**Actual/Potential Drug Interactions Between Directly Acting Antivirals (DAAs) and Anticonvulsants**

| **Anticonvulsant (route of metabolism)** | **Boceprevir (Victrelis®, BOC, SCH 503034) Merck**<br><br>Substrate of CYP3A4, CYP3A5 and aldoketoreductases.[1] Strong, reversible inhibitor of CYP3A4 and p-glycoprotein in vitro.[2] | **Telaprevir (Incivek®, TVR, VX-950) Vertex Pharmaceuticals**<br><br>Substrate and strong inhibitor of CYP3A4 and p-glycoprotein.[3] |
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| Carbamazepine<br>(Parent: CYP3A>> 2C8, 1A2)<br><br>Inducer of CYP3A, 2C9, 2C19, UGT and possibly 1A2 | Potential for ↓ DAA concentration and/or ↓ anticonvulsant concentration.[4]<br><br>Carbamazepine is contraindicated with boceprevir.[5] | Potential for ↓ DAA concentration and/or ↑ anticonvulsant concentration.[4]<br><br>Use combination with caution. Clinical or laboratory monitoring of carbamazepine concentrations and dose titration are recommended to achieve the desired clinical response.[3]<br><br>Consider an alternate agent with non-inducing metabolic properties. |
| Gabapentin<br>(Renal) | No interaction expected based on known pharmacologic characteristics. Monitor and titrate dose according to clinical response. | |
| Lamotrigine<br>(UGT) | No interaction expected based on known pharmacologic characteristics. Monitor and titrate dose according to clinical response. Caution re: risk of rash, including Stevens-Johnson syndrome with lamotrigine, since DAAs may also be associated with rash. | |
| Levetiracetam<br>(24% enzymatic hydrolysis, 66% renal) | No interaction expected based on known pharmacologic characteristics. Monitor and titrate dose according to clinical response.<br>NB: No data exist for levetiracetam for treating psychiatric disorders in the context of HCV. | |
| Lithium<br>(renal) | No interaction expected based on known pharmacologic characteristics. Monitor and titrate dose according to clinical response and serum levels. | |
| Oxcarbazepine<br>(parent - UGT)<br><br>Inhibitor of CYPC19<br>Potent inducer of CYP3A4.<br>Relative to carbamazepine, oxcarbazepine inducing effect is 54% lower[6] | Potential for ↓ DAA concentrations and decreased efficacy. Avoid combination if possible, and consider an alternate anticonvulsant with non-inducing metabolic properties.[7] | |
| Phenobarbital<br>(parent - 2C9/19)<br><br>Potent inducer of CYP3A4, 1A2, 2C9/19, UGT | Potential for ↓ DAA concentrations and/or ↑/↓ anticonvulsant concentrations.<br><br>Phenobarbital is contraindicated with boceprevir.[5] | Potential for ↓ DAA concentrations and/or ↑/↓ anticonvulsant concentrations.<br><br>Use combination with caution. Clinical or laboratory monitoring |

| Anticonvulsant (route of metabolism) | Boceprevir (Victrelis®, BOC, SCH 503034) Merck | Telaprevir (Incivek®, TVR, VX-950) Vertex Pharmaceuticals |
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| | | of phenobarbital concentrations and dose titration are recommended to achieve the desired clinical response.[3]<br><br>Consider an alternate agent with non-inducing metabolic properties. |
| Phenytoin<br>(parent - 70% CYP2C9, minor 2C19)<br><br>Potent inducer of CYP3A4, 2C9/19, UGT | Potential for ↓ DAA concentrations and/or ↑/↓ anticonvulsant concentrations.<br><br>Phenytoin is contraindicated with boceprevir.[5] | Potential for ↓ DAA concentrations and/or ↑/↓ anticonvulsant concentrations.<br><br>Use combination with caution. Clinical or laboratory monitoring of phenobarbital concentrations and dose titration are recommended to achieve the desired clinical response.[3]<br><br>Consider an alternate agent with non-inducing metabolic properties. |
| Pregabalin<br>(renal) | No interaction expected based on known pharmacologic characteristics. Monitor and titrate dose according to clinical response. | |
| Topiramate<br>(renal)<br><br>Induces 3A4 (mild), inhibits 2C19 | Potential for ↓ DAA concentrations. Monitor and titrate dose according to clinical response.<br>NB: No data exist for topiramate for treating psychiatric disorders in the context of HCV. | |
| Valproic acid, divalproex<br>(Parent – 50% UGT, <10% CYP)<br><br>Inhibitor of UGT,CYP2C9/19 | No interaction expected based on known pharmacologic characteristics. Monitor and titrate dose according to clinical response and serum levels. Monitor for potential hepatotoxicity.[8] | |

Legend: CYP = cytochrome P450, P-gp = p-glycoprotein, UGT = Uridine 5'-diphospho-glucuronosyltransferases

References:


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