

Р†РќРЎРЎР РЈРЉРІР†РЇ

**PrP»CЦ PjPμPrPëC‡PSPsPiPs P•P°CíC,PsCíCíPIP°PSPSCЦ P»C-PεP°CĤCíCĤPεPsPiPs
P•P°CíPsP±Cí**

[illegible]

P•P—PћPќPŷPћP›

(EZANTAL)

$P \dot{Y} P \in P \gg P^\circ P_\Gamma$:

PrC-CHC†P° CH₂PμC†PsPIPëPSP°: P»PμCH₂PeP°PSC-PrPëPïC-PS (lercanidipine);

1 C, P°P±P»PμC, PεP° PjC-Cl'C, PëC, CH 10 PjPi P°P±Ps 20 PjPi P»PμCηPεP°PSC-PrPëPiC-PSCr
PiC-PrCηPsC...P»PsCηPëPrCr (Cr PIPëPiP»CΠPrC- P»PμCηPεP°PSC-PrPëPiC-PSCr
PiC-PrCηPsC...P»PsCηPëPrCr PiPμPjC-PiC-PrCηP°C, Cr);

PrPsPiPsPjC-P¶PSC- C¶PµC±PsPIPëPSPë: P»P°PeC,PsP·P°, PjPsPSPsPiC-PrC¶P°C,;
C†PµP»C¶P»PsP·P° PjC-PeC¶PsPeC¶PëC¶C, P°P»C-C±PSP°; PSP°C,C¶C-C¶
PeC¶PsC¶PeP°C¶PjPµP»PsP·P°; PïPsPIC-PrPsPS; PïPsP»C-C¶PsC¶P±P°C,; PjP°PiPSC-C¶
C¶C,PµP°C¶P°C,; PiC-PïC¶PsPjPµP»PsP·P°; PïPsP»C-PµC,PëP»PµPSPiP»C-PePsP»CH 6000
(PjP°PeC¶PsPiPsP» 6000); C,PëC,P°PSCí PrC-PsPeC¶PëPr (P· 171); C,P°P»CHPe; P·P°P»C-P·P°
PsPeC¶PëPr P¶PsPIC,PëPñ (E 172).

P>C-PeP°C₇C₇CH₂PeP° C₇PsC₇PjP°. P₇P°P±P»P₇C₇PeP₇, PIPeC₇P₇C₇-P₇P»C-PIPePsPIP₇C₇ PsP±PsP»PsPSPePsC₇.

PhCfPSPsPIPS- C,,C-P·PëPePs-C...C-PjC-C±PSC- PIP»P°CfC,PëPIPsCfC,C-:
PrPIPsPsPïCfPeP»C- C,P°P±P»PµC,PePë PeCfCfPiP»PsC— C,,PsCfPjPë P¶PsPIC,PsPiPs
PePsP»CHbPsCfCf, PIPeCfPëC,C- PïP»C-PIPePsPIPsCf PsP±PsP»PsPSPePsCf.

P_αP°C₇P_jP°PePsC,P_μC₇P°P_iP_μPIC,PëC_‡PSP° PiC₇C₇P_iP°

P'P»PsPeP°C,PsC $\overline{\text{H}}$ Pë PeP°P»CHC†C-C"PIPëC... PeP°PSP°P»C-PI. PŸP μ P»P μ PeC,PëPIPSC-P°PSC,P°PiPsPSC-C†C,Pë PeP°P»CHC†C-C $\overline{\text{H}}$ P· PïP μ C $\overline{\text{H}}$ P μ PIP°P¶(PSPsC $\overline{\text{H}}$ PrC-C"C $\overline{\text{H}}$ PSP° C†C†PrPëPSPë. P μ PsC...C-PrPSC- PrPëPiC-PrC $\overline{\text{H}}$ PsPiC-C $\overline{\text{H}}$ PëPrPëPSCr.
P>P μ C $\overline{\text{H}}$ PeP°PSC-PrPëPiC-PS. P $\overline{\text{L}}$ PsPr P $\overline{\text{h}}$ PŸP† PŸ08PŸ P $\overline{\text{h}}$ 13.

PαP°CḡPjP°PePsP»PsPiiC≠PSi PIP»P°CḡC,PëPIPSCḡC,C-

$$P \propto P^{\circ} C_T P_j P^{\circ} P_e P_s P_r P_{\ddot{e}} P_s P^{\circ} P_j C - P_e P^{\circ}$$

P>PμCḡPeP°PSC-PrPëPīC-PS бḡ“ C†Pμ P°PSC,P°PiPsPSC-CḡC, PeP°P»CHC†C-Cḡ
PrPëPiC-PrCḡPsPiC-CḡPëPrPëPSPsPIPsC— PiCḡCrPīPë. P†PSPiC-P±CḡC”
C,CḡP°PSCḡPjPμPjP±CḡP°PSPSPëP№ PiPsC,C-Pe PeP°P»CHC†C-Cḡ PICḡPμCḡPμPrPëPSCḡ
PeP°CḡPrC-PsPjC-PsC†PëC,C-PI C,P° PiP»P°PrPePsPjбḡ™ CḡP·PsPIPëC... PeP»C-C,PëPS
CḡCrPrPëPS. PḡPμC...P°PSC-P·Pj P°PSC,PëPiC-PīPμCḡC,PμPSP·PëPIPSsC— PrC-C—
P»PμCḡPeP°PSC-PrPëPīC-PSCḡ P·CḡPjPsPIP»PμPSPëP№ PiCḡCḡPjPëPj
CḡPμP»P°PeCḡCḡCḡPëPj PIPiP»PëPIPsPj PSP° PiP»P°PrPeC- Pjбḡ™ CḡP·Pë CḡCrPrPëPS, P·P°
CḡP°C...CḡPSPsPe CḡPsPiPs P·PjPμPSCḡCḡC”C,CHCḡCḡ P·P°PiP°P»CHPSPëP№
CḡCrPrPëPSPSPëP№ PiPμCḡPëC,,PμCḡPëCḡPSPëP№ PsPiC-Cḡ. PḡPμP·PIP°PḡP°CḡCḡPë PSP°
PePsCḡPsC,PePëP№ PiPμCḡC-PsPr PSP°PiC-PIPIPëPIPμPrPμPSPSCḡ P· PiP»P°P·PjPë PeCḡPsPIC-,
P»PμCḡPeP°PSC-PrPëPīC-PS CḡPëPSPëC,CH PiCḡPsP»PsPSPIPsPIP°PSCḡ
P°PSC,PëPiC-PiPμCḡC,PμPSP·PëPIPSsCḡ PrC-Cḡ P·P° CḡP°C...CḡPSPsPe PIPëCḡPsPePsPiPs
PePsPμC,,C-C†C-C”PSC,P° PjPμPjP±CḡP°PSPSPsPiPs CḡPsP·PiPsPrC-P»Cḡ. P—P°PIPrCḡPePë
PIPëCḡPsPeC-P№ CḡCrPrPëPSPSC-P№ CḡPμP»PμPeC,PëPIPSsCḡC,C- PiCḡPμPiP°CḡP°C, PSPμ
CḡPëPSPëC,CH PSPμPiP°C,PëPIPSsC— C-PSPsC,CḡPsPiPSPsC— PrC-C—. P”PsCḡC,CḡP°
P°CḡC,PμCḡC-P°P»CHPSP° PiC-PiPsC,PμPSP·C-Cḡ P· CḡPμC,,P»PμPeC,PsCḡPSPsCḡ
C,P°C...C-PeP°CḡPrC-C”Cḡ PIPëPSPëPeP°C” CḡC-PrPePs P·P°PIPrCḡPePë
PiPsCḡC,CḡPiPsPIPsPjCḡ CḡPsP·PIPëC,PeCḡ PIP°P·PsPrPëP»P°C,P°C†C-C— PiCḡPë
PiCḡPëP№PsPjC- P»PμCḡPeP°PSC-PrPëPīC-PSCḡ.

PīPe C- PrP»Cḡ C-PSCḡPëC... P°CḡPëPjPμC,CḡPëCḡPSPëC... 1,4-
PrPëPiC-PrCḡPsPiC-CḡPëPrPëPSC-PI, P°PSC,PëPiC-PiPμCḡC,PμPSP·PëPIPSsP°
P°PeC,PëPIPSsC-CḡC,CH P»PμCḡPeP°PSC-PrPëPīC-PSCḡ PI PsCḡPSPsPIPSsPjCḡ
PsP±CḡPjPsPIP»PμPSP° P№PsPiPs S-PμPSP°PSC,C-PsPjPμCḡPsPj.

PḡP»C-PSC-CḡPSP° PμC,,PμPeC,PëPIPSsC-CḡC,CH C- P±PμP·PiPμPeP°
P·P°CḡC,PsCḡCḡPIP°PSPSCḡ P»PμCḡPeP°PSC-PrPëPīC-PSCḡ PI PrPsP·C- 10бḡ“20 PjPi 1 CḡP°P·
PSP° PrPsP±Cḡ P±CḡP»Pë PIPëPICḡPμPSC- PI PiPsPrPIC-P№PSPsPjCḡ CḡP»C-PiPsPjCḡ
PiP»P°C†PμP±Ps-PePsPSC,CḡPsP»CHPsPIP°PSPsPjCḡ PeP»C-PSC-CḡPSPsPjCḡ
PrPsCḡP»C-PrPḡPμPSPSC- (Cḡ CḡPePsPjCḡ 1200 PiP°C†C-C”PSC,C-PI PsC,CḡPëPjCḡPIP°P»Pë
P»PμCḡPeP°PSC-PrPëPīC-PS, 603 PiP°C†C-C”PSC,Pë PsC,CḡPëPjCḡPIP°P»Pë PiP»P°C†PμP±Ps)
C,P° PI P°PeC,PëPIPSs PePsPSC,CḡPsP»CHPsPIP°PSPëC... C- PI
PSPμPePsPSC,CḡPsP»CHPsPIP°PSPëC... PrPsPIPiPsC,CḡPëPIP°P»PëC... PeP»C-PSC-CḡPSPëC...
PrPsCḡP»C-PrPḡPμPSPSCḡC... C-P· P·P°PiP°P»CHPSPsCḡ PeC-P»CHPeC-CḡC,Cḡ 3676
PiP°C†C-C”PSC,C-PI P· P°CḡC,PμCḡC-P°P»CHPSPsCḡ PiC-PiPμCḡC,PμPSP·C-C”Cḡ.

P”Ps P±C-P»CHCḡPsCḡC,C- PrPsCḡP»C-PrPḡPμPSCH P±CḡP»Pë P·P°P»CḡCḡPμPSC-
PiP°C†C-C”PSC,Pë P· PμCḡPμPSC†C-P°P»CHPSPsCḡ PiC-PiPμCḡC,PμPSP·C-C”Cḡ
P»PμPiPePsPiPs P°P±Ps PiPsPjC-CḡPSPsPiPs CḡC,CḡPiPμPSCḡ C,CḡPḡPePsCḡC,C-
(PIPeP»CḡCḡP°CḡCḡPë PiP°C†C-C”PSC,C-PI P»C-C,PSCHPsPiPs PIC-PeCḡ C,P° C...PIPsCḡPëC...
PSP° C†CḡPeCḡPsPIPëP№ PrC-P°P±PμC,,) CḡPeC- PsC,CḡPëPjCḡPIP°P»Pë
P»PμCḡPeP°PSC-PrPëPīC-PS CḡPe PjPsPSPsC,PμCḡP°PiC-Cḡ P°P±Ps Cḡ
PePsPjP±C-PSP°C†C-C— P· C-PSPiC-P±C-C,PsCḡP°PjPë PḡPμPḡ, PrC-CḡCḡPμC,PëPeP°PjPë
P°P±Ps β-P±P»PsPeP°C,PsCḡP°PjPë.

