

# 29 - Adverse effects

## Adverse effects

358 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 doses tested, in Table 3.6 we provide a summary of dosing recommendations, considering available evidence and clinical experience. Novel formulations of oral ketamine are under development.<sup>17</sup> Adverse effects Ketamine generally leads to significant dissociative symptoms when given at antidepressant doses.<sup>18</sup> These symptoms include perceptual distortions and can lead to significant anxiety. As a result, it is necessary that any patients administered ketamine should be observed by a trained clinician during dosing and for 1 hour after administration. Although a rare event, ketamine has also been reported to induce laryngospasm and so the observing clinician should be trained in intermediate or advanced life support. When ketamine is given at lower doses by oral or sublingual routes, it is less likely to induce strong dissociative symptoms so, once a test dose has been given under clinical supervision, it may be possible for administration to take place in a non-clinical (home) setting, although patients should be advised not to drive, operate heavy machinery or partake in other high-risk activities for at least 1 hour after administration. In addition, consideration must be given by the prescribing clinician to the risks of diversion and illegal use. Ketamine can have significant effects on blood pressure and heart rate. Before administration, a physical examination including baseline blood pressure, full blood count, liver function test, thyroid function test plus ECG is recommended. Physical monitoring (blood pressure and heart rate) during and after ketamine administration is also indicated. In longer-term illicit use, ketamine is associated with urinary pain, epithelial bladder barrier damage, reduced bladder capacity, ureter stenosis and kidney failure.<sup>19</sup> Although this ketamine-induced cystitis is a recognised complication of recreational use of ketamine, its occurrence in therapeutic use of ketamine in depression has so far not been widely reported but remains a concern.<sup>20</sup> Table 3.6 Dosing recommendations for different routes of ketamine administration and intranasal esketamine in treatment-resistant depression.

Route	Dose	Details	Frequency	Comments
IV	2-6	0.5mg/kg, increasing up to 1.0mg/kg if no response (limited support for doses higher than 0.5mg/kg) <sup>16</sup>	(titrate from 0.25mg/kg in older people)	Infuse over 40 minutes Induction phase: once or twice a week Maintenance phase: according to response, weekly then every 2 weeks, or even monthly (consider supplementing with oral/sublingual doses between IV treatments) Must be administered in clinical setting Cognitive effects (confusion, dissociation, etc.) do occasionally occur Associated with transient increase in BP, tachycardia and arrhythmias. Pretreatment ECG required. Monitor BP before and after infusion. Observe during and for 1 hour after infusion

(Continued)

Depression and anxiety disorders CHAPTER 3 Route Dose Details Frequency Comments SC21,22  
0.5mg/kg, increasing up to 1.0mg/kg if no response (titrate from 0.25mg/kg in older people)

■ SC bolus injection to appropriate SC site ■ ■ As per IV above ■ ■ As per IV above ■ ■ May be better tolerated than IV or IM routes<sup>21</sup> IM<sup>23,24</sup> ■ ■ 0.5mg/kg, increasing up to 1.0mg/kg if no response (titrate from 0.25mg/kg in older people) ■ ■ IM bolus injection to appropriate IM site ■ ■ As per IV above ■ ■ As per IV above Oral<sup>25–27</sup> ■ ■ 0.5–5.0mg/kg depending on dosing strategy ■ ■ Oral capsules ■ ■ Regular lower doses: ■ ■ 0.5–2.0mg/kg every 1–3 days ■ ■ Intermittent higher doses to supplement IV/SC/IM treatment: ■ ■ 2.0–5.0mg/kg once or twice a week ■ ■ Can be taken at home ■ ■ Lower doses show good tolerability, however, antidepressant effects not as rapid as IV/SC/IM ■ ■ Higher doses may be practical alternative to maintain response to IV/ SC/IM treatment. Titrate dose according to response/adverse effects. Sublingual<sup>27–29</sup> ■ ■ 0.5–3.0mg/kg depending on dosing strategy ■ ■ Ketamine solution (held under tongue for 5 minutes and swallowed) ■ ■ Sublingual ketamine lozenges ■ ■ Regular lower doses: ■ ■ 0.5–1.5mg/kg every 1–3 days ■ ■ Limited evidence for very low sublingual dosing (10mg every 2–3 days or weekly)<sup>30</sup> ■ ■ Intermittent higher doses to supplement IV/SC/IM treatment: ■ ■ 1.5–3.0mg/kg once or twice a week ■ ■ Can be taken at home ■ ■ Lower doses show good tolerability, however putative antidepressant effects not as rapid as IV/ SC/IM ■ ■ Higher doses may be used as practical alternative to maintain response to IV/SC/IM treatment. Titrate dose according to response/adverse effects. Intranasal esketamine<sup>31–34</sup> ■ ■ 56–84mg (28mg in older people) ■ ■ 28mg in two sprays (1 spray per nostril) ■ ■ Repeat after 5 minutes, depending on total dose required ■ ■ Twice weekly, then weekly, then every 2 weeks ■ ■ Must be administered in clinical setting ■ ■ Cognitive effects (confusion, dissociation, etc.) do occasionally occur ■ ■ Associated with transient increase in BP, tachycardia and arrhythmias. Pretreatment ECG recommended. Monitor BP before and after dose. ■ ■ Observe for approximately 2 hours after dose Table 3.6 (Continued)

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