Key Considerations when Selecting Adjunctive Medications

1. Drug–drug interactions
   - 76% of available ASMs have known interactions with other ASMs
   - Dose adjustment of existing or added treatment, and/or monitoring of drug levels, is therefore often required

2. Liver and kidney function
   - 75% of ASMs require dose adjustment, or should be administered with caution in patients with impaired hepatic function
   - 70% of ASMs require dose adjustment, or should be administered with caution in patients with impaired renal function

3. Psychiatric warnings
   - All ASMs carry a standard label warning for risk of suicidal behaviour and ideation
   - Psychiatric history may be a relevant consideration when selecting adjunctive anti-seizure treatment

4. Fetal risk
   - Birth defects, including neural tube defects, other major malformations, reduced IQ, and neurodevelopmental deficits, have been reported following fetal exposure to valproate
   - Fetal exposure to topiramate may be associated with increased risk of cieth lip/palate
   - Theoretical risk of fetal harm based on teratogenicity data in animals exists for all ASMs, although data on fetal exposure at therapeutic doses in humans is limited for most ASMs
   - Decisions to add multiple ASMs require careful consideration of risks versus benefits in females of childbearing age

5. Paediatric approval
   - 68% of ASMs are approved in patients aged as young as 4 years (and younger for some ASMs)
   - VNS implant is the only neurostimulation option approved for paediatric use

Non-pharmacological interventions should also be considered for patients with DRE

VNS: vagal nerve stimulation.
DDI: drug–drug interaction.
CNS: central nervous system.
DBS: deep brain stimulation.
DRE: drug-resistant epilepsy.
DDI: drug–drug interaction.
ASMs: antiseizure medications.
TCAs: tricyclic antidepressants.
SSRIs: selective serotonin reuptake inhibitors.
MAOIs: monoamine oxidase inhibitors.
SSNRIs: serotonin-norepinephrine reuptake inhibitors.
NEAIDs: noradrenaline reuptake inhibitors.