**Supplementary Table 1. Drugs which may inhibit nausea and/ or vomiting and cited as treatments of gastroparesis but lack adequate pharmacological and clinical evaluation**

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| **Drug or Drug Class** | **Limitation** | **Mechanism of anti-emetic action** |
| Histamine H1 receptor antagonists(now classified as inverse agonists)1* Promethazine: H1 and mACh receptor antagonist; higher concentrations antagonise at D2 receptors
* Diphenhydramine: H1 and mACh M2 receptor antagonist
 | Used2,3 but no controlled trials in patients with gastroparesis or FD | Motion sickness inhibited because H1 receptors in the vestibular system and the brainstem integrative circuitry (‘vomiting centre’) are blocked4,5 with additional anti-emetic activity conferred by antagonism at muscarinic receptors, particularly for diphenhydramine. These drugs may also exhibit some anti-emetic activity against postoperative emesis6,7. mACh receptor antagonism may reduce gastric emptying.8 |
| Marijuana or Tetrahydrocannabinol (THC) derivatives* Dronabinol
* Nabilione
 | No controlled trials. Case reports with THC derivatives or self-use of marijuana with other anti-emetics.9,10,11 THC derivatives may delay gastric emptying. Marijuana may cause cannabinoid hyperemesis syndrome9 | Dronabinol approved and used as anti-emetic drugs in patients receiving anti-cancer chemotherapy12. These agents are CB1 receptor agonists, acting in the dorsal vagal complex and the visceral insular cortex.1 |
| Alpha2-adrenoceptor agonism* Clonidine
 | Small trials in diabetic gastroparesis; increased gastric emptying of liquid meal and reduced symptoms,13 or no effect on gastric emptying of solid meal with reduced nausea, vomiting.14 | The mechanism of the antiemetic effect of clonidine is unclear but thought to be related to activation of the α2-adrenoceptor within the AP14, although inhibition of sympathetic tone may contribute to reduction of PONV15. |
| Dopamine D2 receptor antagonists* Haloperidol: Brain penetration confers disadvantages and potential advantages A reduced need for analgesic medication and symptoms of nausea and vomiting reported in patients at emergency treatment department16
* Trimethobenzamide (Tigan): Can block apomorphine-induced vomiting in dogs17 and responses to dopamine.18 Said to be useful.19
* Thiethylperazine: Blocks responses to dopamine21 Case study suggests ability to reduce symptoms of gastroparesis20
 | No controlled trials.  | D2 receptor antagonist with anti-emetic activity likely to occur within the AP |
| Levosulpiride* May improve symptoms in diabetic or idiopathic gastroparesis, including nausea, vomiting and early satiety.22,23 Accelerates gastric emptying
 | Small studies, without placebo control. | D2 receptor antagonist and a 5-HT4 receptor agonist with brain-penetrant properties24  |
| Tricyclic antidepressants* prochlorperazine, chlorpromazine, fluphenazine, levomepromazine
 | No clear scientific rationale. Case reports and small trials | Used as anti-emetic drugs, usually in patients receiving anti-cancer chemotherapy. Most likely effective because of antagonism at the H1, muscarinic, α2 adrenoceptor and/ or 5-HT3 receptor1 |

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