Supplementary Table 2 Description of PBPK model analysis results on Japanese Product Labels※

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| Drug Name (Generic Name) | Cerdelga® (Eliglustat) | Farydak® (Panobinostat) | Imbruvica® (Ibrutinib) |
| Intended purpose of PBPK | * PK in different genotype of CYP2D6 subjects * DDI magnitude with terbinafine and fluconazole | DDI magnitude with rifampin | DDI magnitude with inhibitors and inducers of CYP3A4 |
| Items predicted using PBPK | * AUC of eliglustat in CYP2D6 PM * Cmax and AUC of eliglustat with inhibitors of CYP2D6 and CYP3A | AUC of panobinostat | AUC of ibrutinib |
| Description of PBPK simulation in the label | * Simulations of eliglustat AUC using PBPK models after 100 mg daily dosing in CYP2D6 PM estimated comparable with AUC in CYP2D6 IM after twice daily dosing of eliglustat. * Simulations using PBPK models estimated increase in eliglustat Cmax and AUC 8.85-fold and 11.7-fold in the presence of terbinafine and fluconazole, respectively. * Comparison of systemic exposure of eliglustat after 800 mg dosing with estimated systemic exposure using PBPK models when co-administered with both inhibitors of CYP2D6 and CYP3A in CYP2D6 EM, or with inhibitors of CYP3A in CYP2D6 IM and PM are described. | Simulations using PBPK models estimated an approximately 70% decrease in AUC in the presence of rifampin. | Estimated AUC of ibrutinib using PBPK models with itraconazole, clarithromycin, voriconazole, erythromycin, diltiazem, fluvoxamine, azithromycin, carbamazepine, efavirenz are described. |
| Dosing recommendations in the label using PBPK analysis results | Contraindications:   * Co-administration with both inhibitors of CYP2D6 and CYP3A in CYP2D6 EM. * Co-administration with inhibitors of CYP3A in CYP2D6 IM and PM. | Dosing with strong inducers of CYP3A is not recommended because this may decrease panobinostat blood concentration. | Dosing with ketoconazole, itraconazole and clarithromycin is contraindications.  Consider alternative agents with no CYP3A inhibition or induction. |

* The English descriptions of the Japanese Product labels in this table are provided for reference purposes only. In the event of any inconsistency between the Japanese original product label and the English translation, the former shall prevail.