

Р†РќРЎРЎР РЈРљРІР†РЇ

**PrP»CŮ PjPµPrPëC‡PSPsPiPs P•P°CŦC,PsCŦCŦPIP°PSPSCŮ P»C-PeP°CŦCŦCŦPePsPiPs
P•P°CŦPs±CŦ**

PᵤPᵛP•PŸPₕPᵝ

(PLETOL)

$P\check{Y}P\epsilon P\gg P^{\circ}P\Gamma$:

$PrC-CHC\equiv P^{\circ}$ $CH_2P\mu C\equiv PsPIP\ddot{e}PSP^{\circ}$: cilostazol;

$$1 \text{ C}, \text{P}^\circ\text{P} \pm \text{P} \gg \text{P}_\mu\text{C}, \text{P}_\epsilon\text{P}^\circ \text{ P}_j\text{C}-\text{C}\dot{\text{I}}\text{C}, \text{P}\ddot{\text{e}}\text{C}, \text{CH} \text{ C}\dagger\text{P}\ddot{\text{e}}\text{P} \gg \text{P}_\text{s}\text{C}\dot{\text{I}}\text{C}, \text{P}^\circ\text{P} \cdot \text{P}_\text{s}\text{P} \gg \text{Cr} \text{ 50 P}_j\text{P}_i \text{ P}^\circ\text{P} \pm \text{P}_\text{s} \text{ 100 P}_j\text{P}_i;$$

C,P°P±P»PµC,PePë PïPs 50 PjPi: PrPsPïPsPjC-P¶PSC- C¶PµC‡PsPIPëPSPë:

$$\text{PeC}\bar{\text{T}}\text{P}\text{Sc} \dots \text{PjP}^\circ \text{P} \gg \text{CH} \text{ PeCrPeCrC}\bar{\text{T}}\text{CrPrP} \cdot \text{C}\bar{\text{U}}\text{PSP}\bar{\text{e}}\text{PN}_0,$$
$$\text{PiC-PrC}\bar{\text{H}}\text{PsPeC}\bar{\text{I}}\text{P}\ddot{\text{e}}\text{PjP}\mu\text{C,P}\ddot{\text{e}}\text{P}\gg\text{PiC}\bar{\text{H}}\text{PsPiC-P}\gg\text{C}\dagger\text{P}\mu\text{P}\gg\text{C}\bar{\text{H}}\text{P}\gg\text{PsP}\cdot\text{P}^\circ\text{ P}\cdot 5, \text{C}\dagger\text{P}\mu\text{P}\gg\text{C}\bar{\text{H}}\text{P}\gg\text{PsP}\cdot\text{P}^\circ$$
$$\text{PjC-PeCHPsPeCHPëCfC, P°P} \gg \text{C-C} \ddagger \text{PSP}^\circ \text{ 101, PjP°PiPSC-CH CfC, P} \mu \text{P°CHP°C,, C} \ddagger \text{P} \mu \text{P} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ$$
$$\text{PjC-PeC}\bar{\text{H}}\text{PsPeC}\bar{\text{H}}\text{P}\bar{\text{e}}\text{C}\bar{\text{I}}\text{C,P}^\circ\text{P}\rangle\text{C-C}\bar{\text{I}}\text{PSP}^\circ \text{ 12, PeP}^\circ\text{P}\rangle\text{CHC}\bar{\text{I}}\text{C-C}\bar{\text{H}}\text{PeP}^\circ\text{C}\bar{\text{H}}\text{PjP}\bar{\text{u}}\text{P}\rangle\text{PsP}^\circ\text{P}^\circ;$$

C,P°P±P»PuC,PePë PïPs 100 PjPi: PrPsPïPsPjC-P¶PSC- C¶PuC¶PsPIPëPSPë:

$$\text{PeC}\bar{\text{T}}\text{P}\text{Sc} \dots \text{PjP}^\circ\text{P} \gg \text{CH} \text{ PeCr'}\text{PeCr'}\text{C}\bar{\text{T}}\text{Cr'}\text{PrP} \cdot \text{C}\bar{\text{L}}\text{PSP}\bar{\text{e}}\text{PN}_0,$$
$$\text{PiC-PrCHPsPeClPëPjPuC,PëP} \gg \text{PiCHPsPiC-P} \gg \text{C†PuP} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ \quad \text{P} \cdot 5, \text{C†PuP} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ$$
$$\text{PjC-PeCHPsPeCHPëCfC,P°P»C-C†PSP° 101, PiP°PiPSC-CH CfC,PuP°CHP°C,, PeP°P»CHC†C-CH}$$
$$P \in P^\circ \subset \mathcal{H} P \mid P \mu P \gg P_S P \cdot P^\circ.$$
$$\mathbf{P} \triangleright \mathbf{C} - \mathbf{P} \mathbf{e} \mathbf{P}^{\circ} \mathbf{C} \mathbf{f} \mathbf{C} \mathbf{f} \mathbf{C} \mathbf{h} \mathbf{P} \mathbf{e} \mathbf{P}^{\circ} \mathbf{C} \mathbf{,,} \mathbf{P} \mathbf{s} \mathbf{C} \mathbf{f} \mathbf{P} \mathbf{j} \mathbf{P}^{\circ} . \mathbf{P} \check{\mathbf{y}} \mathbf{P}^{\circ} \mathbf{P} \pm \mathbf{P} \gg \mathbf{P} \mu \mathbf{C} , \mathbf{P} \mathbf{e} \mathbf{P} \check{\mathbf{e}} .$$
$$PhCI\dot{P}SPsPIPSC-C_{\text{„}}C-P\cdot P\ddot{e}PePs-C...C-PjC-C\ddot{z}PSC-PIP\gg P^{\circ}CI\dot{C},P\ddot{e}PIPsCI\dot{C},C-:$$

C,P°P±P»PμC,PePë PïPs 50 PjPi: PeCḥCrPiP»C-, PïP»P°CḤPeC- C,P°P±P»PμC,PePë PIC-Pr

$$P_{\pm}C-P \gg P_S P_i P_S \quad P_r P_S \quad P_j P^o P_N P_l P_{\parallel} P_u \quad P_{\pm}C-P \gg P_S P_i P_S \quad P_e P_S P \gg C H P_S C H C_r, P.$$

PiC₇P^oPiC-C₇PIP^oPSPSCIPj B«50B» P· PsPrPSPsPiPs P±PsPeCf;

C,P°P±P»PuC,PePë PïPs 100 PjPi: PeCĤCrPiP»C-, PïP»P°CĤPeC- C,P°P±P»PuC,PePë PIC-Pr

$$P \pm C - P \gg PsPiPs \quad PrPs \quad PjP^{\circ}PN_{\circ}P \quad P \pm C - P \gg PsPiPs \quad PePsP \gg CHPsCHCr, P.$$
$$\text{PiCHP}^\circ\text{PIC-CHPIP}^\circ\text{PSPSCUPj B}\ll 100\text{B}\gg \text{P}\cdot \text{PsPrPSPsPiPs P}\pm\text{PsPeCr}.$$

PꝛP°CḦPjP°PePsC,PuCḦP°PīPuPIC,PëC±PSP° PiCḦCḡPīP°.

$$\text{PhPSC}, \text{P}\ddot{\text{e}}\text{C}, \text{C}\ddot{\text{H}}\text{P}\text{S}\text{P}\text{I}\text{P}\pm\text{P}\text{S}\text{C}, \text{P}\ddot{\text{e}}\text{C}\mp\text{PSC}-\text{P}\cdot\text{P}^{\circ}\text{C}\dot{\text{I}}\text{P}\text{S}\text{P}\pm\text{P}\ddot{\text{e}}. \text{P}\dagger\text{PSPiC}-\text{P}\pm\text{C}-\text{C}, \text{P}\text{S}\text{C}\ddot{\text{H}}\text{P}\ddot{\text{e}}$$
$$\text{P}^\circ\text{PiC}\bar{\text{H}}\text{PuPiP}^\circ\text{C}^\dagger\text{C}-\text{C}-\text{C}, \text{C}\bar{\text{H}}\text{PsPiP}\pm\text{PsC}^\dagger\text{P}\bar{\text{e}}\text{C}, \text{C}-\text{PI} \text{P}^\circ\text{P}^\circ \text{PIP}\bar{\text{e}}\text{PSC}\text{IIC}, \text{PePsPj} \text{PiPuPiP}^\circ\text{C}\bar{\text{H}}\text{P}\bar{\text{e}}\text{PSC}^\dagger.$$

РљРѕРј РћРјРјРј В01А С23.

$$P\alpha P^{\circ}C\bar{H}PjP^{\circ}PePsP\gg PsPiC-C\neq PSC-PIP\gg P^{\circ}C\bar{I}C,P\ddot{e}PIPsC\bar{I}C,C-.$$

PαP°CḡPjP°PePsPrPëPSP°PjC-PeP°.

PjPëP»PsCfC,P°P·PsP» C" C-PSPiC-P±C-C,PscḡPsPj P°PiCḡPμPiP°C†C-C—
C,CḡPsPjP±PsC†PëC,C-PI. PμCḡPμPiP°CḡP°C, PiPsPeCḡP°C%oCfC" P·PrP°C,PSC-CfC,CH
PiPμCḡPμPSPsCfPëC,Pë C,,C-P·PëC±PSC- PSP°PIP°PSC,P°PḡPμPSPSCḡ, CḡPeCf
PsC†C-PSCḡCḡC,CH P·P° P°P±CfPsP»CḡC,PSPsCḡ PrPëCfC,P°PSC†C-C"ḡ PiCḡPë
PiPμCḡPμPjC-PḡPSC-PMë PeCfP»CHPiP°PiPsCfC,C- (P°P±Ps P·P° PjP°PeCfPëPjP°P»CHPSPsCḡ
PrPëCfC,P°PSC†C-C"ḡ C...PsPrCHP±Pë (PḡP"PI)) C,P° PiPsC±P°C,PePsPiPsCḡ
PrPëCfC,P°PSC†C-C"ḡ PiPμCḡPμPjC-PḡPSPsC— PeCfP»CHPiP°PiPsCfC,C- (P°P±Ps P·P°
P±PμP·P±PsP»C-CfPSPsCḡ PrPëCfC,P°PSC†C-C"ḡ C...PsPrCHP±Pë (P'P"PI)) Cf
C,PμCfC,CfPIP°PSPSC- PSP° P±C-PiPsPIC-PMë PrPsCḡC-PḡC†C-. P—P°
CḡPμP·CfP»CHC,P°C,P°PjPë PrPsCfP»C-PrPḡPμPSCḡ PiCḡPë CḡC-P·PSPëC...
PSP°PIP°PSC,P°PḡPμPSPSCḡC... P±CfP»Ps PICfC,P°PSPsPIP»PμPSPs P·PSP°C±PSPμ
P°P±CfPsP»CḡC,PSPμ PiPsPeCḡP°C%oPμPSPSCḡ PSP° 42 PjPμC,CḡPë PḡP"PI PiCḡPë
P·P°CfC,PscfCfPIP°PSPSC- PiCḡPμPiP°CḡP°C,Cf PiPsCḡC-PIPSḡPSPs P·C,P°PePsCḡ
PiCḡPëB PiCḡPëPMëPsPjC- PiP»P°C†PμP±Ps. PjPμ PIC-PrPiPsPIC-PrP°C"
PIC-PrPSPsCfPSPsPjCf PiPsPeCḡP°C%oPμPSPSCḡ PSP° 100 % PiPsCḡC-PIPSḡPSPs P·
PiP»P°C†PμP±Ps. PjPμPMë PμC,,PμPeC, P±CfPI PrPμC%oPs PSPëPḡC±PëPj Cf
C...PiPsCḡPëC... PSP° C†CfPeCḡPsPIPëPMë PrC-P°P±PμC,,.