P”PsPrP°C,PePsPIPs PrPs PeP»C-PSC-CḡPSPëC... PrPsCḡP»C-PrPḡPμPSCH,
PiCḡPsPIPμPrPμPSPëC... PrP»Cḡ PiC-PrC,PIPμCḡPrPḡPμPSPSCḡ C,PμCḡP°PiPμPIC,PëCḡPSPëC...
PiPsPeP°P·P°PSCH, PiPsPrP°P»CHCḡPμ PSPμPIPμP»PëPePμ
PSPμPePsPSC,CḡPsP»CHPsPIP°PSPμ, P°P»Pμ CḡP°PSPrPsPjC-P·PsPIP°PSPμ
PrPsCḡP»C-PrPḡPμPSPSCḡ PiCḡPμPiP°CḡP°C,Cḡ P·P° CḡCḡP°CḡC,Cḡ PiP°C†C-C”PSC,C-PI P·
C,CḡPḡPePsCḡ P°CḡC,PμCḡC-P°P»CHPSPsCḡ PiC-PiPμCḡC,PμPSP·C-C”Cḡ (CḡPμCḡPμPrPSC”
B± CḡC,P°PSPrP°CḡC,PSPμ PIC-PrC...PëP»PμPSPSCḡ CḡC-PIPSsCḡ

PrC-P°CfC,PsP»C-C†PSPsPiPs P°CfC,PμCfC-P°P»CHbPSPsPiPs C,PëCfPeCr 114,5 B± 3,7 PjPj CfC, CfC, PiCfPsPrPμPjPsPSCfC,CfCrPIP°P»Ps PSPsCfPjP°P»C-P·P°C†C-Cf P°CfC,PμCfC-P°P»CHbPSPsPiPs C,PëCfPeCr Cr 40 % C-P· 25 PïP°C†C-C"PSC,C-PI, CΠPeC-PiCfPëPNëPjP°P»Pë PiCfPμPïP°CfP°C, Cr PrPsP·C- B B B B B B B B 20 PjPi 1 CfP°P· PSP° PrPsP±Cr, C,P° Cr 56 % C-P· 25 PïP°C†C-C"PSC,C-PI, CΠPeC- PiCfPëPNëPjP°P»Pë P»PμCfPeP°PSC-PrPëPiC-PS Cr PrPsP·C- 10 PjPi 2 CfP°P·Pë PSP° PrPsP±Cr. Pj PïPsPrPIC-PNëPSPsPjCr CfP»C-PiPsPjCr CfP°PSPPrPsPjC-P·PsPIP°PSPsPjCr PïP»P°C†PμP±Ps- PePsPSC,CfPsP»CHbPsPIP°PSPsPjCr PrPsCfP»C-PrP¶PμPSPSC- Cr PïP°C†C-C"PSC,C-PI P· C-P·PsP»CHbPsPIP°PSPsCf CfPëCfC,PsP»C-C†PSPsCf PiC-PiPμCfC,PμPSP·C-C"Cf P»PμCfPeP°PSC-PrPëPiC-PS PμC,,PμPeC,PëPIPSPs P·PSPëP¶CfPIP°PI CfPëCfC,PsP»C-C†PSPëPNë P°CfC,PμCfC-P°P»CHbPSPëPNë C,PëCfPe C-P· CfPμCfPμPrPSCbPsPiPs PïPsC†P°C,PePsPIPsPiPs P·PSP°C†PμPSPSCΠ 172,6 B± 5,6 PjPj CfC, CfC, PrPs 140,2 B± 8,7 PjPj CfC, CfC,.

P"C-C,Pë

PμP»C-PSC-C†PSC- PrPsCfP»C-PrP¶PμPSPSCΠ Cr PrPëC,CΠC†C-PNë PïPsPiCrP»CΠC†C-C— PSPμ PiCfPsPIPsPrPëP»PëCfCΠ.

PαP°CfPjP°PePsPeC-PSPμC,PëPeP°

PbP±CfPsCfP±C†C-CΠ

P>PμCfPeP°PSC-PrPëPiC-PS PïPsPIPSC-CfC,Cf PICfPjPsPeC,CrC"C,CHbCfCΠ PiC-CfP»CΠ PiCfPëPNëPsPjCr PIPSCfC,CfC-C€PSCbPs Cr PrPsP·C- 10b¶"20 PjPi, PjP°PeCfPëPjP°P»CHbPSP° PePsPSC†PμPSC,CfP°C†C-CΠ Cr PïP»P°P·PjC- PeCfPsPIC- (C_{max}) 3,30 PSPi/PjP» B± 2,09 Cf. PI. C,P° 7,66 PSPi/PjP» B± 5,90 Cf. PI. PIC-PrPïPsPIC-PrPSPs CfPμC"CfC,CfCrC"C,CHbCfCΠ PiCfPëP±P»PëP·PSPs C†PμCfPμP· 1,5b¶"3 PiPsPrPëPSPë.

P"PIP° PμPSP°PSC,C-PsPjPμCfPë P»PμCfPeP°PSC-PrPëPiC-PSCr PrPμPjPsPSCfC,CfCrCfC,CHb PïPsPrC-P±PSPëPNë PiCfPsC,,C-P»CHb CfC-PIPSCΠ Cr PïP»P°P·PjC- PeCfPsPIC-: C†P°Cf PrPsCfCΠPiPSPμPSPSCΠ C_{max} C,P°PePëPNë CfP°PjPëPNë, C_{max} C,P° AUC (PïP»PsC%°P° PiC-Pr C,,P°CfPjP°PePsPeC-PSPμC,PëC†PSPsCf PeCfPëPIPsCf B«PePsPSC†PμPSC,CfP°C†C-CΠ- C†P°CfB») PI CfPμCfPμPrPSCbPsPjCr Cr 1,2 CfP°P·P° PIPëC%°C- PrP»CΠ S- PμPSP°PSC,C-PsPjPμCfP°, C- PïPμCfC-PsPr PSP°PiC-PIPIPëPIPμPrPμPSPSCΠ PrPIPsC... PμPSP°PSC,C-PsPjPμCfC-PI, PïPs CfCrC,C-, PsPrPSP°PePsPIPëPNë. P'P·P°C"PjPsPiPμCfPμC,PIPsCfPμPSPSCΠ PμPSP°PSC,C-PsPjPμCfC-PI *in vivo* PSPμ CfPiPsCfC,PμCfC-PiP°P»PsCfCf.

P'PSP°CfP»C-PrPsPe PIPëCfPsPePsPiPs PjPμC,P°P±PsP»C-P·PjCr PiCfPë PiPμCfPIPëPSPSPsPjCr PiCfPsC...PsPrP¶PμPSPSC- C†PμCfPμP· PïPμC†C-PSPeCr P°P±CfPsP»CfC,PSP° P±C-PsPrPsCfC,CrPïPSC-CfC,CHb P»PμCfPeP°PSC-PrPëPiC-PSCr, P·P°CfC,PsCfPsPIP°PSPsPiPs PïP°C†C-C"PSC,PsPj PiC-CfP»CΠ PIP¶PëPIP°PSPSCΠ C—P¶C-, CfC,P°PSPsPIPëC,CHb PiCfPëP±P»PëP·PSPs 10 %, C...PsC†P° PIPsPSP° P·PjPμPSC€CfPIP°P»P°CfCΠ PrPs 1/3 C†CHbPsPiPs P·PSP°C†PμPSPSCΠ, CΠPeC%°Ps PiCfPμPïP°CfP°C, P·P°CfC,PsCfPsPICrPIP°P»Pë P·PrPsCfPsPIC- PrPsP±CfPsPIPsP»CHbC†C- PSP°C,C%°Pμ. PïPeC%°Ps PiCfPμPïP°CfP°C, PiCfPëPNëPjP°C,Pë PSPμ PiC-P·PSC-C€Pμ PSC-P¶ C†PμCfPμP· 2 PiPsPrPëPSPë PiC-CfP»CΠ PIP¶PëPIP°PSPSCΠ PrCrP¶Pμ P¶PëCfPSPsC— C—P¶C-, PNëPsPiPs P±C-PsPrPsCfC,CrPïPSC-CfC,CHb P·P±C-P»CHbC€CfC"C,CHbCfCΠ Cr 4 CfP°P·Pë. PÿPsPjCr P»PμCfPeP°PSC-PrPëPiC-PS CfP»C-Pr PiCfPëPNëPjP°C,Pë PrPs PIP¶PëPIP°PSPSCΠ C—P¶C-.

P PsP·PiPsPrC-P»

P PsP·PiPsPrC-P» C-P· PiP»P°P·PjPë PeCḡPsPIC- Cr C,PeP°PSPëPSPë C,P° PsCḡPiP°PSPë C”
 C€PiPëPrPePëPj C,P° PsP±C€PëCḡPSPëPj. PŸC,CrPiC-PSCH P·PiBḡ™ CḡP·CrPiP°PSPSCḡ
 P»PμCḡPeP°PSC-PrPëPiC-PSCr P· P±C-P»PeP°PjPë CḡPëCḡPsPiP°C,PePë PeCḡPsPIC-
 PiPμCḡPμPiPëC%CrC” 98 %. PhCḡPeC-P»CHPePë CḡC-PIPμPSCḡ P±C-P»PeP° Cr PiP»P°P·PjC-
 PeCḡPsPIC- P·PjPμPSC€PμPSPëPnë Cr PiP°C†C-C”PSC,C-PI C-P· C,CḡP¶PiPëPjPë
 PiPsCḡCrC€PμPSPSCḡPjPë C,,CrPSPeC†C-C— PSPëCḡPsPe C,P° PiPμC†C-PSPePë, PIC-P»CHPSP°
 C,,CḡP°PeC†C-Cḡ PiCḡPμPiP°CḡP°C,Cr PjPsP¶Pμ P·P±C-P»CHC€CrPiP°C,PëCḡCḡ.

P’C-PsC,CḡP°PSCḡC,,PsCḡPjP°C†C-Cḡ

P»PμCḡPeP°PSC-PrPëPiC-PS PμPeCḡC,PμPSCḡPëPiPSPs PjPμC,P°P±PsP»C-P·CrC”C,CHCḡCḡ
 C-P·PsC,,PμCḡPjPμPSC,PsPj CYP3Pḡ4, PSPμP·PjC-PSPμPSPëPnë PiCḡPμPiP°CḡP°C, Cr CḡPμC†C-
 C†Pë PeP°P»C- PSPμ PiPëCḡPiP»CḡC”C,CHCḡCḡ. P’C-PS PiPμCḡPμC,PIPsCḡCḡC”C,CHCḡCḡ
 PiPμCḡPμPiP°P¶PSPs Cr PSPμP°PeC,PëPiPSC- PjPμC,P°P±PsP»C-C,Pë, PiCḡPëP±P»PëP·PSPs 50
 % PiCḡPëPnëPSCḡC,PsC— PrPsP·Pë PiPëPiPsPrPëC,CHCḡCḡ C-P· CḡPμC†PμCḡ.

P·PeCḡPiPμCḡPëPjPμPSC,Pë *in vitro* P· P»CHPrCḡCHPePëPjPë PjC-PeCḡPsCḡPsPjP°PjPë
 PiPμC†C-PSPePë CḡPIC-PrC†P°C,CH, C%Ps P»PμCḡPeP°PSC-PrPëPiC-PS PrPμC%Ps
 PiCḡPëPiPSC-C†CrC” CYP3A4 C,P° CYP2D6 PiCḡPë PePsPSC†PμPSC,CḡP°C†C-CḡC...
 PIC-PrPiPsPIC-PrPSPs Cr 160 C- 40 CḡP°P·C-PI PiPëC%PëC..., PSC-P¶ PnëPsPiPs C_{max} Cr
 PiP»P°P·PjC- PeCḡPsPIC-, CḡPeP° PrPsCḡCḡPiP°C”C,CHCḡCḡ PiC-CḡP»Cḡ PiCḡPëPnëPsPjCr
 PrPsP·Pë 20 PjPi. PḡCḡC-Pj C†CHPsPiPs, PrPsCḡP»C-PrP¶PμPSPSCḡ P»C-PeP°CḡCḡCHPePsC—
 PiP·P°C”PjPsPrC-C— Cr P»CHPrPμPnë PiCḡPsPrPμPjPsPSCḡC,CḡCrPiP°P»Pë, C%Ps
 P»PμCḡPeP°PSC-PrPëPiC-PS Cr PiP»P°P·PjC- PeCḡPsPIC- PSPμ P·PjC-PSCHC” CḡC-PIPμPSCḡ
 PjC-PrP°P·PsP»P°PjCr, C,PëPiPsPiPsPiPs CḡCrP±CḡC,CḡP°C,Cr CYP3A4, P°P±Ps
 PjPμC,PsPiCḡPsP»PsP»Cr, C,PëPiPsPiPsPiPs CḡCrP±CḡC,CḡP°C,Cr CYP2D6; C,P°PePëPj
 C†PëPSPsPj, PiCḡPë P·P°CḡC,PsCḡCrPiP°PSPSC- P»PμCḡPeP°PSC-PrPëPiC-PSCr Cr
 C,PμCḡP°PiPμPIC,PëC†PSPëC... PrPsP·P°C... PSPμ PsC†C-PeCrC”C,CHCḡCḡ
 P±C-PsC,CḡP°PSCḡC,,PsCḡPjP°C†C-C— PiCḡPμPiP°CḡP°C,C-PI, C%Ps
 PjPμC,P°P±PsP»C-P·CrCḡC,CHCḡCḡ CYP3A4 P°P±Ps CYP2D6.

P’PëPiPμPrPμPSPSCḡ

P·P»C-PjC-PSP°C†C-Cḡ PiCḡPsC...PsPrPëC,CH PI PsCḡPSPsPiPSPsPjCr C€P»CḡC...PsPj
 P±C-PsC,CḡP°PSCḡC,,PsCḡPjP°C†C-C—. PŸPμCḡPμPrPSC-Pnë C,PμCḡPjC-PSP°P»CHPSPëPnë
 PiPμCḡC-PsPr PSP°PiC-PIPiPëPiPμPrPμPSPSCḡ CḡC,P°PSPsPiPëC,CH 8Bḡ“10 PiPsPrPëPS, P°
 C,PμCḡP°PiPμPIC,PëC†PSP° PrC-Cḡ C,CḡPëPiP°C” 24 PiPsPrPëPSPë PiPSP°CḡP»C-PrPsPe
 PiPëCḡPsPePsPiPs CḡC,CrPiPμPSCḡ P·PiBḡ™ CḡP·CrPiP°PSPSCḡ P»PμCḡPeP°PSC-PrPëPiC-PSCr
 P· P»C-PiC-PrP°PjPë PeP»C-C,PëPSPSPëC... PjPμPjP±CḡP°PS. PμCḡPë PiPsPIC,PsCḡPSPsPjCr
 P·P°CḡC,PsCḡCrPiP°PSPSC- PeCrPjCrP»CḡC†C-Cḡ PSPμ CḡPiPsCḡC,PμCḡC-PiP°P»P°CḡCH.

