Pharm-02A16 Briefly outline the pharmacology of flumazenil. 45%

Flumazenil is a competitive antagonist at the benzodiazepine receptor, commonly used in the reversal of benzodiazepines

**Physicochemical properties**

Flumazenil is 1,4-imidazobenzodiazepine derivative  
Clear colourless solution  
Ampoules containing 500 microg in 5 mL  
Dose = 100 ~ 200 microg boluses at 60 second intervals, up to 1 mg

**Pharmacokinetic properties**

**Absorption:** usually iv administration; also good oral absorption but high first pass metabolism (< 25% bioavailability)

**Distribution:** 50% protein bound, $V_d \approx 1 \text{ L/kg}$

**Metabolism:** by hepatic microsomal enzymes → inactive carboxylic acid and glucuronide metabolites

**Elimination:** < 0.1% excreted unchanged in urine, CL 10 mL/kg/min (quite high),

**Pharmacodynamic properties**

**Mechanism of action:** competitive antagonist selective for the benzodiazepine binding site of GABA\(_A\) receptor. It has minimal agonist activity.

**Onset of action:** within 2 minutes

**Duration of action:** 30 ~ 60 minutes  
Half-life of benzodiazepines usually longer than flumazenil → re-sedation possible

**CNS:** anxiety; reverse sedation associated with benzodiazepines; may precipitate seizures, especially at high doses and in susceptible pts

**CVS:** ↑HR; ↑MAP

**RESP:** reverses respiratory depression from benzodiazepines

**Examiner’s comments** - The pass rate for this question was 45%.

The question asked for straightforward factual information. To pass, the candidate needed to describe the chemical identity, presentation, pharmacokinetics (briefly) and pharmacodynamics of the drug. It was difficult to score enough points to pass without at least a brief mention of each of these points. Many candidates gave lengthy and often incorrect descriptions of the kinetics of the drug.
More complete answer usually gave a dose or dosage range for the drug and referred to the clinical problem of re-sedation, due to the longer half-lives of the most commonly used benzodiazepines compared with flumazenil.