PjPëP»PsCfC,P°P·PsP» PIPëCḡPIP»CḡC" PIP°P·PsPrPëP»P°C,P°C,PscḡPSPëPMë PμC,,PμPeC,,
C%oPs P±CfP»Ps PiC-PrC,PIPμCḡPrPḡPμPSPs PIPëPjC-CḡCḡPIP°PSPSCḡPj PeCḡPsPiPsC,PscPeCf
PSPëPḡPSC-C... PeC-PSC†C-PIPsPe P·P° PrPsPiPsPjPsPiPsCḡ C,PμPSP·PsPjPμC,CḡPëC±PSPsC—
PiP»PμC,PëP·PjPsPiCḡP°C,,C-C—. PjPëP»PsCfC,P°P·PsP» C,P°PePsPḡ C-PSPiC-P±CfC"
PiCḡPsP»C-C,,PμCḡP°C†C-Cḡ PeP»C-C,PëPS PiP»P°PrPePëC... Pjḡḡ CḡP·C-PI C,P°
C-PSPiC-P±CfC" CḡPμP°PeC†C-Cḡ PIPëPIC-P»CHPSPμPSPSCḡ C,CḡPsPjP±PsC†PëC,C-PI
C,CḡPsPjP±PsC†PëC,P°CḡPSPsPiPs C,,P°PeC,PscḡP° CḡPsCfC,Cf C,P° PF-4 Cf
C,CḡPsPjP±PsC†PëC,P°C... P»CḡPrPëPSPë.

P"PsCfP»C-PrPḡPμPSPSCḡ PiCḡPsPrPμPjPsPSCfC,CḡCfPIP°P»Pë, C%oPs C†PëP»PsCfC,P°P·PsP»
CfPiCḡPëC±PëPSCḡC" PsP±PsCḡPsC,PSPμ PiCḡPëPiPSC-C±PμPSPSCḡ P°PiCḡPμPiP°C†C-C—
C,CḡPsPjP±PsC†PëC,C-PI. P†PSPiC-P±CfPIP°PSPSCḡ PμC,,PμPeC,PëPiPSPμ PiCḡPsC,Pë
PSPëP·PePë P°PiCḡPμPiP°PSC,C-PI (PIPeP»CḡC±P°CḡC±Pë P°CḡP°C...C-PrPsPSPsPICf
PePëCfP»PsC,Cf, PePsP»P°PiPμPS, P°PrPμPSPsP·PëPSPrPëC,,PsCfC,,P°C, (PḡP"Pα) C,P°
P°PrCḡPμPSP°P»C-PS); Cf PiP°C†C-C"PSC,C-PI C-PSPiC-P±CfPIP°PSPSCḡ C,CḡPëPiP°C" PrPs
12 PiPsPrPëPS, P° PiC-CfP»Cḡ P·P°PIPμCḡCëPμPSPSCḡ PiCḡPëPMëPsPjCf
C†PëP»PsCfC,P°P·PsP»Cf PIC-PrPSPsPIP»PμPSPSCḡ P°PiCḡPμPiP°C†C-C—
PiCḡPsC...PsPrPëP»Ps PI PjPμPḡP°C... 48-96 PiPsPrPëPS P±PμP· PμC,,PμPeC,Cf
CḡPëPePsCëPμC,Cf (PiC-PiPμCḡP°PiCḡPμPiP°C†C-C—). PḡP°PePsPḡ PICfC,P°PSPsPIP»PμPSPs
PIP»PëPI C†PëP»PsCfC,P°P·PsP»Cf PSP° P»C-PiC-PrPë, CḡPeC- C†PëCḡPeCfP»CḡCḡC,CH Cf
PiP»P°P·PjC- PeCḡPsPIC-. PμCḡPëPMëPsPj PiCḡPμPiP°CḡP°C,Cf P·PSPëPḡCfC" CḡC-PIPμPSCḡ
C,CḡPëPiP»C-C†PμCḡPëPrC-PI C,P° PiC-PrPIPëC%oCfC" CḡC-PIPμPSCḡ HDL-
C...PsP»PμCfC,PμCḡPsP»Cf. PḡCḡPëPiP°P»Pμ P·P°CfC,PscfCfPIP°PSPSCḡ PiCḡPμPiP°CḡP°C,Cf
PSPμ PIPëPeP»PëPeP°P»Ps P·P±C-P»CHCëPμPSPSCḡ CḡC-PIPSḡ P»PμC,P°P»CHPSPsCfC,C-
CfPμCḡPμPr PiP°C†C-C"PSC,C-PI PiPsCḡC-PIPSḡPSPs P· PiP»P°C†PμP±Ps.

PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°.

PμCḡPë CḡPμPiCfP»CḡCḡPSPsPjCf PiCḡPëPMëPsPjC- C†PëP»PsCfC,P°P·PsP»Cf PI PrPsP·C- 100
PjPi 2 CḡP°P·Pë PSP° PrPsP±Cf Cf PiP°C†C-C"PSC,C-PI C-P· P·P°C...PiPsCḡCḡPIP°PSPSCḡPjPë
PiPμCḡPëC,,PμCḡPëC±PSPëC... CfCfPrPëPS CfC,P°P±C-P»CHPSPëPMë CfC,P°PS

PrPsCfCjPiP°C"C,CHCfCj PiCfjPsC,CjPiPsPj 4 PrPSC-PI. PpP°PeCfPpPjP°P»CHbPSP°
 PePsPSCtPmPSC,CfjP°CtC-Cj (PŸ_{max}) CtPpP»PsCfC,P°P·PsP»Cr C,P° PnPsPiPs
 PjPmCfjPiPpPSPSPpC... PjPmC,P°P±PsP»C-C,C-PI PiC-PrPiPpC%CrC"C,CHCfCj PjPmPSCf
 PiCfjPsPiPsCfjCtC-PnPsPs P· PiC-PrPiPpC%PmPSPSCjPj PrPsP·Pp, PiCfjPsC,Pm PiP»PsC%P°
 PiC-Pr PeCfjPpPiPsCf B«PePsPSCtPmPSC,CfjP°CtC-Cj-CtP°CfB» (AUC)
 CtPpP»PsCfC,P°P·PsP»Cr C,P° PnPsPiPs PjPmC,P°P±PsP»C-C,C-PI
 P·P±C-P»CHbCfCfC"C,CHCfCj PiCfjPp±P»PpP·PSPs PiCfjPsPiPsCfjCtC-PnPsPs PrPs
 PrPsP·CrPiP°PSPSCj. PjPiPSPpPn PjPmCfjC-PsPr PSP°PiC-PIPiPpPiPmPrPmPSPSCj
 CtPpP»PsCfC,P°P·PsP»Cr CfPeP»P°PrP°C" 10,5 PiPsPrPpPSPp. PtCfPSCfC" PrPiP°
 PiPsP»PsPiPSPpC... PjPmC,P°P±PsP»C-C,Pp bŸ" PrPmPiC-PrCfjPsCtPpP»PsCfC,P°P·PsP» C,P° 4'-
 C,CfjP°PSCf-PiC-PrCfjPsPeCfPpCtPpP»PsCfC,P°P·PsP», C%Ps PjP°CfC,CHb P±P»PpP·CHbPeC-
 PiPsPeP°P·PSPpPePp PSP°PiC-PIPiPpPiPmPrPmPSPSCj. P" PmPiC-PrCfjPsPjPmC,P°P±PsP»C-C,
 PjP°C" Cr 4-7 CfjP°P·C-PI PiPpC%Cr P°PSC,PpC,CfjPsPjP±PsC,PpCtPSCf
 P°PeC,PpPiPSC-CfC,CHb, PSC-PŸ PiPpC...C-PrPSP° CfjPmCtPsPiPpPSP°, P° 4'-C,CfjP°PSCf-
 PiC-PrCfjPsPeCfPpPjPmC,P°P±PsP»C-C, bŸ" 1/5 PIC-Pr P°PeC,PpPiPSPsCfC,C-
 CtPpP»PsCfC,P°P·PsP»Cr. PpPsPSCtPmPSC,CfjP°CtC-C— PI PiP»P°P·PjC- PeCfjPsPIC-
 (PsC,CfjPpPjP°PSC- P·P° PrPsPiPsPjPsPiPsCf AUC) PrPmPiC-PrCfjPs- C,P° 4'-C,CfjP°PSCf-
 PiC-PrCfjPsPeCfPpPjPmC,P°P±PsP»C-C,C-PI PiCfjPp±P»PpP·PSPs CfPeP»P°PrP°CfC,CHb 41 %
 C,P° 12 % PIC-Pr PePsPSCtPmPSC,CfjP°CtC-C— CtPpP»PsCfC,P°P·PsP»Cr PIC-PrPiPsPIC-PrPSPs.

PpPmC,P°P±PsP»C-P·Pj

PiPpP»PsCfC,P°P·PsP» PiPpPiPsPrPpC,CHCfCj PiPmCfjPmPiP°PŸPSPs P·P° PrPsPiPsPjPsPiPsCf
 PjPmC,P°P±PsP»C-P·PjCr C,P° PiPsPrP°P»CHbCfPsPiPs PiPpPiPmPrPmPSPSCj PnPsPiPs
 PjPmC,P°P±PsP»C-C,C-PI P·C- CfPmCtPmCf. PmPmCfjPiPpPSPSC- C-P·PsC,,PmCfjPjPmPSC,Pp
 CtPpC,PsC...CfjPsPjCr P 450, CjPeC- P±PmCfjCfC,CHb CrCtP°CfC,CHb Cr PnPsPiPs
 PjPmC,P°P±PsP»C-P·PjC-, bŸ" CYP3A4, PjPmPSCfPsCf PjC-CfjPsCf bŸ" CYP2C19 C,P° C%Pm
 PjPmPSCfPsCf PjC-CfjPsCf bŸ" CYP1A2.