P»C-PSC-PnëPSC-CḡC,CH / PSPμP»C-PSC-PnëPSC-CḡC,CH

PμCḡPë PiPμCḡPsCḡP°P»CHPSPsPjCr P·P°CḡC,PsCḡCrPiP°PSPSC-
 P»PμCḡPeP°PSC-PrPëPiC-PSCr PnëPsPiPs PePsPSC†PμPSC,CḡP°C†C-Cḡ Cr PiP»P°P·PjC-
 PeCḡPsPIC- PSPμ C” PiCḡCḡPjPs PiCḡPsPiPsCḡC†C-PnëPSPsCḡ PrPs PiCḡPëPnëPSCḡC,PsC—
 PrPsP·Pë (PSPμP»C-PSC-PnëPSP° PeC-PSPμC,PëPeP°). PμC-CḡP»Cḡ PiCḡPëPnëPsPjCr 10 PjPi, 20
 PjPi C- 40 PjPi C_{max} Cr PiP»P°P·PjC- PeCḡPsPIC-, CḡPeC- CḡPiPsCḡC,PμCḡC-PiP°P»PëCḡCḡ,
 PjP°P»Pë CḡPiC-PIPIC-PrPSPsC€PμPSPSCḡ 1:3:8, P° PiP»PsC%C- PiC-Pr PeCḡPëPiPëPjPë
 P·P°P»PμP¶PSPsCḡC,C- PePsPSC†PμPSC,CḡP°C†C-C— Cr PiP»P°P·PjC- PeCḡPsPIC- PIC-Pr
 C†P°CḡCr PjP°P»Pë CḡPiC-PIPIC-PrPSPsC€PμPSPSCḡ 1:4:18, C%Ps PiPeP°P·CrC” PSP°
 PiPsCḡC,CrPiPsPiPμ PSP°CḡPëC†PμPSPSCḡ PjPμC,P°P±PsP»C-P·PjCr PiCḡPë PiPμCḡC€PsPjCr

РiСҫPсC...PsPrP¶PµPSPSC-. PŷP°PePëPj C‡PëPSPsPj, P±C-PsPrPsCГC,CrPіPSC-CГC,CH
P»PµCҫPeP°PSC-PrPëPіC-PSCr P·P±C-P»CHCЄCрC”C,CHCГCЦ P· PіC-PrPIPëC%PµPSPSCЦPj
PrPsP·Pë.

P”PsPrP°C,PePsPIP° C-PSC,,PsCҫPjP°C‡C-CЦ C%PsPrPs PsPeCҫPµPjPëC... PiCҫCrPі
PiP°C‡C-C”PSC,C-PI

P’CрP»Ps PiPsPeP°P·P°PSPs, C%Ps C,,P°CҫPjP°PePsPeC-PSPµC,PëPeP°
P»PµCҫPeP°PSC-PrPëPіC-PSCr Cr PiP°C‡C-C”PSC,C-PI P»C-C,PSCHPsPiPs PIC-PeCr C,P° Cr
PіP°C‡C-C”PSC,C-PI P· PrPëCГC,,CrPSPeC‡C-C”Cҫ PSPëCҫPsPe P°P±Ps PiPµC‡C-PSPePë
CГP»P°P±PePsPiPs P°P±Ps CГPµCҫPµPrPSCHPsPiPs CГC,CrPiPµPSCЦ C,CЦP¶PePsCГC,C-
CГC...PsP¶P° PSP° C,P°PeCr, C%Ps CГPiPsCГC,PµCҫC-PiP°C”C,CHCГCЦ Cr
P·P°PiP°P»CHPSC-PM PiCҫCrPіC- PiP°C‡C-C”PSC,C-PI. Pj C...PIPsCҫPëC... C-P· C,CЦP¶PePëPj
CГC,CrPiPµPSPµPj PrPëCГC,,CrPSPeC‡C-C— PSPëCҫPsPe P°P±Ps Cr
PrC-P°P»C-P·PsP·P°P»PµP¶PSPëC... C...PIPsCҫPëC... PePsPSC‡PµPSC,CҫP°C‡C-CЦ
P»C-PeP°CҫCГCHPePsPiPs P·P°CГPsP±Cr P±CrP»P° P±C-P»CHCЄ PIPëCГPsPePsCҫ
(PiCҫPëP±P»PëP·PSPs 70 %). Pj C...PIPsCҫPëC... C-P· CГPµCҫPµPrPSC-Pj P°P±Ps C,CЦP¶PePëPj
CГC,CrPiPµPSPµPj PiPsCҫCrCєPµPSPSCЦ C,,CrPSPeC‡C-C— PiPµC‡C-PSPePë CГPëCГC,PµPjPSP°
P±C-PsPrPsCГC,CrPіPSC-CГC,CH P»PµCҫPeP°PSC-PrPëPіC-PSCr, C-PjPsPIC-CҫPSPs,
P·P±C-P»CHCЄCрC”C,CHCГCЦ, PsCГPeC-P»CHPePë PIC-PS
PjPµC,P°P±PsP»C-P·CрC”C,CHCГCЦ PiPsP»PsPIPSPëPj C‡PëPSPsPj Cr PiPµC‡C-PSC‡C-.

РЉP»C-PSC-C‡PSC- C...P°CҫP°PeC,PµCҫPëCГC,PëPePë

PµPsPeP°P·P°PSPSCЦ

P·CГPµPSC‡C-P°P»CHPSP° PiC-PiPµCҫC,PµPSP·C-CЦ P»PµPiPePsPiPs P°P±Ps
PiPsPjC-CҫPSPsPiPs CГC,CrPiPµPSCЦ C,CЦP¶PePsCГC,C-.

PµCҫPsC,PëPiPsPeP°P·P°PSPSCЦ

- PµC-PrPIPëC%PµPSP° C‡CrC,P»PëPIC-CГC,CH PrPs P»PµCҫPeP°PSC-PrPëPіC-PSCr P°P±Ps
PrPs P±CrPrCH-CЦPePsPiPs PePsPjPiPsPSPµPSC,P° P»C-PeP°CҫCГCHPePsPiPs P·P°CГPsP±Cr;
- PsP±CГC,CҫCrPeC‡C-CЦ PIPëPIC-PrPSPsPiPs PIC-PrPrC-P»Cr P»C-PIPsPiPs
CєP»CrPSPsC‡PeP°;
- PSPµP»C-PePsPIP°PSP° P·P°CГC,C-PM PSP° CГPµCҫC‡PµPIP°
PSPµPrPsCГC,P°C,PSC-CГC,CH;
- PSPµCГC,P°P±C-P»CHPSP° CГC,PµPSPsPeP°CҫPrC-CЦ C‡Pë PSPµC%PsPrP°PIPSC-PM
(PiCҫPsC,CЦPiPsPj 1 PjC-CГCЦC‡CЦ) C-PSC,,P°CҫPeC, PjC-PsPeP°CҫPrP°;
- C,CЦP¶PeP° PiPµC‡C-PSPePsPIP° PSPµPrPsCГC,P°C,PSC-CГC,CH;
- C,CЦP¶PeP° PSPëCҫPePsPIP° PSPµPrPsCГC,P°C,PSC-CГC,CH (PeP»C-CҫPµPSCГ
PeCҫPµP°C,PëPSC-PSCr <30 PjP»/C...PI), PIPeP»CҫC‡P°CҫC‡Pë PiP°C‡C-C”PSC,C-PI PSP°
PiPµPjPsPrC-P°P»C-P·C-;

- PsPrPSPsC $\ddagger$ P $^{\circ}$ Cl $\ddagger$ PSP μ P $\cdot$ P $^{\circ}$ Cl $\ddagger$ C,PsCl $\ddagger$ CrPIP $^{\circ}$ PSPSC $\ddagger$ P $\cdot$ P $\ddot{\text{P}}$ sC,CrP $\ddagger$ PSP $\ddot{\text{P}}$ PjP $\ddot{\text{e}}$
C-PSPiC-P $\pm$ C-C,PsC $\ddot{\text{H}}$ P $^{\circ}$ PjP $\ddot{\text{e}}$ CYP3P $\ddot{\text{H}}$ 4, C $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PSPsPj, PiC $\ddot{\text{H}}$ P μ PN $\ddot{\text{e}}$ PiC $\ddot{\text{H}}$ CrC,PsPj
C $\ddagger$ P $\ddot{\text{e}}$ PiC $\ddot{\text{H}}$ P μ PN $\ddot{\text{e}}$ PiC $\ddot{\text{H}}$ CrC,PsPIP $\ddot{\text{e}}$ Pj Cl $\ddagger$ PsPePsPj.

***P $\cdot$ P $^{\circ}$ C $\ddot{\text{H}}$ PjPsPrC-C $\ddagger$ P $\cdot$ C-PSC $\ddot{\text{e}}$ P $\ddot{\text{e}}$ PjP $\ddot{\text{e}}$ P $\gg$ C-PeP $^{\circ}$ C $\ddot{\text{H}}$ Cl $\ddagger$ CHPeP $\ddot{\text{e}}$ PjP $\ddot{\text{e}}$ P $\cdot$ P $^{\circ}$ Cl $\ddagger$ PsP $\pm$ P $^{\circ}$ PjP $\ddot{\text{e}}$ C,P $^{\circ}$
C-PSC $\ddot{\text{e}}$ C- PIP $\ddot{\text{e}}$ PrP $\ddot{\text{e}}$ PIP $\cdot$ P $^{\circ}$ C $\ddot{\text{H}}$ PjPsPrC-PN $\ddot{\text{e}}$***

P μ C $\ddot{\text{H}}$ PsC,P $\ddot{\text{e}}$ PiPsPeP $^{\circ}$ P $\cdot$ P $^{\circ}$ PSPs PsPrPSPsC $\ddagger$ P $^{\circ}$ Cl $\ddagger$ PSP μ P $\cdot$ P $^{\circ}$ Cl $\ddagger$ C,PsCl $\ddagger$ C $\ddot{\text{e}}$ PIP $^{\circ}$ PSPSC $\ddagger$

P $\ddagger$ PSPiC-P $\pm$ C-C,PsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ CYP3A4

P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PS PjP μ C,P $^{\circ}$ P $\pm$ PsP $\gg$ C-P $\cdot$ CrC $\ddot{\text{H}}$ C,CHC $\ddagger$ Cl $\ddagger$ P $\ddot{\text{e}}$ C-Pr PrC-C $\ddot{\text{H}}$
C $\ddot{\text{H}}$,P μ C $\ddot{\text{H}}$ PjP μ PSC,Cr CYP3A4, C,PsPjCr C-PSPiC-P $\pm$ C-C,PsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ C,P $^{\circ}$ C-PSPCr $\ddagger$ PeC,PsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$
C $\ddagger$ CHPsPiPs C $\ddot{\text{H}}$,P μ C $\ddot{\text{H}}$ PjP μ PSC,Cr, Cl $\ddagger$ PeC- P $\ddot{\text{e}}$ C $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PN $\ddot{\text{e}}$ PjP $^{\circ}$ CHC,CH PsPrPSPsC $\ddagger$ P $^{\circ}$ Cl $\ddagger$ PSPs P $\cdot$
P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSPsPj, PjPsP $\ddagger$ CrC,CH PIP $\ddot{\text{e}}$ P $\gg$ P $\ddot{\text{e}}$ PIP $^{\circ}$ C,P $\ddot{\text{e}}$ PSP $^{\circ}$ PjP μ C,P $^{\circ}$ P $\pm$ PsP $\gg$ C-P $\cdot$ Pj
C,P $^{\circ}$ PIP $\ddot{\text{e}}$ PIP μ PrP μ PSPSC $\ddagger$ P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$. P $\ddot{\text{H}}$ PsCl $\ddagger$ P $\gg$ C-PrP $\ddagger$ P μ PSPSC $\ddagger$
PIP $\cdot$ P $^{\circ}$ C $\ddot{\text{H}}$ PjPsPrC-C— P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$ P $\cdot$ P $\ddot{\text{P}}$ sC,CrP $\ddagger$ PSP $\ddot{\text{P}}$ Pj
C-PSPiC-P $\pm$ C-C,PsC $\ddot{\text{H}}$ PsPj CYP3A4 PeP μ C,PsPePsPSP $^{\circ}$ P $\cdot$ PsP $\gg$ PsPj
PiC $\ddot{\text{H}}$ PsPrP μ PjPsPSC $\ddagger$ C,C $\ddot{\text{H}}$ CrPIP $^{\circ}$ P $\gg$ P $\ddot{\text{e}}$ P $\cdot$ PSP $^{\circ}$ C $\ddagger$ PSP μ PiC-PrPIP $\ddot{\text{e}}$ C $\%_{\text{P}}$ P μ PSPSC $\ddagger$ C $\ddot{\text{H}}$ C-PIPSC $\ddagger$
P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$ Cr PiP $\gg$ P $^{\circ}$ P $\cdot$ PjC- PeC $\ddot{\text{H}}$ PsPIC- (15-PeC $\ddot{\text{H}}$ P $^{\circ}$ C,PSP μ
PiC-PrPIP $\ddot{\text{e}}$ C $\%_{\text{P}}$ P μ PSPSC $\ddagger$ PiPsPeP $^{\circ}$ P $\cdot$ PSP $\ddot{\text{e}}$ PeP $^{\circ}$ AUC C,P $^{\circ}$ 8-PeC $\ddot{\text{H}}$ P $^{\circ}$ C,PSP μ
PiC-PrPIP $\ddot{\text{e}}$ C $\%_{\text{P}}$ P μ PSPSC $\ddagger$ C max P μ CrC,PsPjP μ C $\ddot{\text{H}}$ P $^{\circ}$ S-P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$).

