compounded into topical and rectal formulations (5). *Citalopram* IV is available outside of the US (8).

- **Psychostimulants:** While data on psychostimulants for depression have been mixed (see *Fast Facts* # 61 & 309) and their provision as a Schedule II medication limits who may prescribe them, they are often considered for depressed patients with a prognosis shorter than a few months since their onset of action is typically days compared with weeks to a month with more usually prescribed anti-depressants. Methylphenidate is available as a solution for patients who can swallow small amounts or for whom use of an enteric tube is feasible. For patients with strict “nothing by the GI tract” orders, there is a commercially available transdermal methylphenidate patch (9). The patch should be applied 2 hours prior to desired effect (ideally near the patient’s hip where it is felt to have best absorption) and removed 9 hours after (10). The patch costs about 7 times more than a tablet or elixir.
- **Ketamine** is an N-methyl-D-aspartate (NMDA) receptor antagonist which has been studied for use in depression (10-13). While the most effective dosing and delivery strategy has not yet been determined, many studies have assessed IV dosing of 0.5 mg/kg either using single doses or repeated doses every 1-2 weeks. See *Fast Fact* #132.

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