P'PpPiPmPrPmPSPSCj

P"PsP»PsPiPSPpPn CfP»CjC... PiPpPiPmPrPmPSPSCj bŸ" P·C- CfPmCtPmCf (74 %),
 P·P°P»PpCfPePsPIC- PeC-P»CHbPePsCfC,C- PiPpPrC-P»CjCfC,CHCfCj P· PeP°P»PsPj.
 PkPmP·PSP°CtPSC- PeC-P»CHbPePsCfC,C- PSPmP·PjC-PSPmPSPsPiPs CtPpP»PsCfC,P°P·PsP»Cr
 PiPpPrC-P»CjCfC,CHCfCj P·C- CfPmCtPmCf, P° PjPmPSCf PSC-PŸ 2 % PnPsPiPs PrPsP·Pp
 PiPpPrC-P»CjC"C,CHCfCj Cr PiPpPiP»CjPrC- PrPmPiC-PrCfjPsCtPpP»PsCfC,P°P·PsP»Cr.
 PmCfjPp±P»PpP·PSPs 30 % PIC-Pr PiPsCtP°C,PePsPiPsC— PrPsP·Pp PiPpPrC-P»CjC"C,CHCfCj
 P·C- CfPmCtPmCf CjPe 4'-C,CfjP°PSCf-PiC-PrCfjPsPeCfPpPjPmC,P°P±PsP»C-C.,
 P—P°P»PpCfPePsPiP° PeC-P»CHbPeC-CfC,CHb PiPpPrC-P»CjC"C,CHCfCj CjPe CfCfPjP°
 PjPmC,P°P±PsP»C-C,C-PI, PŸPsPrPmPS P· CjPePpC... PSPm PiPmCfjPmPiPpC%CrC" 5 % PIC-Pr
 P·P°PiP°P»CHbPSPsC— PeC-P»CHbPePsCfC,C-.

P PsP·PiPsPrC-P»

PiPpP»PsCfC,P°P·PsP» P·PiPŸ™ CjP·CrC"C,CHCfCj P· P±C-P»PeP°PjPp PSP° 95-98 %,
 PiPmCfjPmPiP°PŸPSPs P· P°P»CHbP±CrPjC-PSPsPj. P" PmPiC-PrCfjPsPjPmC,P°P±PsP»C-C, C,P° 4'-
 C,CfjP°PSCf-PiC-PrCfjPsPeCfPpPjPmC,P°P±PsP»C-C, P·PiPŸ™ CjP·CrCfC,CHCfCj P·
 P±C-P»PeP°PjPp PSP° 97,4 % C,P° 66 % PIC-PrPiPsPIC-PrPSPs.

PkPmPjP°C" PiC-PrC,PIPmCfjPrPŸPmPSPSCj P·PrP°C,PSPsCfC,C- CtPpP»PsCfC,P°P·PsP»Cr
 C-PSPrCrPeCfPiP°C,Pp PjC-PeCfjPsCfPsPjP°P»CHbPSC- C,,PmCfjPjPmPSC,Pp PiPmCtC-PSPpPp.
 PpP°CfjPjP°PePsPeC-PSPmC,PpPeP° CtPpP»PsCfC,P°P·PsP»Cr C,P° PnPsPiPs

PjPμC,P°P±PsP»C-C,C-PI PSPμ P·P°P»PμP¶P°P»P° P·PSP°C‡PSPsC¶ PjC-C¶PpsC¶ PIC-Pr PIC-PeCf P°P±Ps C¶C,P°C,C- PIP°C‡C-C”PSC,C-PI PIC-PePsPj 50-80 C¶PpsPeC-PI.

PJ PIP°C‡C-C”PSC,C-PI P· C,C¶P¶PePsC¶ PSPeC¶PePsPIPsC¶ PSPμPrPsC¶C,P°C,PSC-C¶C,C¶ PIC-P»CHbPSP° C,,C¶P°PeC‡C-C¶ C‡Pp»PsC¶C,P°P·PsP»Cf P±CfP»P° PSP° 27 % PIPeC%PsC¶, P° PŸ_{max} C,P° AUC P±CfP»Pp PIC-PrPpPsPIC-PrPSPs PSP° 29 % C,P° 39 % PSPeP¶C‡PpPp, PSC-P¶ Cf PsC¶C-P± P· PSPsC¶PjP°P»CHbPSPsC¶ C,,CfPSPeC‡C-C”C¶ PSPeC¶PsPe. PŸ_{max} C,P° AUC PrPμPIC-PrC¶PpsPjPμC,P°P±PsP»C-C,Cf P±CfP»Pp PIC-PrPpPsPIC-PrPSPs PSP° 41 % C,P° 47 % PSPeP¶C‡PpPp Cf PIP°C‡C-C”PSC,C-PI P· C,C¶P¶PePpPp PpPsC¶CfC¶PμPSPSC¶PpPp PSPeC¶PsPe PpPsC¶C-PIPsC¶PSPs P· PIP°C‡C-C”PSC,P°PjPp P· PSPsC¶PjP°P»CHbPSPsC¶ C,,CfPSPeC‡C-C”C¶ PSPeC¶PsPe. PŸ_{max} C,P° AUC 4'-C,C¶P°PSCf- PiC-PrC¶PpsPeC¶PpPp»PsC¶C,P°P·PsP»Cf P±CfP»Pp PSP° 173 % C,P° 209 % PIC-PrPpPsPIC-PrPSPs PIPeC%PpPp Cf PIP°C‡C-C”PSC,C-PI P· C,C¶P¶PePsC¶ PSPeC¶PePsPIPsC¶ PSPμPrPsC¶C,P°C,PSC-C¶C,C¶. PkPμPjP°C” PrP°PSPeC... C%PsPrPs PIP°C‡C-C”PSC,C-PI P· PpPsPjC-C¶PSPsC¶ C,P° C,C¶P¶PePsC¶ PpμC‡C-PSPePsPIPsC¶ PSPμPrPsC¶C,P°C,PSC-C¶C,C¶.

РљР»С-РSC-С‡РSC- С...Р°С¶Р°РеС,РμС¶РеС¶С,РөРөРө.

РμРsРeР°Р·Р°РSPSC¶.

P”P»C¶ P·P±C-P»CHbC¶PμPSPSC¶ PjP°PeC¶PpP°P»CHbPSPsC— P±PμP·P±PsP»C-C¶PSPsC— PrPpC¶C,P°PSC‡C-C— C...PsPrCHbP±Pp Cf PIP°C‡C-C”PSC,C-PI P· PpμC¶PμPjC-P¶PSPsC¶ PeCfP»CHbPiP°PIC-C¶C,C¶, C¶PeC- PSPμ PjP°C¶C,CH P±PsP»C¶ Cf C¶C,P°PSC- C¶PpPsPePsC¶ C,P° PsP·PSP°Pe PSPμPeC¶PsP·Cf PpμC¶PpC,,PμC¶PpC‡PSPeC... C,PeP°PSPePS (P·P°C...PIPsC¶PpIP°PSPSC¶ PpμC¶PpC,,PμC¶PpC‡PSPeC... P°C¶C,PμC¶C-PN, C¶C,P°PrC-C¶ II P·P° PαPsPSC,PμPNPSPsPj).

P—P°C¶C,PsC¶PsPICfPIP°C,Pp C¶Pe C,PμC¶P°PiC-C¶ PrC¶CfPiPsC— P»C-PSC-C— PrP»C¶ PIP°C‡C-C”PSC,C-PI, Cf C¶PePpC... P·PjC-PSP° C¶C,PpP»C¶ P¶PpC,C,C¶ (PIPeP»C¶C‡P°C¶C‡Pp PIC-PrPjPsPICf PIC-Pr PeCfC¶C-PSPSC¶ C,P° PePsPSC,C¶PsP»CHbPsPIP°PSC- PpC¶PsPiC¶P°PjPp P·P°PSC¶C,CH C¶PpPsC¶C,PsPj) C,P° C-PSC€C- PIC-PrPpPsPIC-PrPSC- P·P°C...PsPrPp PSPμ PpC¶PpP·PIPμP»Pp PrPs P·PSP°C‡PSPsPiPs PpPsC¶P»P°P±P»PμPSPSC¶ C¶PpPjPiC,PsPjC-PI PpμC¶PμPjC-P¶PSPsC— PeCfP»CHbPiP°PIPsC¶C,C-.

РμС¶РsС,РөРiРsРeР°Р·Р°РSPSC¶.

- P’C-PrPsPjP° PiC-PpμC¶C‡CfC,P»PpPIC-C¶C,CH PrPs C‡Pp»PsC¶C,P°P·PsP»Cf P°P±Ps PrPs P±CfPrCHb-C¶PePsPiPs PePsPjPiPsPSPμPSC,P° PpC¶PμPiP°C¶P°C,Cf;
- C,C¶P¶PeP° PSPeC¶PePsPIP° PSPμPrPsC¶C,P°C,PSC-C¶C,CH (PeP»C-C¶PμPSCf PeC¶PμP°C,PpPSC-PSCf £ 25 PjP»/C...PI);
- PpPsPjC-C¶PSP° P°P±Ps C,C¶P¶PeP° PpμC‡C-PSPePsPIP° PSPμPrPsC¶C,P°C,PSC-C¶C,CH;
- P·P°C¶C,C-PN,PSP° C¶PμC¶C‡PμPIP° PSPμPrPsC¶C,P°C,PSC-C¶C,CH;
- PIP°PiC-C,PSC-C¶C,CH;

- P±CfPrCH-CΠPeP° PIC-PrPsPjP° CÍC...PëP»CHΨPSC-CÍC,CH PrPs PeCΨPsPIPSC,PμC±C-
(PSP°PíCΨPëPeP»P°Pr, PIPëCΨP°P·PeP° C€P»CfPSPeP° P°P±Ps
PrPIP°PSP°PrC†CΠC,PëPíP°P»PsC— PePëC€PePë CÍ CÍC,P°PrC-C— P·P°PiPsCÍC,CΨPμPSPSCΠ,
PSPμC%PsPrP°PIPS-C-PNë PiPμPjPsCΨP°PiC-C†PSPëPNë C-PSCÍCfP»CHC, (PíCΨPsC,CΠPiPsPj 6
PjC-CÍCΠC†C-PI), PíCΨPsP»C-C,,PμCΨP°C,PëPIPSP° C,,PsCΨPjP° PrC-P°P±PμC,PëC†PSPSC—
CΨPμC,PëPSPsPíP°C,C-C—, CÍP»P°P±PsPePsPSC,CΨPsP»CHPsPIP°PSP°
P°CΨC,PμCΨC-P°P»CHΨPSP° PiC-PíPμCΨC,PμPSP·C-CΠ);