P $\ddot{\text{Y}}$ P $\gg$ C-Pr CrPSP $\ddot{\text{e}}$ PeP $^{\circ}$ C,P $\ddot{\text{e}}$ PsPrPSPsC $\ddagger$ P $^{\circ}$ Cl $\ddagger$ PSPsPiPs P $\cdot$ P $^{\circ}$ Cl $\ddagger$ C,PsCl $\ddagger$ CrPIP $^{\circ}$ PSPSC $\ddagger$
P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$ P $\cdot$ C-PSPiC-P $\pm$ C-C,PsC $\ddot{\text{H}}$ P $^{\circ}$ PjP $\ddot{\text{e}}$ CYP3A4 (P $\cdot$
PeP μ C,PsPePsPSP $^{\circ}$ P $\cdot$ PsP $\gg$ PsPj, C-C,C $\ddot{\text{H}}$ P $^{\circ}$ PePsPSP $^{\circ}$ P $\cdot$ PsP $\gg$ PsPj, C $\ddot{\text{H}}$ P $\ddot{\text{e}}$ C,PsPSP $^{\circ}$ PIC-C $\ddot{\text{H}}$ PsPj,
P μ C $\ddot{\text{H}}$ P $\ddot{\text{e}}$ C,C $\ddot{\text{H}}$ PsPjC-C $\ddagger$ P $\ddot{\text{e}}$ PSPsPj, C,C $\ddot{\text{H}}$ PsP $\gg$ P μ P $^{\circ}$ PSPPrPsPjC-C $\ddagger$ P $\ddot{\text{e}}$ PSPsPj,
PeP $\gg$ P $^{\circ}$ C $\ddot{\text{H}}$ P $\ddot{\text{e}}$ C,C $\ddot{\text{H}}$ PsPjC-C $\ddagger$ P $\ddot{\text{e}}$ PSPsPj).

P $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PS

P μ C $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PsPrPSPsC $\ddagger$ P $^{\circ}$ Cl $\ddagger$ PSPsPjCr P $\cdot$ P $^{\circ}$ Cl $\ddagger$ C,PsCl $\ddagger$ CrPIP $^{\circ}$ PSPSC- P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$
C- C $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PSC $\ddagger$ PiC-PrPIP $\ddot{\text{e}}$ C $\%_{\text{CrC}}$ C,CHC $\ddagger$ Cl $\ddagger$ C $\ddot{\text{H}}$ C-PIP μ PSCH PsP $\pm$ PsC...
C $\ddot{\text{H}}$ P μ C $\ddagger$ PsPIP $\ddot{\text{e}}$ PS Cr PiP $\gg$ P $^{\circ}$ P $\cdot$ PjC- PeC $\ddot{\text{H}}$ PsPIC-. P $\ddot{\text{H}}$ PsCl $\ddagger$ P $\gg$ C-PrP $\ddagger$ P μ PSPSC $\ddagger$ P $\cdot$ P $^{\circ}$ CrC $\ddagger$ P $^{\circ}$ Cl $\ddagger$ C,CH
PjPsP $\gg$ PsPrP $\ddot{\text{e}}$ C... P $\cdot$ PrPsC $\ddot{\text{H}}$ PsPIP $\ddot{\text{e}}$ C... PrPsP $\pm$ C $\ddot{\text{H}}$ PsPIP $\ddot{\text{e}}$ P $\gg$ CHC $\ddagger$ C-PI PiPsPeP $^{\circ}$ P $\cdot$ P $\gg$ Ps, C $\%_{\text{Ps}}$
P $\cdot$ P $^{\circ}$ Cl $\ddagger$ C,PsCl $\ddagger$ CrPIP $^{\circ}$ PSPSC $\ddagger$ C $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PSC $\ddagger$ C $\ddagger$ P μ C $\ddot{\text{H}}$ P μ P $\cdot$ 3 PiPsPrP $\ddot{\text{e}}$ PSP $\ddot{\text{e}}$
PiC-Cl $\ddagger$ P $\gg$ C $\ddagger$ PiC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PN $\ddot{\text{e}}$ PsPjCr P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$ PSP μ P $\cdot$ PjC-PSCHPIP $^{\circ}$ P $\gg$ Ps
C $\ddot{\text{H}}$ C-PIP μ PSCH P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$ Cr PiP $\gg$ P $^{\circ}$ P $\cdot$ PjC- PeC $\ddot{\text{H}}$ PsPIC-, PIPsPrPSPsC $\ddagger$ P $^{\circ}$ Cl $\ddagger$
PiPsPeP $^{\circ}$ P $\cdot$ PSP $\ddot{\text{e}}$ Pe AUC C $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PSC $\ddagger$ P $\cdot$ P $\pm$ C-P $\gg$ CHC $\ddot{\text{e}}$ CrPIP $^{\circ}$ PIC $\ddagger$ Cl $\ddagger$ PSP $^{\circ}$ 27 %.
PhPrPSP $^{\circ}$ Pe PsPrPSPsC $\ddagger$ P $^{\circ}$ Cl $\ddagger$ PSP μ P $\cdot$ P $^{\circ}$ Cl $\ddagger$ C,PsCl $\ddagger$ CrPIP $^{\circ}$ PSPSC $\ddagger$ P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$
C- C $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PSC $\ddagger$ PiC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ P $\cdot$ PIPsPrP $\ddot{\text{e}}$ C,CH PrPs 3-PeC $\ddot{\text{H}}$ P $^{\circ}$ C,PSPsPiPs
P $\cdot$ P $\pm$ C-P $\gg$ CHC $\ddot{\text{e}}$ P μ PSPSC $\ddagger$ C $\ddot{\text{H}}$ C-PIPSC $\ddagger$ P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PSC $\ddagger$ Cr PiP $\gg$ P $^{\circ}$ P $\cdot$ PjC-
PeC $\ddot{\text{H}}$ PsPIC- C,P $^{\circ}$ P $\cdot$ P $\pm$ C-P $\gg$ CHC $\ddot{\text{e}}$ P μ PSPSC $\ddagger$ PiPsPeP $^{\circ}$ P $\cdot$ PSP $\ddot{\text{e}}$ PeP $^{\circ}$ AUC
C $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PSC $\ddagger$ PSP $^{\circ}$ 21 %.

P $\ddagger$ P $\ddot{\text{e}}$ PeP $\gg$ PsCl $\ddagger$ PiPsC $\ddot{\text{H}}$ P $\ddot{\text{e}}$ PS C,P $^{\circ}$ P $\gg$ P μ C $\ddot{\text{H}}$ PeP $^{\circ}$ PSC-PrP $\ddot{\text{e}}$ PiC-PS PSP μ Cl $\ddagger$ P $\gg$ C-Pr
P $\cdot$ P $^{\circ}$ Cl $\ddagger$ C,PsCl $\ddagger$ PsPIC $\ddagger$ PIP $^{\circ}$ C,P $\ddot{\text{e}}$ C $\ddot{\text{H}}$ P $^{\circ}$ P $\cdot$ PsPj.

P $\ddot{\text{H}}$ C $\ddot{\text{H}}$ P μ PN $\ddot{\text{e}}$ PiC $\ddot{\text{H}}$ CrC, P $^{\circ}$ P $\pm$ Ps PiC $\ddot{\text{H}}$ P μ PN $\ddot{\text{e}}$ PiC $\ddot{\text{H}}$ CrC,PsPIP $\ddot{\text{e}}$ PN $\ddot{\text{e}}$ Cl $\ddagger$ C-Pe

$P\ddot{I}P\epsilon$ C- $PrP \gg C\dot{I} C-PSC\epsilon P\ddot{e}C \dots PrP\ddot{e}P\dot{I}C-PrC\dot{H}PsP\dot{I}C-C\dot{H}P\ddot{e}PrP\ddot{e}PSC-PI$, $PjP\mu C, P^{\circ}P \pm PsP \gg C-P \cdot Pj$
 $P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PSC\acute{r}$ $C\acute{r}P\dot{I}PsPIC-P \gg CH\dot{B}PSC\dot{H}C''C, CH\dot{B}C\dot{I}C\dot{I} P\dot{I}C-Pr PIP\dot{I}P \gg P\ddot{e}PIP\dot{I}PsPj$
 $C\dot{I}PsPeC\acute{r} P\dot{I}C\dot{H}P\mu PN\epsilon P\dot{I}C, C\dot{H}C\acute{r}C, P^{\circ} P \cdot P\dot{I}PsPrP^{\circ}P \gg CH\dot{B}C\epsilon P\ddot{e}Pj P\dot{I}C-PrPIP\ddot{e}C\%P\mu P\dot{I}PSC\dot{I}Pj$
 $C\dot{I}P\ddot{e}C\dot{I}C, P\mu PjPSP\dot{S}C- PrPsC\dot{I}C, C\acute{r}P\dot{I}PSP\dot{S}C\dot{I}C, C- P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PSC\acute{r} C, P^{\circ}$
 $P\dot{I}C-PrC\dot{I}P\ddot{e}P \gg P\mu P\dot{I}PSC\dot{I}Pj P\dot{I}C-P\dot{I}PsC, P\mu P\dot{I}PSP \cdot P\ddot{e}PIP\dot{I}PSP\dot{S}C- PrC-C- . P\acute{K}P\mu C\dot{I}P \gg C-Pr$
 $P\dot{I}C\dot{H}P\ddot{e}PN\epsilon PjP^{\circ}C, P\ddot{e} PsPrPSP\dot{S}C\ddagger P^{\circ}C\dot{I}PSP\dot{S} P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PS C, P^{\circ}$
 $P\dot{I}C\dot{H}P\mu PN\epsilon P\dot{I}C, C\dot{H}C\acute{r}C, P^{\circ}P \pm Ps P\dot{I}C\dot{H}P\mu PN\epsilon P\dot{I}C, C\dot{H}C\acute{r}C, PsPIP\ddot{e}PN\epsilon C\dot{I}C-Pe.$

$P\acute{K}P\mu C\dot{H}P\mu PePsPjP\mu P\dot{I}PSP\dot{S}PIP^{\circ}PSP\dot{S} PsPrPSP\dot{S}C\ddagger P^{\circ}C\dot{I}PSP\mu P \cdot P^{\circ}C\dot{I}C, PsC\dot{I}C\acute{z}PIP^{\circ}PSPSC\dot{I}I$

$P\ddagger PSP\dot{r}C\acute{z}PeC, PsC\dot{H}P\ddot{e} CYP3A4$

$P\acute{K}P\mu PsP \pm C \dots C-PrPSP\dot{S} P \cdot PsP \pm P\mu C\dot{H}P\mu P\dot{I}PSC-C\dot{I}C, C\dot{H} P \cdot P^{\circ}C\dot{I}C, PsC\dot{I}PsPIC\acute{r}PIP^{\circ}C, P\ddot{e}$
 $P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PS PsPrPSP\dot{S}C\ddagger P^{\circ}C\dot{I}PSP\dot{S} P \cdot C-PSPrC\acute{r}PeC, PsC\dot{H}P^{\circ}PjP\ddot{e} CYP3A4,$
 $C, P^{\circ}PeP\ddot{e}PjP\ddot{e} C\dot{I}Pe P\dot{I}C\dot{H}PsC, P\ddot{e}C\dot{I}C\acute{r}PrPsPjPSC- P \cdot P^{\circ}C\dot{I}PsP \pm P\ddot{e} (C, P\mu PSC-C, PsC-PS,$
 $C, P\mu P\dot{I}PSP\dot{S}P \pm P^{\circ}C\dot{H}P \pm C-C, P^{\circ}P \gg, PeP^{\circ}C\dot{H}P \pm P^{\circ}PjP^{\circ}P \cdot P\mu P\dot{I}C-PS) C, P^{\circ} C\dot{H}P\ddot{e}C, P^{\circ}PjP\dot{I}C-C\ddagger P\ddot{e}PSP\dot{S}Pj$
 $C\ddagger P\mu C\dot{H}P\mu P \cdot PjPsP\dot{I}P \gg P\ddot{e}PIP\mu P \cdot PSP\ddot{e}P\dot{I}P\mu P\dot{I}PSPSC\dot{I} P^{\circ}PSC, P\ddot{e}P\dot{I}C-P\dot{I}P\mu C\dot{H}C, P\mu P\dot{I}PSP \cdot P\ddot{e}PIP\dot{I}PSP\dot{S}C-$
 $PrC-C- P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PSC\acute{r}. Pj C\ddagger P\ddot{e}C \dots PIP\ddot{e}P\dot{I}P^{\circ}PrPeP^{\circ}C \dots$
 $C\dot{H}P\mu PePsPjP\mu P\dot{I}PSP\dot{r}PsPIP^{\circ}PSP\dot{S} C\ddagger P^{\circ}C\dot{I}C, C-C\epsilon P\ddot{e}PN\epsilon PePsPSC, C\dot{H}PsP \gg CH C\dot{H}C-PIPSC\dot{I}I$
 $P^{\circ}C\dot{H}C, P\mu C\dot{H}C-P^{\circ}P \gg CH\dot{B}PSP\dot{S}PiPs C, P\ddot{e}C\dot{I}PeC\acute{r}.$

$P\dot{H}P \gg PePsPiPsP \gg CH\dot{B}$

$P\ddot{Y}P \gg C-Pr C\acute{r}PSP\ddot{e}PeP^{\circ}C, P\ddot{e} PIP\dot{I}P\ddot{e}PIP^{\circ}PSPSC\dot{I}I P^{\circ}P \gg PePsPiPsP \gg CH C\ddagger P\mu C\dot{H}P\mu P \cdot PjPsP\dot{I}P \gg P\ddot{e}PIP\mu$
 $P\dot{I}PsC, P\mu PSC\ddagger C-C\dot{H}PIP^{\circ}PSPSC\dot{I}I PIP^{\circ}P \cdot PsPrP\ddot{e}P \gg P^{\circ}C, P^{\circ}C\ddagger C-PN\epsilon PSP\dot{S}PiPs P\mu C, P\mu PeC, C\acute{r}$
 $P^{\circ}PSC, P\ddot{e}P\dot{I}C-P\dot{I}P\mu C\dot{H}C, P\mu P\dot{I}PSP \cdot P\ddot{e}PIP\dot{I}PSP\ddot{e}C \dots P \gg C-PeP^{\circ}C\dot{H}C\dot{I}CH\dot{B}PeP\ddot{e}C \dots P \cdot P^{\circ}C\dot{I}PsP \pm C-PI.$

$P'P \cdot P^{\circ}C''PjPsPrC-C-, C\dot{I}PeC- P\dot{I}PsC, C\dot{H}P\mu P \pm C\acute{z}CHC, CH\dot{B} PePsC\dot{H}P\mu PeC\ddagger C-C- PrPsP \cdot P\ddot{e}$

$P\ddot{Y}C\acute{z}P \pm C\dot{I}C, C\dot{H}P^{\circ}C, P\ddot{e} CYP3A4$

$P\ddot{Y}P \gg C-Pr P \pm C\acute{r}C, P\ddot{e} PsP \pm P\mu C\dot{H}P\mu P\dot{I}PSP\ddot{e}Pj P\dot{I}C\dot{H}P\ddot{e} PsPrPSP\dot{S}C\ddagger P^{\circ}C\dot{I}PSP\dot{S}PjC\acute{r}$
 $P \cdot P^{\circ}C\dot{I}C, PsC\dot{I}C\acute{r}PIP^{\circ}PSPSC- P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PSC\acute{r} P \cdot C-PSC\epsilon P\ddot{e}PjP\ddot{e}$
 $C\dot{I}C\acute{r}P \pm C\dot{I}C, C\dot{H}P^{\circ}C, P^{\circ}PjP\ddot{e} CYP3A4, C, P^{\circ}PeP\ddot{e}PjP\ddot{e} C\dot{I}Pe C, P\mu C\dot{H}C, P\mu P\dot{I}PSP^{\circ}PrP\ddot{e}PS,$
 $P^{\circ}C\dot{I}C, P\mu PjC-P \cdot PsP \gg, P^{\circ}PSC, P\ddot{e}P^{\circ}C\dot{H}P\ddot{e}C, PjC-C\ddagger PSP\ddot{e}PjP\ddot{e} P\dot{I}C\dot{H}P\mu P\dot{I}P^{\circ}C\dot{H}P^{\circ}C, P^{\circ}PjP\ddot{e} P\ddagger P\ddagger P\ddagger$
 $PeP \gg P^{\circ}C\dot{I}C\acute{r}, C, P^{\circ}PeP\ddot{e}PjP\ddot{e} C\dot{I}Pe P^{\circ}PjC-PsPrP^{\circ}C\dot{H}PsPS, PePIC-PSC-PrP\ddot{e}PS, C\dot{I}PsC, P^{\circ}P \gg PsP \gg.$

$P\dot{H}C-PrP^{\circ}P \cdot PsP \gg P^{\circ}Pj$

$P\mu C\dot{H}P\ddot{e} PsPrPSP\dot{S}C\ddagger P^{\circ}C\dot{I}PSP\dot{S}PjC\acute{r} P \cdot P^{\circ}C\dot{I}C, PsC\dot{I}C\acute{r}PIP^{\circ}PSPSC- 20 PjPi$
 $P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PSC\acute{r} C, P^{\circ} PjC-PrP^{\circ}P \cdot PsP \gg P^{\circ}PjC\acute{r} C\acute{r} PrPsP \pm C\dot{H}PsPIP\dot{I}PsP \gg CH\dot{B}C\ddagger C-PI$
 $P \gg C-C, PSCH\dot{B}PsPiPs PIC-PeC\acute{r} P^{\circ}P \pm C\dot{I}PsC\dot{H}P \pm C\ddagger C-C\dot{I}I P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PSC\acute{r}$
 $P\dot{I}C-PrPIP\ddot{e}C\%C\acute{r}PIP^{\circ}P \gg P^{\circ}C\dot{I}CH\dot{B} (P\dot{I}C\dot{H}P\ddot{e}P \pm P \gg P\ddot{e}P \cdot PSP\dot{S} PSP^{\circ} 40 \%), P^{\circ} C\epsilon PIP\ddot{e}PrPeC-C\dot{I}C, CH\dot{B}$
 $P^{\circ}P \pm C\dot{I}PsC\dot{H}P \pm C\ddagger C-C- P \cdot PSP\ddot{e}P\dot{I}C\acute{r}PIP^{\circ}P \gg P^{\circ}C\dot{I}CH\dot{B} (t_{\max} P\dot{I}PsPrPsPIP\dot{I}C\acute{r}PIP^{\circ}P \gg P^{\circ}C\dot{I}CH\dot{B} P \cdot 1,75$
 $PrPs 3 P\dot{I}PsPrP\ddot{e}PS). P\dot{L}PsPSC\ddagger P\mu PSC, C\dot{H}P^{\circ}C\ddagger C-C\dot{I}I PjC-PrP^{\circ}P \cdot PsP \gg P^{\circ}PjC\acute{r} PSP\mu$
 $P \cdot PjC-PSCH\dot{B}PIP^{\circ}P \gg P^{\circ}C\dot{I}CH\dot{B}.$

$P\dot{H}P\mu C, PsP\dot{I}C\dot{H}PsP \gg PsP \gg$

$P\dot{H}PrPSP\dot{S}C\ddagger P^{\circ}C\dot{I}PSP\mu P \cdot P^{\circ}C\dot{I}C, PsC\dot{I}C\acute{r}PIP^{\circ}PSPSC\dot{I}I P \gg P\mu C\dot{H}PeP^{\circ}PSC-PrP\ddot{e}P\dot{I}C-PSC\acute{r} P \cdot$
 $PjP\mu C, PsP\dot{I}C\dot{H}PsP \gg PsP \gg PsPj \text{ в } \dot{H} \beta-P \pm P \gg PsPeP^{\circ}C, PsC\dot{H}PsPj, C\dot{I}PeP\ddot{e}PN\epsilon PIP\ddot{e}PIP\dot{I}PsPrP\ddot{e}C, CH\dot{B}C\dot{I}C\dot{I}$
 $P\dot{I}P\mu C\dot{H}P\mu PIP^{\circ}P\dot{I}PSP\dot{S} C\ddagger P\mu C\dot{H}P\mu P \cdot P\dot{I}P\mu C\ddagger C-PSPeC\acute{r}, \text{ в } \dot{H} \text{ " } PSP\mu P \cdot PjC-PSCH\dot{B}C''$
 $P \pm C-PsPrPsC\dot{I}C, C\acute{r}P\dot{I}PSC-C\dot{I}C, CH\dot{B} PjP\mu C, PsP\dot{I}C\dot{H}PsP \gg PsP \gg C\acute{r}, P^{\circ}P \gg P\mu P\dot{I}C\dot{H}P\ddot{e}P \cdot PIP\dot{I}PsPrP\ddot{e}C, CH\dot{B}$

C†PμPNε P¶Pμ PīPsPeP°P·PSPëPe PrP»C¶ PNεPsPiPs P°PeC,PëPIPSsPiPs PjPμC,P°P±PsP»C-C,C† β-
PiC-PrC¶PsPeC†PëPePëC†P»PsC,Pë B¶“ PSP° 28 %. P¶P°P»PsPNεPjPsPIC-C¶PSPs, C%oPs
C,P°PeC- P·PjC-PSPë PjP°C¶C,CH PeP»C-PSC-C†PSPμ P·PSP°C†PμPSPSC¶. P´Pμ
PsC†C-PeC†C”C,CHC†C¶ PIP·P°C”PjPsPrC-C— PjC-P¶ C†PëPjPë PīC¶PμPīP°C¶P°C,P°PjPë,
C¶PeC%oPs P»PμC¶PeP°PSC-PrPëPiC-PS PīC¶PëPNεPjP°C,Pë P·C¶P°PSPeC†, P°
C†PëPjPIP°C†C,P°C,PëPS B¶“ PIPμC†PμC¶C-, C¶Pe PIPeP°P·P°PSPs PrP»C¶ C†CHPsPiPs
PīC¶PμPīP°C¶P°C,C†.

P”C-C¿C¶PμC,PëPePë, C-PSPiC-P±C-C,PsC¶Pë
P°PSPiC-PsC,PμPSP·PëPSPiPμC¶PμC,PIPsC¶C¶PIP°P»CHPSPsPiPs C„PμC¶PjPμPSC,C¿ (P¶PμP¶)

P»PμC¶PeP°PSC-PrPëPiC-PS PjPsP¶PSP° P·P°C†C,PsC†PsPIC†PIP°C,Pë PsPrPSPsC†P°C†PSPs P·
PrC-C†C¶PμC,PëPeP°PjPë C,P° C-PSPiC-P±C-C,PsC¶P°PjPë P¶PμP¶.

P†PSCεC- P»C-PeP°C¶C†CHPeC- P·P°C†PsP±Pë, C¶PeC- PIPiP»PëPIP°C¶C,CH PSP°
P°C¶C,PμC¶C-P°P»CHPSPëPNε C,PëC†Pe

PīPe C- PrP»C¶ PIC†C-C... P°PSC,PëPiC-PiPμC¶C,PμPSP·PëPIPSsPiPs... PīC¶PμPīP°C¶P°C,C-PI,
PjPsP¶P»PëPIPμ PīPsC†PëP»PμPSPSC¶ PiC-PiPsC,PμPSP·PëPIPSsPiPs PμC„PμPeC,C† PīC¶Pë
PsPrPSPsC†P°C†PSPsPjC† P·P°C†C,PsC†C†PIP°PSPSC- P»PμC¶PeP°PSC-PrPëPiC-PSC† P·
C-PSCεPëPjPë P»C-PeP°C¶C†CHPePëPjPë P·P°C†PsP±P°PjPë, C¶PeC- PIPiP»PëPIP°C¶C,CH
PSP° P°C¶C,PμC¶C-P°P»CHPSPëPNε C,PëC†Pe, C,P°PePëC... C¶Pe α-P±P»PsPeP°C,PsC¶Pë
PrP»C¶ C†PëPjPiC,PsPjP°C,PëC†PSPsPiPs P»C-PeC†PIP°PSPSC¶ P·P°C...PIPsC¶C¶PIP°PSC¶
C†PμC†PsPIPsPiPs PjC-C...C†C¶P°, C,C¶PëC†PëPeP»C-C†PSC- P°PSC,PëPrPμPīC¶PμC†P°PSC,Pë,
PSPμPNεC¶PsP»PμPiC,PëPePë.

P´P°PIPiP°PePë, PjPsP¶Pμ C†PiPsC†C,PμC¶C-PiP°C,PëC†C¶ P·PSPëP¶PμPSPSC¶
PiC-PiPsC,PμPSP·PëPIPSsPiPs PμC„PμPeC,C† PīC¶Pë PsPrPSPsC†P°C†PSPsPjC†
P·P°C†C,PsC†C†PIP°PSPSC- P· PePsC¶C,PëPePsC†C,PμC¶PsC—PrP°PjPë.

P¶C†PsP±P»PëPIPsC†C,C- P·P°C†C,PsC†C¿PIP°PSPSC¶

P¶PëPSPrC¶PsPj C†P»P°P±PePsC†C,C- C†PëPSC¿C†PsPIPsPiPs PIC¿P·P»P°

P»PμC¶PeP°PSC-PrPëPiC-PS C†P»C-Pr P· PsP±PμC¶PμP¶PSC-C†C,C¶
P·P°C†C,PsC†PsPIC†PIP°C,Pë PīP°C†C-C”PSC,P°Pj C-P· C†PëPSPrC¶PsPjPsPj
C†P»P°P±PePsC†C,C- C†PëPSC†C†PsPIPsPiPs PIC†P·P»P° (P±PμP· C-PjPiP»P°PSC,PsPIP°PSPsPiPs
PeP°C¶PrC-PsC†C,PëPjC†P»C¶C,PsC¶P°).

P”PëC†C„C¿PSPeC†C-C¶ P»C-PIPsPiPs CεP»C¿PSPsC†PeP° C†PμC¶C†C¶

P†PsC†P° PiPμPjPsPrPëPSP°PjC-C†PSPs PePsPSC,C¶PsP»CHPsPIP°PSC-
PrPsC†P»C-PrP¶PμPSPSC¶ PSPμ PIPëC¶PIPëP»Pë PīPsPiC-C¶CεPμPSPSC¶
CεP»C†PSPsC†PePsPIPs— C„C†PSPeC†C-C—, P· PsP±PμC¶PμP¶PSC-C†C,C¶ C†P»C-Pr
PīC¶PëP·PSP°C†P°C,Pë PīC¶PμPīP°C¶P°C, PīC¶Pë PrPëC†C„C†PSPeC†C-C— P»C-PIPsPiPs
CεP»C†PSPsC†PeP° C†PμC¶C†C¶.