- C€P»CfPSPSC†PePsPIP° C,P°C...C-PeP°CΨPrC-CΠ, C,,C-P±CΨPëP»CΠC†C-CΠ
C€P»CfPSPSC†PeC-PI P°P±Ps PjCfP»CHC,PëP»PsPeCfP»CΠCΨPSP° C€P»CfPSPSC†PePsPIP°
PμPeC,PsPíC-CΠ PI P°PSP°PjPSPμP·C- CÍ PíP°C†C-C”PSC,C-PI, CΠPeC- PíCΨPsC...PsPrPëP»Pë
P°P±Ps PSPμ PíCΨPsC...PsPrPëP»Pë PIC-PrPíPsPIC-PrPSCÍ C,PμCΨP°PíC-CΨ, P° C,P°PePsP¶
PíPsPrPsPIP¶PμPSPSCΠ C-PSC,PμCΨPIP°P»CÍ QT;

- C,CΠP¶PeP° C,P°C...C-P°CΨPëC,PjC-CΠ PI P°PSP°PjPSPμP·C-;

- PsPrPSPSC†P°CÍPSPμ P»C-PeCfPIP°PSPSCΠ PrPIPsPjP° P°P±Ps P±C-P»CHC€Pμ
PrPsPrP°C,PePsPIPëPjPë P°PSC,PëC,CΨPsPjP±PsC†PëC,P°CΨPSPëPjPë P·P°CÍPsP±P°PjPë P°P±Ps
P°PSC,PëPePsP°PiCfP»CΠPSC,P°PjPë (PSP°PíCΨPëPeP»P°Pr,
P°C†PμC,PëP»CÍP°P»C-C†PëP»PsPIP° PePëCÍP»PsC,P°, PeP»PsPíC-PrPsPiCΨPμP»CH,
PiPμPíP°CΨPëPS, PIP°CΨC,,P°CΨPëPS, P°C†PμPSPsPeCfPjP°CΨPsP», PrP°P±C-PíP°C,CΨP°PS,
CΨPëPIP°CΨPsPeCÍP°P±P°PS P°P±Ps P°PíC-PeCÍP°P±P°PS);

- PSPμCÍC,P°P±C-P»CHΨPSP° CÍC,PμPSPsPeP°CΨPrC-CΠ, C-PSC,,P°CΨPeC,
PjC-PsPeP°CΨPrP° PíCΨPsC,CΠPiPsPj PsCÍC,P°PSPSC-C... 6 PjC-CÍCΠC†C-PI P°P±Ps
PePsCΨPsPSP°CΨPSPμ PIC,CΨCfC†P°PSPSCΠ PíCΨPsC,CΠPiPsPj PsCÍC,P°PSPSC-C... 6
PjC-CÍCΠC†C-PI.

P·P°CÍPsP±Pë. PŸCÍPjC-CÍPSPëPNë PíCĤPëPNëPsPj C†PëP»PsCÍC,P°P·PsP»CÍ C,P°
PeP»PsPíC-PrPsPíCĤPµP»CĤ PSPµ PIPíP»PëPIP°PI PSP° PeC-P»CHPeC-CÍC,CH
C,CĤPsPjP±PsC†PëC,C-PI, PíCĤPsC,CĤPsPjP±C-PSPsPIPëPNë C†P°CÍ (PµPŞ) P°P±Ps
P°PeC,PëPIPsPIP°PSPëPNë C†P°CÍC,PePsPIPëPNë C,CĤPsPjP±PsPíP»P°CÍC,PëPSPsPIPëPNë
C†P°CÍ (PĥPŞPŸPŞ). PjCÍC- P·PrPsCĤPsPIC- PrPsP±CĤPsPIPsP»CHC†C- PjP°P»Pë
PíPsPrPsPIP¶PµPSPëPNë C†P°CÍ PeCĤPsPIPsC,PµC†C- PíCĤPë PíCĤPëPNëPsPjC-
PeP»PsPíC-PrPsPíCĤPµP»CĤ CµPe PjPsPSPsC,PµCĤP°PíC-C— C,P° PíCĤPë
CÍCÍPjC-CÍPSPsPjCÍ P·P°CÍC,PsCÍCÍPIP°PSPSC- P· C†PëP»PsCÍC,P°P·PsP»PsPj, C%Ps
PSPµ PíCĤPëP·PIPsPrPëP»Ps PrPs P·PSP°C†PSPsPiPs CÍCÍPjP°CĤPSPsPiPs PIPíP»PëPICÍ
PSP° C†P°CÍ PeCĤPsPIPsC,PµC†C-. PµCĤPsC,Pµ PíPsC,CĤC-P±PSPs
PrPsC,CĤPëPjCÍPIP°C,PëCÍCµ PsP±PµCĤPµP¶PSPsCÍC,C- PíCĤPë
PePsPjP±C-PSPsPIP°PSPsPjCÍ P·P°CÍC,PsCÍCÍPIP°PSPSC- C†PëP»PsCÍC,P°P·PsP»CÍ P·
P±CÍPrCH-CµPePëPjPë P°PSC,PëC,CĤPsPjP±PsC,PëC†PSPëPjPë P·P°CÍPsP±P°PjPë.
PŸP»C-Pr CĤPsP·PiP»CµPSCÍC,Pë PjPsP¶P»PëPIC-CÍC,CH PíPµCĤC-PsPrPëC†PSPsPiPs
PjPsPSC-C,PsCĤPëPSPiCÍ C†P°CÍCÍ PeCĤPsPIPsC,PµC†C-. P>C-PeCÍPIP°PSPSCµ
C†PëP»PsCÍC,P°P·PsP»PsPj PíCĤPsC,PëPíPsPeP°P·P°PSPs PíP°C†C-C”PSC,P°Pj, CµPeC-
PíCĤPëPNëPjP°CĤC,CH PrPIP° P°P±Ps P±C-P»CHC€Pµ PrPsPrP°C,PePsPIPëC...
P°PSC,PëC,CĤPsPjP±PsC†PëC,P°CĤPSPëC.../P°PSC,PëPePsP°PiCÍP»CµPSC,PSPëC...
P·P°CÍPsP±C-PI. P’C-P»CHC€ PIPëCÍPsPeP° C†P°CÍC,PsC,P° PIPëPíP°PrPeC-PI
PeCĤPsPIPsPIPëP»PëPIC-PI CÍPíPsCÍC,PµCĤC-PíP°P»P°CÍCµ PíCĤPë
PsPrPSPsC†P°CÍPSPsPjCÍ P·P°CÍC,PsCÍCÍPIP°PSPSC- PeP»PsPíC-PrPsPíCĤPµP»CĤ,
PĥPŸPĤ C- C†PëP»PsCÍC,P°P·PsP»CÍ PI PíCĤPsC†PµCÍC- PrPsCÍP»C-PrP¶PµPSPSCµ
CASTLE.

PµPµCĤPsCĤP°P»CHPSC- P°PSC,PëPePsP°PiCÍP»CµPSC,Pë (PSP°PíCĤPëPeP»P°Pr,
PIP°CĤC,,P°CĤPëPS). PµCĤPë PsPrPSPsCĤP°P·PsPIPsPjCÍ PíCĤPëPNëPsPjC- PSPµ P±CÍP»Ps
PIPëCµPIP»PµPSPs PíCĤPëPiPSC-C†PµPSPSCµ PjPµC,P°P±PsP»C-P·PjCÍ PIP°CĤC,,P°CĤPëPSCÍ
P°P±Ps PIPíP»PëPICÍ PSP° PíP°CĤP°PjPµC,CĤPë PePsP°PiCÍP»CµC†C-C— (PµPŞ, PĥPŞPŸPŞ,
C†P°CÍ PeCĤPsPIPsC,PµC†C-). PµCĤPsC,Pµ CĤPµPePsPjPµPSPPrPsPIP°PSPs
PrPsC,CĤPëPjCÍPIP°C,PëCÍCµ PsP±PµCĤPµP¶PSPsCÍC,C- PíP°C†C-C”PSC,P°Pj, CµPeC-
PíCĤPëPNëPjP°CĤC,CH C†PëP»PsCÍC,P°P·PsP» P· P±CÍPrCH-CµPePëPj
P°PSC,PëPePsP°PiCÍP»CµC†C-PNëPSPëPj P·P°CÍPsP±PsPj, C,P° PíCĤPsPIPsPrPëC,Pë
PíPµCĤC-PsPrPëC†PSPëPNë PjPsPSC-C,PsCĤPëPSPi PrP»Cµ PjC-PSC-PjC-P·P°C†C-C—
PjPsP¶P»PëPIPsCÍC,C- PeCĤPsPIPsC,PµC†C-. P>C-PeCÍPIP°PSPSCµ C†PëP»PsCÍC,P°P·PsP»PsPj
PíCĤPsC,PëPíPsPeP°P·P°PSPs PíP°C†C-C”PSC,P°Pj, CµPeC- PíCĤPëPNëPjP°CĤC,CH PrPIP° P°P±Ps
P±C-P»CHC€Pµ PrPsPrP°C,PePsPIPëC...
P°PSC,PëC,CĤPsPjP±PsC†PëC,P°CĤPSPëC.../P°PSC,PëPePsP°PiCÍP»CµPSC,PSPëC...
P·P°CÍPsP±C-PI.

P†PSPiC-P±C-C,PsCĤPë C†PëC,PsC...CĤPsPjCÍ P 450 (CYP). PíPëP»PsCÍC,P°P·PsP»
P·PSP°C†PSPsCĤ PjC-CĤPsCĤ PjPµC,P°P±PsP»C-P·CÍC”C,CHCÍCµ C,,PµCĤPjPµPSC,P°PjPë CYP,
PsCÍPsP±P»PëPIPs CYP3A4 C,P° CYP2C19, C- PjPµPSC€PsCĤ PjC-CĤPsCĤ BĤ” CYP1A2.
P”PµPiC-PrCĤPsPjPµC,P°P±PsP»C-C,, CµPePëPNë PjP°C” P°PSC,PëC,CĤPsPjP±PsC†PëC,P°CĤPSCÍ
P°PeC,PëPIPsC-CÍC,CH CÍ 4-7 CĤP°P·C-PI PIPëC%óCÍ, PSC-P¶ C†PëP»PsCÍC,P°P·PsP»,
C-PjPsPIC-CĤPSPs, CÍC,PIPsCĤCĤC”C,CHCÍCµ PiPsP»PsPIPsPëPj C†PëPSPsPj PíC-Pr PrC-C”CĤ
CYP3A4. 4'-C,CĤP°PSCÍ-PíC-PrCĤPsPeCÍPëPjPµC,P°P±PsP»C-C, P· P°PeC,PëPIPsC-CÍC,CĤ,
C%Ps PrPsCĤC-PIPsCĤC” 1/5 P°PeC,PëPIPsPSCÍC,C- C†PëP»PsCÍC,P°P·PsP»CÍ,
C-PjPsPIC-CĤPSPs,B CÍC,PIPsCĤCĤC”C,CHCÍCµ P·P° PrPsPíPsPjPsPiPsCĤ CYP2C19.
PŸP°PePëPj C†PëPSPsPj, P·P°CÍPsP±Pë, C%Ps PíCĤPëPiPSC-C†CÍCĤC,CH CYP3A4

(PSP°PīCḡPēPeP»P°Pr, PrPμCḡPeC- PjP°PeCḡPsP»C-PrPē, P°P·PsP»PsPIC-
PīCḡPsC,PēPīCḡPēP±PePsPIC- P·P°CḡPsP±Pē, C-PSPiC-P±C-C,PScḡPē PīCḡPsC,PμP°P·) P°P±Ps
CYP2C19 (PSP°PīCḡPēPeP»P°Pr, C-PSPiC-P±C-C,PScḡPē PīCḡPsC,PSPSPSPiPs PSP°CḡPsCḡP°),
PīC-PrPIPēC%CrCḡC,CH P·P°PiP°P»CHPSCr C,,P°CḡPjP°PePsP»PsPiC-C±PSCr
P°PeC,PēPIPSC-CḡC,CH PSP° 32 % C,P° 42 % PIC-PrPīPsPIC-PrPSPs C,P° PjPsPḡCḡC,CH
PīC-PrPIPēC%CrPIP°C,Pē PīPsP±C-C±PSC- PμC,,PμPeC,Pē C†PēP»PsCḡC,P°P·PsP»Cḡ. PḡPsPḡPμ
P±CḡC,Pē PSPμPsP±C...C-PrPSPēPj P·PSPēPḡPμPSPSCḡ PrPsP·Pē C†PēP»PsCḡC,P°P·PsP»Cḡ PrPs
50 PjPi 2 CḡP°P·Pē PSP° PrPsP±Cḡ P·P°P»PμPḡPSPs PIC-Pr C-PSPrPēPIC-PrCḡP°P»CHPSPsC-
PμC,,PμPeC,PēPIPSPsCḡC,C- C,P° PīPμCḡPμPSPsCḡPēPjPsCḡC,C-.

PμCḡPēPNēPsPj 100 PjPi C†PēP»PsCḡC,P°P·PsP»Cḡ PSP° 7-PNē PrPμPSCḡ
P·P°CḡC,PScḡCḡPIP°PSPSCḡ PμCḡPēC,CḡPsPjC-C†PēPSCr (PīPsPjC-CḡPSPēPNē
C-PSPiC-P±C-C,PScḡ CYP3A4) 500 PjPi 3 CḡP°P·Pē PSP° PrPsP±Cḡ PīCḡPēP·PIPSPPrPēP»Ps PrPs
PīC-PrPIPēC%PμPSPSCḡ AUC C†PēP»PsCḡC,P°P·PsP»Cḡ PrPs 74 %, CḡPePμ
CḡCḡPīCḡPsPIPsPrPḡCḡPIP°P»PsCḡCḡ P·PSPēPḡPμPSPSCḡPj PSP° 24 % AUC PNēPsPiPs
PrPμPiC-PrCḡPsPjPμC,P°P±PsP»C-C,Cḡ, P°P»Pμ P· PīPsPjC-C,PSPēPj PīC-PrPIPēC%PμPSPSCḡPj
AUC 4'-C,CḡP°PSCḡ-PiC-PrCḡPsPeCḡPēPjPμC,P°P±PsP»C-C,Cḡ. P— CḡCḡP°C...CḡPIP°PSPSCḡPj
P·PSP°C†PμPSCḡ AUC P·P°PiP°P»CHPSP° C,,P°CḡPjP°PePsP»PsPiC-C±PSP°
P°PeC,PēPIPSC-CḡC,CH C†PēP»PsCḡC,P°P·PsP»Cḡ P·P±C-P»CHC€CḡC''C,CHCḡCḡ PSP° 34 %
PīCḡPē PsPrPSPsC†P°CḡPSPsPjCḡ PNēPsPiPs PīCḡPēPNēPsPjC- P· PμCḡPēC,CḡPsPjC-C†PēPSPsPj.
PḡP° PīC-PrCḡC,P°PIC- C†PēC... PrP°PSPēC... CḡPμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P°
C†PēP»PsCḡC,P°P·PsP»Cḡ CḡC,P°PSPsPIPēC,CH 50 PjPi 2 CḡP°P·Pē PSP° PrPsP±Cḡ PīCḡPē
PsPrPSPsC†P°CḡPSPsPjCḡ PīCḡPēPNēPsPjC- P· PμCḡPēC,CḡPsPjC-C†PēPSPsPj C,P° P·
PīPsPrC-P±PSPēPjPē P»C-PeP°CḡCḡCHPePēPjPē P·P°CḡPsP±P°PjPē (PSP°PīCḡPēPeP»P°Pr, C-P·
PeP»P°CḡPēC,CḡPsPjC-C†PēPSPsPj).

PŸCḡPjC-CḡPSPēPNē PīCḡPēPNēPsPj PsPrPSPsCḡP°P·PsPIPēC... PrPsP· PePμC,PSPePsPSP°P·PsP»Cḡ
(CḡPēP»CHPSPēPNē C-PSPiC-P±C-C,PScḡ CYP3A4) 400 PjPi C,P° C†PēP»PsCḡC,P°P·PsP»Cḡ 100
PjPi PīCḡPēP·PIPSPPrPēPi PrPs PīC-PrPIPēC%PμPSPSCḡ AUC C†PēP»PsCḡC,P°P·PsP»Cḡ PSP° 117
, CḡPePμ CḡCḡPīCḡPsPIPsPrPḡCḡPIP°P»PsCḡCḡ P·PSPēPḡPμPSPSCḡPj PSP° 15 % AUC
PrPμPiC-PrCḡPsPjPμC,P°P±PsP»C-C,Cḡ C,P° PīC-PrPIPēC%PμPSPSCḡPj PSP° 87 % AUC 4'-
C,CḡP°PSCḡ-PiC-PrCḡPsPeCḡPēPjPμC,P°P±PsP»C-C,Cḡ. P— CḡCḡP°C...CḡPIP°PSPSCḡPj
P·PSP°C†PμPSCḡ AUC P·P°PiP°P»CHPSP° C,,P°CḡPjP°PePsP»PsPiC-C±PSP°
P°PeC,PēPIPSC-CḡC,CH C†PēP»PsCḡC,P°P·PsP»Cḡ P·P±C-P»CHC€CḡC''C,CHCḡCḡ PSP°
35 % PīCḡPē PsPrPSPsC†P°CḡPSPsPjCḡ P·P°CḡC,PScḡCḡPIP°PSPSC- P·
PePμC,PSPePsPSP°P·PsP»PsPj. PḡP° PīC-PrCḡC,P°PIC- C†PēC... PrP°PSPēC...
CḡPμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P° C†PēP»PsCḡC,P°P·PsP»Cḡ CḡC,P°PSPsPIPēC,CH
50 PjPi 2 CḡP°P·Pē PSP° PrPsP±Cḡ PīCḡPē PsPrPSPsC†P°CḡPSPsPjCḡ PīCḡPēPNēPsPjC- P·
PePμC,PSPePsPSP°P·PsP»PsPj C,P° P· PīPsPrC-P±PSPēPjPē P·P°CḡPsP±P°PjPē
(PSP°PīCḡPēPeP»P°Pr, P· C-C,CḡP°PePsPSP°P·PsP»PsPj).

P—P°CḡC,PScḡCḡPIP°PSPSCḡ 100 PjPi C†PēP»PsCḡC,P°P·PsP»Cḡ 2 CḡP°P·Pē PSP° PrPsP±Cḡ P·
PrPēP»C,C-P°P·PμPjPsPj (CḡP»P°P±PePēPNē C-PSPiC-P±C-C,PScḡ CYP3A4) 180 PjPi 1 CḡP°P·
PSP° PrPsP±Cḡ PīCḡPēP·PIPSPPrPēP»Ps PrPs PīC-PrPIPēC%PμPSPSCḡ AUC
C†PēP»PsCḡC,P°P·PsP»Cḡ PSP° 44 %, CḡPePμ CḡCḡPīCḡPsPIPsPrPḡCḡPIP°P»PsCḡCḡ
P·P±C-P»CHC€PμPSPSCḡPj AUC PrPμPiC-PrCḡPsPjPμC,P°P±PsP»C-C,Cḡ PSP° 4 % C,P°
P·P±C-P»CHC€PμPSPSCḡPj AUC 4'-C,CḡP°PSCḡ-PiC-PrCḡPsPeCḡPēPjPμC,P°P±PsP»C-C,Cḡ PSP°
43 %. P— CḡCḡP°C...CḡPIP°PSPSCḡPj P·PSP°C†PμPSCḡ AUC P·P°PiP°P»CHPSP°
C,,P°CḡPjP°PePsP»PsPiC-C±PSP° P°PeC,PēPIPSC-CḡC,CH C†PēP»PsCḡC,P°P·PsP»Cḡ
P·P±C-P»CHC€CḡC''C,CHCḡCḡ PSP° 19 % PīCḡPē PsPrPSPsC†P°CḡPSPsPjCḡ PīCḡPēPNēPsPjC- P·

PrPëP»C,C-P°P·PμPjPsPj. P°CḡCfPSC,CfCḡCfPëCfCḡ PSP° C†PëC... PrP°PSPëC...,
PePsCḡPëPiCfPIP°PSPSCḡ PrPsP·Pë PSPμ PīPsC,CḡC-P±PSPs.

PμCḡPëPNëPsPj PsPrPSPsCḡP°P·PsPIPsC— PrPsP·Pë 100 PjPi C†PëP»PsCfC,P°P·PsP»Cf P· 240 PjP»
PiCḡPμPNëPīC,,CḡCfC,PsiPIPsPiPs CfPsPeCf (C-PSPiC-P±C-C,PSCḡ PePëCëPePsPIPsPiPs CYP3A4)
PSPμ PIPëCḡPIP»CḡPI PīPsPjC-C,PSPsPiPs PμC,,PμPeC,Cf PSP°
C,,P°CḡPjP°PePsPeC-PSPμC,PëPeCf C†PëP»PsCfC,P°P·PsP»Cf. Pj P·PIḡḡ CḡP·PeCf P· C†PëPj
PePsCḡPëPiCfPIP°PSPSCḡ PrPsP·Pë PSPμ PīPsC,CḡC-P±PSPs. PμCḡPsC,Pμ PIPḡPëPIP°PSPSCḡ
PIPμP»PëPePëC... PsP±CfCḡPiC-PI PiCḡPμPNëPīC,,CḡCfC,PsiPIPsPiPs CfPsPeCf PjPsPḡPμ
PjP°C,Pë PeP»C-PSC-C†PSPs P·PSP°C†CfC%PëPNë PIPiP»PëPI PSP°
C,,P°CḡPjP°PePsPeC-PSPμC,PëPeCf C†PëP»PsCfC,P°P·PsP»Cf.