P†CεPμPjC-C†PSP° C...PIPsC¶PsP±P° C†PμC¶C†C¶

P´C†P»Ps PIPëC†P»PsPIP»PμPSPs PīC¶PëPiC†C%oPμPSPSC¶, C%oPs PrPμC¶PeC-
PrPëPiC-PrC¶PsPiC-C¶PëPrPëPSPë PePsC¶PsC,PePsC— PrC-C— PjPsP¶C†C,CH P±C†C,Pë

PĭPsPI'CIIP·P°PSC- P· PĭC-PrPIPĕC%oPμPSPĕPj CĭPμCĭC†PμPIPs-CĭC†PrPĕPSPSPĕPj
 CĭPĕP·PĕPePsPj Cĭ PĭP°C†C-C"°PSC,C-PI P· C-CĕPμPjC-C†PSPsCĭ C...PIPsCĭPsP±PsCĭ
 CĭPμCĭC†Cĭ. PĭPsC†P° P·P—PĭPĕPĭPĕP C" PĭCĭPμPĭP°CĭP°C,PSPj
 PrPsPIPIPsC,CĭPĕPIP°P»PSC— PrC-C—, PĭCĭPsC,Pμ C,P°PePĕPj C...PIPsCĭPĕPj
 PĭCĭPμPĭP°CĭP°C, CĭP»C-Pr P·P°CĭC,PSCĭPsPICĭPIP°C,Pĕ P· PsP±PμCĭPμP¶PSC-CĭC,Cĭ.
 P"°PμCĭPeC- PrPĕPiC-PrCĭPsPĭC-CĭPĕPrPĕPSPĕ CĭC-PrPePs PjPsP¶CĭC,Cĭ
 PĭCĭPĕP·PIPsPrPĕC,Pĕ PrPs PĭCĭPμPePsCĭPrC-P°P»CHPSPsPiPs P±PsP»Cĭ P°P±Ps
 CĭC,PμPSPsPeP°CĭPrC-C—. P"°CĭP¶Pμ CĭC-PrPePs Cĭ PĭP°C†C-C"°PSC,C-PI P· CĭP°PSC-CĕPμ
 C-CĭPSCĭCĭC†PsCĭ CĭC,PμPSPsPeP°CĭPrC-C"°Cĭ PjPsP¶P»PĕPIPμ P·P±C-P»CHCĕPμPSPSCĭ
 C†P°CĭC,PSC,Pĕ, C,CĭPĕPIP°P»PSCĭC,C- P°P±Ps C,CĭP¶PePsCĭC,C- C†PĕC... PSP°PĭP°PrC-PI.
 PĕPsP¶CĭC,Cĭ PIC-PrP·PSP°C†P°C,PĕCĭCĭ PĭPsPsPrPĕPSPsPeC- PIPĕPĭP°PrPePĕ
 C-PSC,,P°CĭPeC,Cĭ PjC-PsPeP°CĭPrP°.

PμPμCĭPĕC,PSPSPμP°P»CHPSPĕPN Prc-P°P»C-P.

P—P°CĭC,PSCĭCĭPIP°PSPSCĭ P»PμCĭPeP°PSC-PrPĕPiC-PSCĭ PĭPsPIĕĭ™CĭP·CĭC"°C,CĭCĭCĭ P·
 CĭPsP·PIPĕC,PePsPj PĭPsPjCĭC,PSC-PSPSCĭ PĭPμCĭPĕC,PSPSPμP°P»CHPSPsPiPs
 PμPeCĭCĭPrP°C,Cĭ Cĭ PĭP°C†C-C"°PSC,C-PI PSP° PĭPμCĭPĕC,PSPSPμP°P»CHPSPsPjCĭ
 PrC-P°P»C-P·C-. PμPsPjCĭC,PSC-PSPSCĭ PsP±CĭPjPsPIP»PμPSPs PĭC-PrPIPĕC%oPμPSPsCĭ
 PePsPSC†PμPSC,CĭP°C†C-C"°Cĭ C,CĭPĕPiP»C-C†PμCĭPĕPrC-PI PI PμPeCĭCĭPrP°C,C-
 PsC†PμCĭPμPIPĕPSPĕ. PĭPsC†P° PjPμC...P°PSC-P·Pj PSPμPIC-PrPsPjPĕPN, C†PμPN PμC,,PμPeC,
 PjP°C" C,PμPSPPrPμPSC†C-Cĭ P·PSPĕPeP°C,Pĕ PSPμPIPrPsPIP·C- PĭC-CĭP»Cĭ PIC-PrPjC-PSPĕ
 P»PμCĭPeP°PSC-PrPĕPiC-PSCĭ. P|PμPN PIP·P°C"°PjPsP·PIĕĭ™CĭP·PsPe CĭP»C-Pr PIP·CĭC,Pĕ
 PrPs CĭPIP°PiPĕ P·P°PrP»Cĭ CĭPSPĕPePSPμPSPSCĭ PIPĕPĭP°PrPeC-PI, PePsP»Pĕ
 PĭPsPjCĭC,PSC-PSPSCĭ PĭPμCĭPĕC,PSPSPμP°P»CHPSPsPiPs PμPeCĭCĭPrP°C,Cĭ PjPsP¶Pμ
 P±CĭC,Pĕ PĭPsPjPĕP»PePsPIPs PĭCĭPĕPN PSCĭC,Ps P·P° C-PSC,,PμPeC†C-PN PSPĕPN
 PĭPμCĭPĕC,PSPSC-C, P· PĭPsPrP°P»CHCĕPsCĭ PSPμPĭPsC,CĭC-P±PSPsCĭ
 PĭPsCĭPĭC-C,P°P»C-P·P°C†C-C"°Cĭ C,P° PμPjPĭC-CĭPĕC†PSPĕPj PIPμPrPμPSPSCĭPj
 P°PSC,PĕP±C-PsC,PĕPeC-PI.

P>P°PeC,PSP·P°

P|PμPN P»C-PeP°CĭCĭCHPePĕPN P·P°CĭC-P± PjC-CĭC,PĕC,Cĭ P»P°PeC,PSP·Cĭ.

PμP°C†C-C"°PSC,P°Pj C-P· CĭC-PrPeC-CĭPSPĕPjPĕ CĭPĭP°PrPePsPIPĕPjPĕ PĭCĭPsP±P»PμPjP°PjPĕ
 PSPμPĭPμCĭPμPSPsCĭPĕPjPsCĭC,C- PĭP°P»P°PeC,PSP·Pĕ, P·P°PĭP°P»CHPSPsC—
 P»P°PeC,P°P·PSPsC— PSPμPrPsCĭC,P°C,PSPsCĭC,C- P°P±Ps PĭP»CĭPePsP·Ps-
 PĭP°P»P°PeC,PSP·PSPsC— PjP°P»CHP°P±CĭPsCĭP±C†C-C— PSPμ CĭP»C-Pr
 P·P°CĭC,PSCĭPsPICĭPIP°C,Pĕ C†PμPN P»C-PeP°CĭCĭCHPePĕPN P·P°CĭC-P±.

***P—P°CĭC,PSCĭCĭPIP°PSPSCĭ Cĭ PĭPμCĭC-PsPr PIP°PiC-C,PSPsCĭC,C- P°P±Ps
 PĭPsPrCĭPIP°PSPSCĭ PĭCĭCĭPrPrCĭ***

P'°PiC-C,PSC-CĭC,Cĭ

PĕP»C-PSC-C†PSPĕPN PrPsCĭPIC-Pr P·P°CĭC,PSCĭCĭPIP°PSPSCĭ
 P»PμCĭPeP°PSC-PrPĕPiC-PSCĭ Cĭ PĭPμCĭC-PsPr PIP°PiC-C,PSPsCĭC,C- PIC-PrCĭCĭC,PSC-PN.
 P"°PSCĭP»C-PrPĕ PSP° C,PIP°CĭPĕPSP°C... PSPμ PIPĕCĭPIPĕP»Pĕ C,PμCĭP°C,PSPμPSPsPiPs
 PμC,,PμPeC,Cĭ, P°P»Pμ PIC-PS CĭPĭPsCĭC,PμCĭC-PĭP°PICĭCĭ PĭC-Pr C†P°Cĭ
 P·P°CĭC,PSCĭCĭPIP°PSPSCĭ C-PSCĕPĕC... PrPĕPiC-PrCĭPsPĭC-CĭPĕPrPĕPSPsPIPĕC...

СГРiPcP»CpPе. PкPм СГРмPеPcPjPмPSPpPcPIP°PSPc P·P°CГC,PsCГPcPICpPIP°C,Pë
P»PмСГРPеP°PSC-PrPëPc-PS Cр PиPмСГРC-PcPr PIP°Pc-C,PSPcCГC,C- P°P±Ps P¶C-PSPeP°Pj
СГРмPиСГРPcPrCpPеC,PëPIPSPcPiPs PIC-PeCp, C¶PеC%Ps PIPcPSPë PSPм
P·P°CГC,PsCГPcPICpCГC,CH PмC,,PмPеC,PëPIPSCp PеPcPSC,СГР°CpPиCpC-CГ.

PмPмСГРC-PcPr PiPsPrCзPIP°PSPSC¶ PiCГCзPrPrCГ

PÿPcC±PSPc PSPмPIC-PrPcPjPs, C±Pë PиСГРPcPSPëPеP°C” P»PмСГРPеP°PSC-PrPëPc-PS P°P±Ps
PмPcPiPs PjPмC,P°P±PsP»C-C,Pë Cр PiCГCpPrPSPм PjPsP»PcPеPs, C,PcPjCp СГРPëP·PëPе PrP»C¶
PrPëC,PëPSPë PSPм PjPsP¶Pм P±CpC,Pë PIPëPеP»CГC±PмPSPëPм. PкPм CГP»C-Pr
P·P°CГC,PsCГPcPICpPIP°C,Pë P»PмСГРPеP°PSC-PrPëPc-PS PиC-Pr C±P°CГ PiPsPrCpPIP°PSPSC¶
PiCГCpPrPrCГ.

PмPмСГРC,PëP»CHPSC-CГC,CH

PмP»C-PSC-C±PSC- PrP°PSC- C%PsPrPs PIPиP»PëPICp P»PмСГРPеP°PSC-PrPëPc-PSCp PSP°
C,,PмСГРC,PëP»CHPSC-CГC,CH PIC-PrCГCpC,PSC-. PкP°C¶PIPSC- PrP°PSC- PиСГРPc
PsP±PsСГРPc,PSC- P±C-PcC...C-PjC-C±PSC- P·PjC-PSPë PI PiPsP»C-PICpC-
CГPиPмСГРPjP°C,PsP·Pc—PrC-PI, C%Ps PjPsP¶CpC,CH PIPиP»PëPSCpC,Pë PSP°
PjPsP¶P»PëPIC-CГC,CH P·P°PиP»C-PrPSPмPSPSC¶, Cр PиP°CpC-C”PSC,C-PI, C¶PеC-
P»C-PeCpPIP°P»PëCГC¶ P±P»PcPеP°C,PsСГР°PjPë PеP°P»CHCpC-C”PIPëC... PеP°PSP°P»C-PI. Pj
СГРP°P·C- PиPsPIC,PsСГРPSPcPiPs PSPмCpCГPиC-CëPSPcPiPs P·P°PиP»C-PrPSPмPSPSC¶ *in vitro*
C,P° P·P° PIC-PrCГCpC,PSPcCГC,C- C-PSCëPëC... PиPsC¶CГPSPмPSCH C%PsPrPs CpCHPcPiPs
CГP»C-Pr СГРPcP·PiP»C¶PSCpC,Pë P·P°CГC,PsCГCpPIP°PSPSC¶ P±P»PcPеP°C,PsСГРC-PI
PеP°P»CHCpC-C”PIPëC... PеP°PSP°P»C-PI C¶Pе PjPsP¶P»PëPICp PиСГРPëC±PëPSCp.

**P—PrP°C,PSC-CГC,CH PIPиP»PëPIP°C,Pë PSP° CëPIPëPrPеC-CГC,CH СГРмPмP°PеCpC-C—
PиСГРPë PеPмСГРCзPIP°PSPSC- P°PIC,PsC,СГР°PSCГPиPsСГРC,PsPj P°P±Ps C-PSCëPëPjPë
PjPмC...P°PSC-P·PjP°PjPë**

P’PиP»PëPI P»PмСГРPеP°PSC-PrPëPc-PSCp PSP° P·PrP°C,PSC-CГC,CH PеPмСГРCpPIP°C,Pë
C,СГР°PSCГPиPsСГРC,PSPëPj P·P°CГPcP±PsPj P°P±Ps C-PSCëPëPjPë PjPмC...P°PSC-P·PjP°PjPë
PSPмP·PSP°C±PSPëPм. PhPrPSP°Pе PSPмPcP±C...C-PrPSPc PICГР°C...PsPICpPIP°C,Pë
PjPsP¶P»PëPIC-CГC,CH P·P°PиP°PjPsСГРPcC±PмPSPSC¶, CГP»P°P±PеPsCГC,C-,
PиC-PrPIPëC%PмPSPc— PIC,PsPjP»CHPIP°PSPcCГC,C-, СГРC-PrPеPs бГ”
CГPcPSP»PëPIPcCГC,C-.