P—P°CfC,PsiCfCfPIP°PSPSCḡ C†PëP»PsCfC,P°P·PsP»Cf P· PsPjPμPīCḡP°P·PsP»PsPj
(C-PSPiC-P±C-C,PSCḡPsPj CYP2C19) PīCḡPëP·PIPsPrPëP»Ps PrPs P·P±C-P»CḡCëPμPSPSCḡ AUC
C†PëP»PsCfC,P°P·PsP»Cf PSP° 22 %, CḡPePμ CfCfPīCḡPsPIPsPrPḡCfPIP°P»PsCfCḡ
P·P±C-P»CḡCëPμPSPSCḡPj AUC PrPμPiC-PrCḡPsPjPμC,P°P±PsP»C-C,Cf PSP° 68 % C-
P·PSPëPḡPμPSPSCḡPj AUC 4'C,CḡP°PSCf-PiC-PrCḡPsPeCfPëPjPμC,P°P±PsP»C-C,Cf PSP° 36 %.
P— CfCḡP°C...CfPIP°PSPSCḡPj P·PSP°C†PμPSCḡ AUC P·P°PiP°P»CḡPSP°
C,,P°CḡPjP°PePsP»PsPiC-C†PSP° P°PeC,PëPIPsC-CfC,Cḡ C†PëP»PsCfC,P°P·PsP»Cf
P·P±C-P»CḡCëCfC"C,CḡCfCḡ PSP° 47 % PīCḡPë PsPrPSPsC†P°CfPSPsPjCf PīCḡPëPNëPsPjC- P·
PsPjPμPīCḡP°P·PsP»PsPj. PkP° PīC-PrCfC,P°PIC- C†PëC... PrP°PSPëC...
CḡPμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P° C†PëP»PsCfC,P°P·PsP»Cf CfC,P°PSPsPIPëC,Cḡ 50 PjPi 2
CḡP°P·Pë PSP° PrPsP±Cf PīCḡPë PsPrPSPsC†P°CfPSPsPjCf PīCḡPëPNëPsPjC- P·
PsPjPμPīCḡP°P·PsP»PsPj.

PŸCzP±CfC,CḡP°C,Pë C,,PμCḡPjPμPSC,Cz C†PëC,PsC...CḡPsPjCz P 450. P°CfP»Ps
PIC-PrP·PSP°C†PμPSPs PīC-PrPIPëC%PμPSPSCḡ C†PëP»PsCfC,P°P·PsP»PsPj AUC
P»PsPIP°CfC,P°C,PëPSCf (C†CfC,P»PëPIPëPNë CfCfP±CfC,CḡP°C, CYP3A4) C,P° PNëPsPiPs
β-PiC-PrCḡPsPeCfPëPePëCfP»PsC,Pë PrPs 70 %. PŸP»C-Pr PrPsC,CḡPëPjCfPIP°C,PëCfCḡ
PsP±PμCḡPμPḡPSPsCfC,C- PīCḡPë CfCfPjC-CfPSPsPjCf PīCḡPëPNëPsPjC-
C†PëP»PsCfC,P°P·PsP»Cf P·C- CfCfP±CfC,CḡP°C,P°PjPë CYP3A4 P· PICfP·CḡPePëPj
C,PμCḡP°PiPμPIC,PëC†PSPëPj C-PSPPrPμPeCfPsPj (C,P°PePëPjPë CḡPe C†PëP·P°PīCḡPëPr,
PiP°P»PsC,,P°PSC,CḡPëPS, PīC-PjPsP·PëPr, PīPsC...C-PrPSC- CḡC-PḡPeC-PI). PμPsC,CḡC-P±PSPs
PrPsC,CḡPëPjCfPIP°C,PëCfCḡ PsP±PμCḡPμPḡPSPsCfC,C- PīCḡPë PsPrPSPsC†P°CfPSPsPjCf
PīCḡPëPNëPsPjC- C†PëP»PsCfC,P°P·PsP»Cf P·C- CfC,P°C,PëPSP°PjPë, C%Ps
PjPμC,P°P±PsP»C-P·CfCḡC,CḡCfCḡ C,,PμCḡPjPμPSC,P°PjPë C†PëC,PsC...CḡPsPjCf CYP3A4,
PSP°PīCḡPëPeP»P°Pr P·C- CfPëPjPIP°CfC,P°C,PëPSPsPj, P°C,PsCḡPIP°CfC,P°C,PëPSPsPj C-
P»PsPIP°CfC,P°C,PëPSPsPj.

P†PSPrCzPeC,PsCḡPë C,,PμCḡPjPμPSC,Cz C†PëC,PsC...CḡPsPjCz P 450. P°PīP»PëPI
C-PSPPrCfPeC,PsCḡC-PI CYP3A4 C,P° CYP2C19 (C,P°PePëC... CḡPe PeP°CḡP±P°PjP°P·PμPīC-PS,
C,,PμPSC-C,PsC—PS, CḡPëC,,P°PjPīC-C†PëPS C,P° PīCḡPμPīP°CḡP°C,Pë P·PIC-CḡPsP±PsCḡ)
PSP° C,,P°CḡPjP°PePsPeC-PSPμC,PëPeCf C†PëP»PsCfC,P°P·PsP»Cf PSPμ P±CfPI
PrPsCfP»C-PrPḡPμPSPëPNë. PŸPμPsCḡPμC,PëC†PSPs P°PSC,PëC,CḡPsPjP±PsC,PëC†PSP° PrC-Cḡ
PjPsPḡPμ P±CfC,Pë P·PjC-PSPμPSP°, C,PsPjCf PSPμPsP±C...C-PrPSPs PīCḡPsPIPsPrPëC,Pë
PjPsPSC-C,PsCḡPëPSPi Cf CḡP°P·C- P·P°CfC,PsCfCfPIP°PSPSCḡ C†PëP»PsCfC,P°P·PsP»Cf P·
C-PSPPrCfPeC,PsCḡP°PjPë CYP3A4 C,P° CYP2C19.

PμC-Pr C†P°Cf PrPsCfP»C-PrPḡPμPSCḡ C,CḡC,CḡPSPsPīP°P»C-PSPSCḡ (CḡPePμ
C-PSPPrCfPeCfC" CYP1A2) P·PSPëPḡCfPIP°P»Ps PePsPSC†PμPSC,CḡP°C†C-Cḡ
C†PëP»PsCfC,P°P·PsP»Cf Cf PīP»P°P·PjC- PeCḡPsPIC- PSP° 18 %.

P†PSC€C- PīPsC, PμPSC†C- PNεPSC- PIP·P°C”PjPsPrC-C—

PŸP»C-Pr PrPsC, CħPëPjCrPIP°C, PëC†Cı PsP±PμCħPμP¶PSPsC†C, C- PīCħPë
PsPrPSPsC†P°C†PSPsPjCr P·P°C†C, PsC†C†PIP°PSPSC- C†PëP»PsC†C, P°P·PsP»Cr P· P±CrPrCħ-
CıPePëPj C-PSC€PëPj P·P°C†PsP±PsPj, P·PrP°C, PSPëPj P·PSPëP¶CrPIP°C, Pë
P°CħC, PμCħC-P°P»CħPSPëPNε C, PëC†Pe, C†PμCħPμP· PjPsP¶P»PëPIC-C†C, Cħ
CħPsP·PIPëC, PeCr P°PrPëC, PëPIPSPsPiPs PiC-PiPsC, PμPSP·PëPIPSPsPiPs PμC,, PμPeC, Cr, C%oPs
C†C†PīCħPsPIPsPrP¶CrC”C, CħC†Cı CħPμC,, P»PμPeC, PsCħPSPsCħ C, P°C...C-PeP°CħPrC-C”Cħ.

PħC†PsP±P»PëPIPsC†C, C- P·P°C†C, PsC†CžPIP°PSPSCı.

PμCħPëPNεPSCıC, PSC-C†C, Cħ P»C-PeCrPIP°PSPSCı C†PëP»PsC†C, P°P·PsP»PsPj
C†P»C-Pr CħPμC, PμP»CħPSPs PsC†C-PSCħPIP°C, Pë PīPsCħCıPr P· C-PSC€PëPjPë
PIP°CħC-P°PSC, P°PjPë P»C-PeCrPIP°PSPSCı, C, P°PePëPjPë CıPe
CħPμPIP°C†PeCrP»CıCħPëP·P°C†C-Cı.

P’ C†PëP»Cr C†PIPsPiPs PjPμC...P°PSC-P·PjCr PrC-C— C†PëP»PsC†C, P°P·PsP» PjPsP¶Pμ
C†PīCħPëC†PëPSPëC, Pë C, P°C...C-PeP°CħPrC-Cħ, PIC-PrC†CrC, C, Cı C†PμCħC†PμP±PëC, C, Cı,
C, P°C...C-P°CħPëC, PjC-Cħ C, P°/P°P±Ps P°CħC, PμCħC-P°P»CħPSC† PiC-PiPsC, PμPSP·C-Cħ.
P—P±C-P»CħC€PμPSPSCı C†P°C†C, PsC, Pë C†PμCħC†PμPIPëC... C†PePsCħPsC†PμPSCħ,
P°C†PsC†C-PNεPsPIP°PSPμ P· C†PëP»PsC†C, P°P·PsP»PsPj, C†C, P°PSPsPIPëC, Cħ
PīCħPëP±P»PëP·PSPs PIC-Pr 5 PrPs 7 CrPrP°CħC-PI PSP° C...PIPëP»PëPSC†, C, PsPjCr Cr
PīP°C†C-C”PSC, C-PI C-P· CħPëP·PëPePsPj PrP°PSPsPiPs CıPIPëC%oP° PīCħPμPīP°CħP°C,
PjPsP¶Pμ C†PīCħPëC†PëPSCıC, Pë C†C, PμPSPsPeP°CħPrC-Cħ.