PÿPиPsCГC-P± P·P°CГC,PsCГCзPIP°PSPSC¶ C,P° PrPsP·Pë

P PмPеPcPjPмPSPpPcPIP°PSP° PrPsP·P° CГC,P°PSPcPIPëC,CH 10 PjPi PиPмСГРPcСГРP°P»CHPSPc 1
СГРP°P· PSP° PrPsP±Cp, P·P°CГC,PsCГPcPICpCГC,CH PSPм СГРP°PSC-CëPм PSC-P¶ P·P° 15
C...PIPëP»PëPS PrPs PIP¶PëPIP°PSPSC¶ C—P¶C-. P—P°P»PмP¶PSPc PIC-Pr
C-PSPpPëPIC-PrCpP°P»CHPSPc— СГРмPмP°PеCpC-C— PиP°CpC-C”PSC,P° PSP°
P»C-PeCpPIP°PSPSC¶ PrPsP·Cp PjPsP¶PSP° PиC-PrPIPëC%PëC,Pë PrPs 20 PjPi.

PмC-PrP±C-СГ PrPsP·Pë PjP°C” P±CpC,Pë PиPsCГC,CpPиPsPIPëPj, PsCГPеC-P»CHPеPë
PjP°PеCГPëPjP°P»CHPSP° P°PSC,PëPiC-PиPмСГРC,PмPSP·PëPIPSP° PrC-C¶
СГРPcP·PIPëPIP°C”C,CHCГC¶ PиСГРPc,C¶PiPsPj PrPIPc... C,PëP¶PSC-PI P»C-PeCpPIP°PSPSC¶.

- P·P°CíC, PsCíP sPICrPI P°C, Pë PíCíP uPíP°CíP°C, P±P°P¶P°PSPs PICíP°PSC†C-, PSPu

PjPμPSC€Pμ PSC-P¶ P·P° 15 C...PIPëP»PëPS PrPs CÍPSC-PrP°PSPeCf;

- C†PμPNë P»C-PeP°CĤCÍCHPePëPNë P·P°CÍC-P± PSPμ PjPsP¶PSP° PíCĤPëPNëPjP°C,Pë P·
PiCĤPμPNëPíC,,CĤCfC,PsPj C,P° PiCĤPμPNëPíC,,CĤCfC,PsPIPëPj CÍPsPePsPj.

P''C-C,Pë

P'PμP·PíPμPeP° C,P° PμC,,PμPeC,PëPIPSC-CÍC,CH P·P°CÍC,PsCÍCfPIP°PSPSCĬ
P»C-PeP°CĤCÍCHPePsPiPs P·P°CÍPsP±Cf PrC-C,CĬPj PIC-PePsPj PrPs 18 CĤPsPeC-PI PSPμ
PrPsCÍP»C-PrP¶CfPIP°P»PëCÍCĬ, PrP°PSC- C%PsPrPs P·P°CÍC,PsCÍCfPIP°PSPSCĬ
PrC-C,CĬPj PIC-PrCÍCfC,PSC-.

PμPμCĤPμPrPsP·C¿PIP°PSPSCĬ

PμCĤPsC,CĬPiPsPj PíPμCĤC-PsPrCf PíC-CÍP»CĬCĤPμC''CÍC,CĤP°C†C-PNëPSPsPiPs
P·P°CÍC,PsCÍCfPIP°PSPSCĬ P»PμCĤPeP°PSC-PrPëPíC-PSCf PíPsPIC-PrPsPjP»CĬP»PsCÍCĬ
PíCĤPs PrPμCĬPeC- PIPëPíP°PrPePë PíPμCĤPμPrPsP·CfPIP°PSPSCĬ (PIC-Pr 30BĤ"40 PjPi PrPs
800 PjPi, Cf C,PsPjCf C†PëCÍP»C- CÍPíCĤPsP±P° CÍCfC—C†PëPrCf).

PŸPëPjPíC,PsPjPë

P—P° P°PSP°P»PsPiC-C''CĤ P· C-PSC€PëPjPë PrPëPiC-PrCĤPsPíC-CĤPëPrPëPSP°PjPë, PíCĤPë
PíPμCĤPμPrPsP·CfPIP°PSPSC- P»PμCĤPeP°PSC-PrPëPíC-PSPsPj CÍP»C-Pr PsC†C-PeCfPIP°C,Pë
PIPëPSPëPePSPμPSPSCĬ PSP°PrPjC-CĤPSPsC— PíPμCĤPëC,,PμCĤPëC†PSPsC—
PIP°P·PsPrPëP»P°C,P°C†C-C— C- CĬPIPSPsC— P°CĤC,PμCĤC-P°P»CHPSPsC—
PiC-PíPsC,PμPSP·C-C— C,P° CĤPμC,,P»PμPeC,PsCĤPSPsC— C,P°C...C-PeP°CĤPrC-C—.
PhPrPSP°Pe PíCĤPë PrCfP¶Pμ PIPëCÍPsPePëC... PrPsP·P°C... PíPμCĤPëC,,PμCĤPëC†PSP°
CÍPμP»PμPeC,PëPIPSC-CÍC,CH PjPsP¶Pμ P±CfC,Pë PIC,CĤP°C†PμPSP°, C%Ps PjPsP¶Pμ
CÍPíCĤPëC†PëPSPëC,Pë P±CĤP°PrPëPeP°CĤPrC-CĤ C- PSPμPiP°C,PëPIPSPëPNë
C-PSPsC,CĤPsPíPSPëPNë PμC,,PμPeC,. PkP°PNëPíPsC€PëCĤPμPSC-C€C- PíPsP±C-C†PSC-
CĤPμP°PeC†C-C—, PíPsPíBĤ™ CĬP·P°PSC- P· PíPμCĤPμPrPsP·CfPIP°PSPSCĬPj, BĤ"
P°CĤC,PμCĤC-P°P»CHPSP° PiC-PíPsC,PμPSP·C-CĬ, P·P°PíP°PjPsCĤPsC†PμPSPSCĬ,
PíPsP»PsPIPSPëPNë P±C-P»CH C,P° PíPsCÍPëP»PμPSPμ CÍPμCĤC†PμP±PëC,C,CĬ.

P>C-PeC¿PIP°PSPSCĬ

PμCĤPë C,CĬP¶PeC-PNë P°CĤC,PμCĤC-P°P»CHPSC-PNë PiC-PíPsC,PμPSP·C-C—
PSPμPsP±C...C-PrPSPs PIP¶PëC,Pë P·P°C...PsPrC-PI P°PeC,PëPIPSPsC—
PeP°CĤPrC-PsPIP°CÍPeCfP»CĬCĤPSPsC— PiC-PrC,CĤPëPjPePë, PIPeP»CĤC†P°CĤC†Pë
C†P°CÍC,PëPNë PjPsPSC-C,PsCĤPëPSPi CÍPμCĤC†PμPIPsC— C,P° PrPëC...P°P»CHPSPsC—
C,,CfPSPeC†C-PNë, PSP°PrP°PSPSCĬ PíP°C†C-C''PSC,Cf PíPsCĤPëP·PsPSC,P°P»CHPSPsPiPs
PíPsP»PsP¶PμPSPSCĬ P· PíCĤPëPíC-PrPSCĬC,PëPjPë PSPëP¶PSC-PjPë PeC-PSC†C-PIPeP°PjPë,
PePsPSC,CĤPsP»CH CĤC-PrPëPSPë, C%Ps C†PëCĤPeCfP»CĤC'', C,P°
CÍPμC†PsPIPëPíCfCÍPeP°PSPSCĬ. P— PsPiP»CĬPrCf PSP° PíPsPrPsPIP¶PμPSCf
C,,P°CĤPjP°PePsP»PsPiC-C†PSCf PrC-CĤ P»PμCĤPeP°PSC-PrPëPíC-PSCf Cf CĤP°P·C-
PíPμCĤPμPrPsP·CfPIP°PSPSCĬ C'' PSPμPsP±C...C-PrPSPëPj PSP°PiP»CĬPr P·P° CÍC,P°PSPsPj
CÍPμCĤC†PμPIPs-CÍCfPrPëPSPSPsC— CÍPëCÍC,PμPjPë C,P°PePëC... PíP°C†C-C''PSC,C-PI
C%PsPSP°PNëPjPμPSC€Pμ PíCĤPsC,CĬPiPsPj 24 PíPsPrPëPS. P'PμCĤCfC†Pë PrPs CfPIP°PiPë
PIPëCÍPsPePμ P·PíBĤ™ CĬP·CfPIP°PSPSCĬ P»PμCĤPeP°PSC-PrPëPíC-PSCf P· P±C-P»PeP°PjPë,
PrC-P°P»C-P· PjPsP¶Pμ P±CfC,Pë PSPμPμC,,PμPeC,PëPIPSPëPj. PμP°C†C-C''PSC,Pë P·

PsC†C–PeCfPIP°PSPsC† P†PsPjC–C†PSPsC† P°P±Ps C,C†P¶PePsC†
C–PSC,PsPeC†PëPeP°C†C–C”C† PjP°C†C,C† P±CfC,Pë P†C–Pr PSP°PiP»C†P†PsPj P†
C†PjPsPIP°C... C–PSC,PµPSC†PëPIPSsC— C,PµC†P°P†C–C—.

PµPsP±C–C†PSC– C†PµP°PeC†C–C—

P—PiC–PrPSPs P· PrP°PSPëPjPë PeP»C–PSC–C†PSPëC... PrPsC†P»C–PrP¶PµPSC† C,P°
P†C–C†P»C†C†PµC”C†C,C†P°C†C–PµPSPsPiPs P·P°C†C,PsC†C†PIP°PSPSC† P†PsP±C–C†PSC–
C†PµP°PeC†C–C—, C†PeC– P·C†C†C,C†C–C†P°P»PëC†C† PSP°PµC†P°C†C,C–C†Pµ, б†” C†Pµ
P†PµC†PëC,,PµC†PëC†PSC– PSP°P±C†C†PePë, PiPsP»PsPIPSPëPµ P±C–P»C†,
P†C†PëP†P»PëPIPë, C,P°C...C–PeP°C†PrC–C† C– P†PsC†PëP»PµPSPµ C†PµC†C†PµP±PëC,C,C†.

Pj PSPëP¶C†PµPSP°PIPµPrPµPSC–Pµ C,P°P±P»PëC†C– P†PeP°P·P°PSPs P†PsP±C–C†PSC–
C†PµP°PeC†C–C—, P†C†Ps C†PeC– P†PsPIC–PrPsPjP»C†P»PsC†C† P†C–Pr C†P°C†
PeP»C–PSC–C†PSPëC... PrPsC†P»C–PrP¶PµPSC† C,P°
P†C–C†P»C†C†PµC”C†C,C†P°C†C–PµPSPsPiPs P·P°C†C,PsC†C†PIP°PSPSC†
P†C†PµP†P°C†P°C,C† C† PeC†P°C—PSP°C... C†PIC–C,C† C,P° PrP»C† C†PePëC... P±C†PI
PsP±T’C†C†PSC,PsPIP°PSPëPµ P†C†PëC†PëPSPSPs–PSP°C†P»C–PrPePsPIPëPµ
P·P†б†” C†P·PsPe C–P· P·P°C†C,PsC†C†PIP°PSPSC†Pj P†C†PµP†P°C†P°C,C†.
PµPsP±C–C†PSC– C†PµP°PeC†C–C— PSP°PIPµPrPµPSPs P·PiC–PrPSPs P·
PeP»P°C†PëC,,C–PeP°C†C–C”C† MedDRA C,P° C†P°C†C,PsC,PsC†
PIPëPSPëPePSPµPSPSC†: PrC†P¶Pµ C†P°C†C,Ps (≥ 1/10), C†P°C†C,Ps (≥ 1/100, < 1/10),
PSPµC†P°C†C,Ps (≥ 1/1000, < 1/100), C†C–PrPePs (≥ 1/10000, < 1/1000), PrC†P¶Pµ C†C–PrPePs
(< 1/10000), C†P°C†C,PsC,P° PSPµPIC–PrPsPjP° (PSPµ PjPsP¶PSP° PIPëP·PSP°C†PëC,Pë
P·PiC–PrPSPs P· PSP°C†PIPSPsC† C–PSC,,PsC†PjP°C†C–C”C†). Pj PePsP¶PSC–Pµ
P†C†C†PiC– PIC–PrP†PsPIC–PrPSPs PrPs C†P°C†C,PsC,Pë PIPëPSPëPePSPµPSPSC†
C†PµP°PeC†C–C— P·P°P·PSP°C†PµPSPs P† P†PsC†C†P†PeC† P·PjPµPSC†PµPSPSC† C–C...
C†PµC†PµP·PSPsC†C,C–.