P—P°B PīP°C†C-C”PSC, P°PjPë, CıPeC- PjPsP¶CrC, Cħ P±CrC, Pë C†C...PëP»CħPSC- PrPs
PīC-PrPIPëC%oPμPSPsPiPs CħPëP·PëPeCr C†PμCħPNεPsP·PSPëC... PīPsP±C-C†PSPëC...
PμC,, PμPeC, C-PI P· P±PsPeCr C†PμCħC†Cı PI CħPμP·CrP»CħC, P°C, C-
P·P±C-P»CħC€PμPSPSCı C†P°C†C, PsC, Pë C†PμCħC†PμPIPëC... C†PePsCħPsC†PμPSCħ,
PSP°PīCħPëPeP»P°Pr P·P° PīP°C†C-C”PSC, P°PjPë P·C- C†C, P°P±C-P»CħPSPsCħ
C-C€PμPjC-C†PSPsCħ C...PIPsCħPsP±PsCħ C†PμCħC†Cı, C†P»C-Pr CħPμC, PμP»CħPSPs
C†PīPsC†C, PμCħC-PiP°C, Pë PīC-Pr C†P°C† P»C-PeCrPIP°PSPSCı C†PëP»PsC†C, P°P·PsP»PsPj;
PīPsC, CħC-P±PSPs PICħP°C...PsPIC†PIP°C, Pë, C%oPs C†PëP»PsC†C, P°P·PsP»
PīCħPsC, PëPīPsPeP°P·P°PSPëPNε PīP°C†C-C”PSC, P°Pj, CıPeC- PīPμCħPμPSPμC†P»Pë
PSPμC†C, P°P±C-P»CħPSC† C†C, PμPSPsPeP°CħPrC-Cħ P°P±Ps C-PSC,, P°CħPeC,
PjC-PsPeP°CħPrP°/PePsCħPsPSP°CħPSPμ PIC, CħCrC†P°PSPSCı PīCħPsC, CıPiPsPj
PsC†C, P°PSPSC-C... 6 PjC-C†CıC†C-PI, C, P° PīP°C†C-C”PSC, P°Pj P· C, CıP¶PePsCħ
C, P°C...C-P°CħPëC, PjC-C”Cħ PI P°PSP°PjPSPμP·C-.

PŸP»C-Pr PrPsC, CħPëPjCrPIP°C, PëC†Cı PsP±PμCħPμP¶PSPsC†C, C- PīCħPë
PīCħPëP·PSP°C†PμPSPSC- C†PëP»PsC†C, P°P·PsP»Cr PīP°C†C-C”PSC, P°Pj P· PμPeC, PsPīC-C”Cħ
PīPμCħPμPrC†PμCħPrCı C- C€P»CrPSPsC†PeC-PI, P° C, P°PePsP¶ PīP°C†C-C”PSC, P°Pj C-P·
C,, C-P±CħPëP»CıC†C-C”Cħ P°P±Ps C, CħC-PiPsC, C-PSPSCıPj PīPμCħPμPrC†PμCħPrCı.

PμP°C†C-C”PSC, C-PI PSPμPsP±C...C-PrPSPs PīPsPīPμCħPμPrPëC, Pë PīCħPs
PSPμPsP±C...C-PrPSC-C†C, Cħ P·PIPμCħPSC†C, PëC†Cı PrPs P»C-PeP°CħCı Cr PIPëPīP°PrPeCr
PīPsCıPIPë PeCħPsPIPsC, PμC† P°P±Ps C†PëPSC†C-PI PīC-Pr C†P°C† C, PμCħP°PīC-C—. Pj
CħP°P·C- PīPsCıPIPë PsC†PSPëC... PeCħPsPIPsC, PμC† PīCħPëPNεPsPj C†PëP»PsC†C, P°P·PsP»Cr
PSPμPsP±C...C-PrPSPs PīCħPëPīPëPSPëC, Pë.

PhCTPec-P»CHPePe PictHpmPip°CtH°P°C, P·PrP°C,PSPePN PictHpePipSC-CtCrPIP°P°C,Pë
P°PictHpmPip°CtC-CH C,CHPsPjP±PsCtPëC,C-PI, P·P±C-P»CHC€CtC°°C,CHCtCt CtpëP·PëPe
PeCHPsPIPsC,PµCt Pïc-Pr CtP°Ct C...C-CHCrCHPïc-CtPSPëC... PIC,CHCrCtP°PSCH
(PIPeP»CHCtP°CHCtPë PSPµP·PSP°CtPSC- PIC,CHCrCtP°PSPSCt, PSP°PictHpePeP»P°Pr
PIPëPrP°P»PµPSPSCt P·CrP±P°). PïPeC%Ps PïP°CtC-C°PSC,Cr PSPµPsP±C...C-PrPSPs
PictHpsPIPµCtC,Pë C...C-CHCrCHPïc-CtPSPµ PIC,CHCrCtP°PSPSCt C-
P°PSC,PëP°PictHpmPip°CtC-PN°PSPëPN PµC,,PµPeC, C° PSPµP±P°P¶P°PSPëPj, PictHpePN°PsPj
CtPëP»PsCtC,P°P·PsP»Cr CtP»C-Pr PictHpePipëPSPëC,Pë P·P° 5 PrPSC-PI PrPs
PsPïPµCHP°CtC-C—.

PkP°PrC...PsPrPëP»Pë PïPsPsPrPëPSPsPeC- PïPsPIC-PrPsPjP»PµPSPSCt PictHps
PiPµPjP°P°C,PsP»PsPïc-CtPSC- PIC-PrC...PëP»PµPSPSCt, PIPeP»CHCtP°CHCtPë
C,CHPsPjP±PsCtPëC,PsPïPµPSC-CH, P»PµPN°PePsPïPµPSC-CH, P°PictH°PSCtP»PsCtPëC,PsP·,
PïP°PSCtPëC,PsPïPµPSC-CH C,P° P°PïP»P°CtC,PëCtPSCt P°PSPµPjC-CH. P°C-P»CHC€C-CtC,CH
PïP°CtC-C°PSC,C-PI PIPëPrCtP¶CtPIP°P»Pë Pïc-CtP»Ct PictHpePipëPSPµPSPSCt
PictHpePN°PsPjCr CtPëP»PsCtC,P°P·PsP»Cr. PµCHPsC,Pµ PrPµPeC-P»CHPeP° PIPëPïP°PrPeC-PI
PïP°PSCtPëC,PsPïPµPSC-C— C,P° P°PïP»P°CtC,PëCtPSPsC— P°PSPµPjC-C— PjP°P»Pë
P»PµC,P°P»CHPSPëPN° PSP°CtP»C-PrPsPe.

PµP°CtC-C°PSC,C-PI CtP»C-Pr PïPsPïPµCHPµPrPëC,Pë PictHps PSPµPsP±C...C-PrPSC-CtC,CH
PSPµPip°PN°PSPs PïPsPIC-PrPsPjP»CtC,Pë PictHps P±CtPrCH-CtPeC- PsP·PSP°PePë, CtPeC-
PjPsP¶CtC,CH CtPIC-PrCtPëC,Pë PictHps CHP°PSPSC-PN° CHPsP·PIPëC,PsPe
PïP°P°C,PsP»PsPïc-CtPSPëC... P·PjC-PS PeCHPsPIC-, C,P°PePëC... CtPe Pïc-PïPµCHC,PµCHPjC-Ct
C,P° P±C-P»CH Cr PïPsCHP»C-. PkPµPsP±C...C-PrPSPs PictHpsPIPµCtC,Pë PïPsPIPSPëPN°
P°PSP°P»C-P· PeCHPsPIC-, CtPeC%Ps C° Pïc-PrPsP·CHP° PSP° C-PSC,,PµPeCtC-CH P°P±Ps
PSP°CtPIPSC- P±CtPrCH-CtPeC- C-PSC€C- PeP»C-PSC-CtPSC- PsP·PSP°PePë
PïP°P°C,PsP»PsPïc-CtPSPëC... P·PjC-PS PeCHPsPIC-. PµCHPëPN°PsPj CtPëP»PsCtC,P°P·PsP»Cr
CtP»C-Pr PictHpePipëPSPëC,Pë, CtPeC%Ps C° PeP»C-PSC-CtPSC- P°P±Ps
P»P°P±PsCHP°P°C,PsCHPSC- PrPsPeP°P·Pë PïP°P°C,PsP»PsPïc-CtPSPëC... P·PjC-PS PeCHPsPIC-.

Pj PïP°CtC-C°PSC,C-PI, CtPeC- PictHpePN°PjP°P»Pë PïPsC,CrP¶PSC- C-PSPïc-P±C-C,PsCHPë
CYP3A4 P°P±Ps CYP2C19, CtPïPsCtC,PµCHC-PïP°P»PsCtCt P·P±C-P»CHC€PµPSPSCt
CHC-PIPSCt CtPëP»PsCtC,P°P·PsP»Cr Cr PïP»P°P·PjC- PeCHPsPIC-. Pj C,P°PePëC...
PIPëPïP°PrPeP°C... CHPµPePsPjPµPSPrPsPIP°PSP° PrPsP·P° CtPëP»PsCtC,P°P·PsP»Cr
CtC,P°PSPsPIPëC,CH 50 PjPi 2 CHP°P·Pë PSP° PrPsP±Ct.

PkPµPsP±C...C-PrPSP° PsP±PµCHPµP¶PSC-CtC,CH PictHpe CtCrPjC-CtPSPsPjCr
P·P°CtC,PsCtCrPIP°PSPSC- CtPëP»PsCtC,P°P·PsP»Cr P· C-PSPïc-P±C-C,PsCHP°PjPë P°P±Ps
C-PSPrCtPeC,PsCHP°PjPë CYP 3A4, CYP 2C19 P°P±Ps CtCrP±CtC,CHP°P°C,P°PjPë CYP 3A4.

PkPµPsP±C...C-PrPSPs P· PsP±PµCHPµP¶PSC-CtC,CH PictHpeP·PSP°CtP°P°C,Pë PictHpmPip°CtH°P°C,
PïP°CtC-C°PSC,P°Pj C-P· PïPµCHPµPrCtPµCHPPrPSPsCH P°P±Ps C€P»CrPSPsCtPePsPIPsCH
PµPeC,PsPïc-C°CH, C,,C-P±CHPëP»CtCtC-C°CH P°P±Ps C,CHC-PïPsC,C-PSPSCtPj
PïPµCHPµPrCtPµCHPPrCH.

PkPµPsP±C...C-PrPSP° PsP±PµCHPµP¶PSC-CtC,CH PictHpe CtCrPjC-CtPSPsPjCr
PictHpePN°PsPjC- CtPëP»PsCtC,P°P·PsP»Cr P· P±CtPrCH-CtPePëPjPë C-PSC€PëPjPë
P»C-PeP°CHCtCHPePëPjPë P·P°CtPsP±P°PjPë, C%Ps PjPsP¶CtC,CH P·PSPëP¶CtPIP°P°C,Pë
P°CHC,PµCHC-P°P»CHPSPëPN° C,PëCtPe, PsCtPeC-P»CHPePë C-CtPSCtC° CHPëP·PëPe
P°PrPëC,PëPIPSPsPïPs Pïc-PïPsC,PµPSP·PëPIPSPsPïPs PµC,,PµPeC,Cr P·
CHPµC,,P»PµPeC,PsCHPSPsCH C,P°C...C-PeP°CHPPrC-C°CH.