MedDRA PeP»P°C†PëC,,C–PeP°C†C–C† C†PëC†C,PµPj C,P° PsC†P†PSC–PI	P§P°C†C,Ps	PkPµC†P°C†C,Ps	P C–PrPePs	P§P°C†C,PsC,P° PSPµPIC–PrPsPjP°
P— P±PsPeC± C–PjC±PSPSPsC— C†PëC†C,PµPjPë	б†”	б†”	P†C–PrPIPëC%PµPSP° C†C†C,P»PëPIC–C†C,C†	б†”
P— P±PsPeC± PSPµC†PIPSPsC— C†PëC†C,PµPjPë	P†PsP»PsPIPSPëPµ P±C–P»C†	P·P°P†P°PjPsC†PµPSPSC†	C†PsPSP»PëPIC–C†C,C†, PSPµP†C†PëC,PsPjPSC–C†C,C†	б†”
P— P±PsPeC± C†PµC†C†C†	C,P°C...C–PeP°C†PrC–C†, P†PsC†PëP»PµPSPµ C†PµC†C†PµP±PëC,C,C†	б†”	C†C,PµPSPsPeP°C†PrC–C†	б†”
P— P±PsPeC± C†C±PrPëPS	P†C†PëP†P»PëPIPë	P°C†C,PµC†C–P°P»C†PSP° PiC–PiPsC,PµPSP·C–C†	б†”	б†”
P— P±PsPeC± C†P»C±PSPPePsPiPs– PePëC†PePsPiPs C,C†P°PeC,C±	б†”	PrPëC†P†PµP†C†C–C†, PSC†PrPsC,P°, P±C–P»C† C† P†PµC†C...PSC–Pµ C†P°C†C,PëPSC– P¶PëPiPsC,P°	P±P»C†PIP°PSPSC†, PrC–P°C†PµC†	P†C–P†PµC†C,C†PsC,,C–C† C†C†PµPS*, P†PsPjC†C,PSC–PSPSC† P†PµC†PëC,PsPSPµP°P»C†PSPs–PiPs PµPëC†C†PrP°C,C†*
P— P±PsPeC± PiPµPiP°C,PsP±C–P»C–P°C†PSPsC— C†PëC†C,PµPjPë	б†”	б†”	б†”	P†C–PrPIPëC%PµPSPSC† C†C–PIPSC† C,C†P°PSC†P°PjC–PSP°P· C†PëC†PsPIP°C,PePë PeC†PsPIC–*
P— P±PsPeC± C†PeC–C†Pë C,P° PiC–PrC†PeC–C†PSPsC— C,PeP°PSPëPSPë	б†”	PIPëC†PëP†, C†PIPµC†P±C–P¶	PIPëC†PëP†P°PSPSC†	PSP°P±C†C†Pe*
P— P±PsPeC± C†PePµP»PµC,PSPs– Pjë” C†P·PsPiPsC— C†PëC†C,PµPjPë C,P° C†PiPsP»C±C†PSPsC— C,PeP°PSPëPSPë	б†”	PjC–P°P»PiC–C†	б†”	б†”
P— P±PsPeC± C†PµC†PsPiPëPrC–P»C†PSPsC— C†PëC†C,PµPjPë	б†”	P†PsP»C–C†C†C–C†	P†PsP»P°PeC–C†C†C–C†	б†”
P— P°PiP°P·C†PSC– PiPsC†C†C†PµPSPSC† C,P° C†PµP°PeC†C–C— C±PjC–C†C†C– PIPIPµPrPµPSPSC†	P†PµC†PëC,,PµC†PëC†PSC– PSP°P±C†C†PePë	P°C†C,PµPSC–C†, PiC–PrPIPëC%PµPSP° PIC,PsPjP»C†PIP°PSC–C†C,C†	P±C–P»C† C† P†C†C†PrC†C... б†”	б†”

*P_μPsP±C-C†PSC- C₇P_μP°PeC†C-C— P·C- C†P_iPsPSC,P°PSPSPëC... P_iPsPIC-PrPsPjP»P_μPSCH P_iC-Pr C†P°C† P_iC-C†P»C₁C₇P_μC”C†C,C₇P°C†C-PN₆PSPsPiPs P·P°C†C,PsC†C†PIP°PSPSC₁ C† PeC₇P°C—PSP°C... C†PIC-C,C†.

P>P_μC₇PeP°PSC-PrPëP_iC-PS PSP_μ PIP_iP»PëPIP°C” PSP_μPiP°C,PëPIPSs PSP° C₇C-PIP_μPSCH C†C†PeC₇C† PI PeC₇PsPIC- C,P° C₇C-PIP_μPSCH P»C-P_iC-PrC-PI C† C†PëC₇PsPIP°C,C†C- PeC₇PsPIC-.

PJ P_iP»P°C†P_μP±Ps-PePsPSC,C₇PsP»CHPsPIP°PSPëC... PeP»C-PSC-C†PSPëC... PrPsC†P»C-PrP₁P_μPSPSC₁C... P_iP_μC₇PëC,,P_μC₇PëC†PSC- PSP°P±C₇C₁PePë C†C,P°PSPsPIPëP»PëB B B B B B B B B B B B 0,9 % PSP° C,P»C- P_iC₇PëPN₆PsPjC† P»P_μC₇PeP°PSC-PrPëP_iC-PSC† C† PrPsP·C- 10B₇”20 PjPi C,P° 0,83 % B₇” P_iC₇Pë P_iC₇PëPN₆PsPjC- P_iP»P°C†P_μP±Ps. P_iC₁ C†P°C†C,PsC,P° PrPsC†C₁PiP°P»P° 2 % C† P·P°PiP°P»CHPsPSC-PN₆ P_iPsPiC†P»C₁C†C-C— PrPsC†P»C-PrP₁P_μPSPSC₁, PIPeP»CHC†P°CHC†Pë PrPsPIP_iPsC,C₇PëPIP°P»C- PeP»C-PSC-C†PSC- PIPëP_iC₇PsP±C†PIP°PSPSC₁.

P—P°C†C,PsC†C†PIP°PSPSC₁ PrP_μC₁PePëC... PrPëP_iC-PrC₇PsP_iC-C₇PëPrPëPSC-PI PjPsP₁P_μ C-PSPsPrC- P_iC₇PëP·PIPsPrPëC,Pë PrPs P_iC₇P_μPePsC₇PrC-P°P»CHPsPsPiPs P±PsP»CH P°P±Ps C†C,P_μPSPsPeP°C₇PrC-C—, C† PIPëPSC₁C,PePsPIPëC... PIPëP_iP°PrPeP°C... C† P_iP°C†C-C”PSC,C-PI P·C- C†C,P_μPSPsPeP°C₇PrC-C”CH PjPsP₁P_μ P·P±C-P»CHC€PëC,PëC†C₁ C†P°C†C,PsC,P°, C,C₇PëPIP°P»C-C†C,CH P°P±Ps C,C₁P₁PeC-C†C,CH PSP°P_iP°PrC-PI, PjPsP₁C†C,CH PIC-PrP·PSP°C†P°C,PëC†C₁ C-P·PsP»CHPsPIP°PSC- PIPëP_iP°PrPePë C-PSC,,P°C₇PeC,C† PjC-PsPeP°C₇PrP°.

P_μPsPIC-PrPsPjP»P_μPSPSC₁ P_iC₇Ps P_iC-PrPsP·C₇CHPIP°PSC- P_iPsP±C-C†PSC- C₇P_μP°PeC†C-C—. P_μPsPIC-PrPsPjP»P_μPSPSC₁ P_iC₇Ps P_iPsP±C-C†PSC- C₇P_μP°PeC†C-C— P_iC-C†P»C₁ C₇P_μC”C†C,C₇P°C†C-C— P»C-PeP°C₇C†CHPePsPiPs P·P°C†PsP±C† PjP°C” PIP°P₁P»PëPIP_μ P·PSP°C†P_μPSPSC₁. P_iP_μ PrP°C” P·PjPsPiC† P_iC₇PsPIP_sPrPëC,Pë PjPsPSC-C,PsC₇PëPSP_i C†P_iC-PIPIC-PrPSPsC€P_μPSPSC₁ PePsC₇PëC†C,CH / C₇PëP·PëPe P_iC₇Pë P·P°C†C,PsC†C†PIP°PSPSC- C†CHPsPiPs P»C-PeP°C₇C†CHPePsPiPs P·P°C†PsP±C†. P_μP_μPrPëC†PSPëPj C,P° C,,P°C₇PjP°C†P_μPIC,PëC†PSPëPj P_iC₇P°C†C-PIPSPëPeP°Pj, P° C,P°PePsP₁ P_iP°C†C-C”PSC,P°Pj P°P±Ps C—C... P·P°PePsPSPSPëPj P_iC₇P_μPrC†C,P°PIPSPëPeP°Pj C†P»C-Pr P_iPsPIC-PrPsPjP»C₁C,Pë P_iC₇Ps C†C†C- PIPëP_iP°PrPePë P_iC-PrPsP·C₇CHPIP°PSPëC... P_iPsP±C-C†PSPëC... C₇P_μP°PeC†C-PN₆ C,P° PIC-PrC†C†C,PSPsC†C,C- P_μC,,P_μPeC,PëPIPSsC†C,C- P»C-PeP°C₇C†CHPePsPiPs P·P°C†PsP±C† C†P_μC₇P_μP· P_hPIC,PsPjP°C,PëP·PsPIP°PSC† C-PSC,,PsC₇PjP°C†C-PN₆PSC† C†PëC†C,P_μPjC† P· C,,P°C₇PjP°PePsPSP°PiP»C₁PrC† P·P° P_iPsC†PëP»P°PSPSC₁Pj: <https://aisf.dec.gov.ua>.

P₇P_μC₇PjC-PS P_iC₇PëPrP°C,PSPsC†C,C-

2 C₇PsPePë.

PJPjPsPIPë P·P±P_μC₇C-PiP°PSPSC₁

P—P±P_μC₇C-PiP°C,Pë P_iC₇Pë C,P_μPjPiP_μC₇P°C,C†C₇C- PSP_μ PIPëC‰P_μ 25 B°P₇ PI PsC₇PëPiC-PSP°P»CHPsPSC-PN₆ C†P_iP°PePsPIC†C-.

P—P±P_μC₇C-PiP°C,Pë C† PSP_μPrPsC†C,C†PiPSPsPjC† PrP»C₁ PrC-C,P_μPN₆ PjC-C†C†C-.

PJPiP°PePsPIPeP°

PμPs 10 C,P°P±P»PμC,PsPe Cr P±P»C-CÍC,PμCȚC-, PīPs 3 P°P±Ps 6 P±P»C-CÍC,PμCȚC-PI CȚP°P·PsPj P· C-PSCÍC,CȚCrPeC†C-C"CH PrP»CȚ PjPμPrPëC†PSPsPiPs P·P°CÍC,PsCÍCrPIP°PSPSCȚ Cr PīP°C†C†C- P· PeP°CȚC,PsPSCÍ.

PμPs 30 P°P±Ps 60 C,P°P±P»PμC,PsPe Cr P±P°PSC†C-, PīPs 1 P±P°PSC†C- CȚP°P·PsPj P· C-PSCÍC,CȚCrPeC†C-C"CH PrP»CȚ PjPμPrPëC†PSPsPiPs P·P°CÍC,PsCÍCrPIP°PSPSCȚ Cr PīP°C†C†C- P· PeP°CȚC,PsPSCÍ.

PљP°C,PμPiPsCȚC-CȚ PIC-PrPīCrCÍPeCr

P—P° CȚPμC†PμPīC,PsPj.

P—P°CȚPIPSPëPe

PŷPhP' PќP'Pα B«PњP†PљP PhPГ†PњB».

PњC-CÍC†PμP·PSP°C...PsPrP¶PμPSPSCȚ P·P°CȚPIPSPëPeP°

PJPeCȚP°C—PSP°, 01013, Pj. PљPëC—PI, PIC†P». P'Cr†C-PSP†CrCÍC,CȚC-C—, P±Cr†P. 5.

PμPsPIC-PrPsPjPëC,Pë PīCȚPs PSPμP±P°P¶P°PSPμ CȚPIPëC‰Pμ PīCȚPë P·P°CÍC,PsCÍCrPIP°PSPSC- P»C-PeP°CȚCÍCHPePsPiPs P·P°CÍPsP±Cr P'Pë PjPsP¶PμC,Pμ C†PμCȚPμP· CÍPëCÍC,PμPjCr C„P°CȚPjP°PePsPSP°PiP»CȚPrCr PŷPhP' PќP'Pα B«PњP†PљP PhPГ†PњB» PSP° PSPsPjPμCȚ C,PμP»PμC„PsPSCÍ: 38 (050) 309-83-54 (C†C-P»PsPrPsP±PsPIPs) P°P±Ps PSP° e-mail: pharmacovigilance@microkhim.com.

P'PëCȚPsP±PSPëPe

PŷPhP' PќP'Pα B«PњP†PљP PhPГ†PњB» (PIC-PrPīPsPIC-PrP°P»CHPSPëPNē P·P° PIPëPīCrCÍPe CÍPμCȚC-C—, PSPμ PIPeP»CHC†P°CHC†Pë PePsPSC,CȚPsP»CH/PIPëPīCȚPsP±CrPIP°PSPSCȚ CÍPμCȚC-C—).

AT B«P>CrP±PSPëC„P°CȚPjB» (PIC-PrPīPsPIC-PrP°P»CHPSPëPNē P·P° PIPëCȚPsP±PSPëC†C,PIPs C,P° PePsPSC,CȚPsP»CH/PIPëPīCȚPsP±CrPIP°PSPSCȚ CÍPμCȚC-C—, PSPμ PIPeP»CHC†P°CHC†Pë PIPëPīCrCÍPe CÍPμCȚC-C—).

PњC-CÍC†PμP·PSP°C...PsPrP¶PμPSPSCȚ PIPëCȚPsP±PSPëPeC-PI C,P° P°P†CȚPμCÍP°

PjC-CfC†CЦ PïCђPsPIP°PrP¶PμPSPSCЦ C—C... PrC-CЦP»CHъPSPsCfC,C-

PJPeCђP°C—PSP°, 01013, Pj. PљPөC—PI, PICfP». P'CfPrC-PSPrCfCfC,CђC—C—, P±CfPr. 5.

PJPeCђP°C—PSP°, 37500, PцPsP»C,P°PICfCHъPeP° PsP±P»., Pj. P>CfP±PSPө, PICfP».
P'P°CђPIC-PSPePsPIP°, 16.