РҮР»С-Рr PrPsC,СҲРөРјСrPIP°С,РөСГCЦ PsP±PμCҲPμP¶PSPsCГC,С- PиCҲРө
PиCҲРөP·PSP°С±PμPSPSC- C†PөP»PsCГC,P°P·PsP»Cр P· P±CрPrCH-ClPePөPјPө C-PSC€PөPјPө
P°PSC,PөC,СҲPsPјP±PsC,PөC±PSPөPјPө P·P°CГPsP±P°PјPө.

P·C,,PμPeC, PiP°P»CHPјCрPIP°PSPSCЦ PSP°PiP°PrCр C-PSCГCрP»CHC,Cр, C%oPs
PиCҲPsCЦPIP»CЦC" C†PμPNө PiCҲPμPiP°CҲP°C,, PSPμ PrPsCГP»C-PrP¶CрPIP°PICГCЦ PиCҲРө
P°CГPөPјPiC,PsPјP°C,PөC±PSPsPјCр C-C€PμPјC-C±PSPsPјCр C-PSCГCрP»CHC,С-.

*P—P°CГC,PsCГCзPIP°PSPSCЦ Cз PiPμCҲC-PsPr PIP°PiC-C,PSPsCГC,С- P°P±Ps
PiPsPrCзPIP°PSPSCЦ PiCҲCзPrPrCH.*

P'P°PiC-C,PSC-CГC,CH

P'C-PrCГCрC,PSC- PиC-PrC,PIPμCҲPrP¶PμPSC- PrP°PSC- C%oPsPrPs
P·P°CГC,PsCГCрPIP°PSPSCЦ C†PөP»PsCГC,P°P·PsP»Cр PIP°PiC-C,PSPөPј,
PiPsC,PμPSC†C-PNөPSPөPNө CҲРөP·PөPe PSPμPIC-PrPsPјPөPNө. P"PsCГP»C-PrP¶PμPSPSCЦ PSP°
C,PIP°CҲРөPSP°C... PiPsPeP°P·P°P»Pө CҲPμPiCҲPsPrCрPeC,PөPIPSCр
C,PsPeCГPөC±PSC-CГC,CH. PμPsC,PμPSC†C-PNөPSPөPNө CҲРөP·PөPe PSPμPIC-PrPsPјPөPNө,
C,PsPјCр C†PөP»PsCГC,P°P·PsP» PSPμ PјPsP¶PSP° PiCҲРөPNөPјP°C,Pө Cр PiPμCҲC-PsPr
PIP°PiC-C,PSPsCГC,С-.

PμPμCҲC-PsPr PiPsPrCзPIP°PSPSCЦ PiCҲCзPrPrCH

P"PsCГP»C-PrP¶PμPSPSCЦ PSP° C,PIP°CҲРөPSP°C... PiPsPeP°P·P°P»Pө, C%oPs
C†PөP»PsCГC,P°P·PsP» PјPsP¶Pμ PiCҲPsPSPөPeP°C,Pө Cр PiCҲCрPrPSPμ PјPsP»PsPePs.
PҮPsC±PSC- PrP°PSC- PiCҲPs PiCҲPsPSPөPePSPμPSPSCЦ C†PөP»PsCГC,P°P·PsP»Cр Cр
PiCҲCрPrPSPμ PјPsP»PsPePs P¶C-PSPөPө PIC-PrCГCрC,PSC-. P'CҲP°C...PsPICрCHC±Pө
PјPsP¶P»PөPIPөPNө PSPμPiP°C,PөPIPSPөPNө PIPiP»PөPI PSP° PrPөC,PөPSCр,
P·P°CГC,PsCГCрPIP°PSPSCЦ PiCҲPμPiP°CҲP°C,Cр Cр PiPμCҲC-PsPr PiPsPrCрPIP°PSPSCЦ
PiCҲCрPrPrCH PSPμ CҲPμPePsPјPμPSPPrCрC"С,CHCГCЦ. Pј CҲP°P·C-
PSPμPsP±C...C-PrPSPsCГC,С- P»C-PөCрPIP°PSPSCЦ C†PөP»PsCГC,P°P·PsP»PsPј CГP»C-Pr
PiCҲРөPiPөPSPөC,Pө PiPsPrCрPIP°PSPSCЦ PiCҲCрPrPrCH.

PαPμCҲC,PөP»CHPSC-CГC,CH

P"PsCГP»C-PrP¶PμPSPSCЦ PSP° C,PIP°CҲРөPSP°C... PiPsPeP°P·P°P»Pө, C%oPs
C†PөP»PsCГC,P°P·PsP» PSPμ PIPiP»PөPIP°C" PSP° C,,PμCҲC,PөP»CHPSC-CГC,CH.

*P—PrP°C,PSC-CГC,CH PIPiP»PөPIP°C,Pө PSP° C€PIPөPrPeC-CГC,CH CҲPμP°PeC†C-C—
PiCҲРө PePμCҲCзPIP°PSPSC- P°PIC,PsC,СҲP°PSCГPiPsCҲC,PsPј P°P±Ps C-PSC€PөPјPө
PјPμC...P°PSC-P·PјP°PјPө.*

РҮР»С-Рr PrPsC,СҲРөРјСrPIP°С,РөСГCЦ PsP±PμCҲPμP¶PSPsCГC,С-, PsCГPeC-P»CHPePө
PиCҲРө PiCҲРөPNөPsPјC- PiCҲPμPiP°CҲP°C,Cр PјPsP¶P»PөPIPμ P·P°PiP°PјPsCҲPsC±PμPSPSCЦ.

PҮPiPsCГC-P± P·P°CГC,PsCГCзPIP°PSPSCЦ C,P° PrPsP·Pө.

P"PsP·CзPIP°PSPSCЦ

P PμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P° PiCḡPμPiP°CḡP°C,Cr Bḡ“ PīPs 100 PjPi 2 CḡP°P·Pē PSP° PrPsP±Cr. PŷP°P±P»PμC,PePē PiCḡPēPNḡPjP°CḡC,CH P·P° 30 C...PIPēP»PēPS PrPs PIP¶PēPIP°PSPSC¶ C—P¶C- P°P±Ps C†PμCḡPμP· 2 PiPsPrPēPSPē PiC-ClP»C¶ PIP¶PēPIP°PSPSC¶ C—P¶C-, PICḡP°PSC†C- C,P° PIPiPμC†PμCḡC-.

PμCḡPēPNḡPsPj PiCḡPμPiP°CḡP°C,Cr PiC-Pr C†P°Cl C—PrPē PjPsP¶Pμ PiC-PrPIPēC%CrPIP°C,Pē PNḡPsPiPs PjP°PeClPēPjP°P»CHPSCr PePsPSC†PμPSC,CḡP°C†C-CH PI PīP»P°P·PjC- PeCḡPsPIC-, C%Ps P·P±C-P»CHC€CrC” CḡPēP·PēPe PIPēPSPēPePSPμPSPSC¶ PiPsP±C-C†PSPēC... CḡPμP°PeC†C-PNḡ. P—PSP°C†PSPμ PiPsPeCḡP°C%PμPSPSC¶ ClC,P°PSCr PīP°C†C-C”PSC,C-PI ClPiPsClC,PμCḡC-PiP°C”C,CHClC¶ PiC-ClP»C¶ PiCḡPēPNḡPsPjCr PiCḡPμPiP°CḡP°C,Cr PiCḡPsC,C¶PiPsPj 16-24 C,PēP¶PSC-PI, C-PSPsPrC- PiPsPeCḡP°C%PμPSPSC¶ PIC-PrP·PSP°C†P°P»Pē PIP¶Pμ PiC-ClP»C¶ P»C-PeCrPIP°PSPSC¶ PiCḡPsC,C¶PiPsPj 4-12 C,PēP¶PSC-PI. PīPeC%Ps PiCḡPsC,C¶PiPsPj 6 PjC-ClC¶C†C-PI P»C-PeCrPIP°PSPSC¶ PSPμ P±CrP»Ps PμC,,PμPeC,PēPIPSPēPj, P»C-PeP°Cḡ PīPsPIPēPSPμPS PiCḡPēP·PSP°C†PēC,Pē C-PSC€Cr C,PμCḡP°PiC-CH. PμP°C†C-C”PSC,P°Pj, C¶PeC- PsC,CḡPēPjCrCḡC,CH P»C-PeCrPIP°PSPSC¶ C†PēP»PsClC,P°P·PsP»PsPj, ClP»C-Pr PrPsC,CḡPēPjCrPIP°C,PēClC¶ P·PjC-PS Cr ClPiPsClPsP±C- P¶PēC,C,C¶ (PIC-PrPjPsPIP° PIC-Pr PeCrCḡC-PSPSC¶ C,P° C,,C-P·PēC†PSC- PIPiCḡP°PIPē) C- PiCḡPsPrPsPIP¶CrPIP°C,Pē C,,P°CḡPjP°PePsP»PsPiC-C†PSC- PIC,CḡCrC†P°PSPSC¶ (PSP°PiCḡPēPeP»P°Pr, PiCḡPēPNḡPsPj P»C-PiC-PrPsP·PSPēP¶CrPIP°P»CHPSPēC... C,P° P°PSC,PēC,CḡPsPjP±PsC†PēC,P°CḡPSPēC... P·P°ClPsP±C-PI), C%PsP± P·PjPμPSC€PēC,Pē CḡPēP·PēPe CḡPsP·PIPēC,PeCr ClPμCḡC†PμIPs- ClCrPrPēPSPSPēC... C¶PIPēC%. PīPēP»PsClC,P°P·PsP» PSPμ P·P°PjC-PSCHC” PrP°PSC- PIPēPrPē P»C-PeCrPIP°PSPSC¶.

P—PjPμPSC€PμPSPSC¶ PrPsP·Pē PrPs 50 PjPi 2 CḡP°P·Pē PSP° PrPsP±Cr CḡPμPePsPjPμPSPPrPsPIP°PSPμ PrP»C¶ PiP°C†C-C”PSC,C-PI, C¶PeC- PsC,CḡPēPjCrCḡC,CH P»C-PeP°CḡClCHPeC- P·P°ClPsP±Pē, C%Ps ClPēP»CHPSPs C-PSPiC-P±CrCḡC,CH CYP3A4, PSP°PiCḡPēPeP»P°Pr PrPμC¶PeC- PjP°PeCḡPsP»C-PrPē, P°P·PsP»CHPSC- C,,CrPSPiC-C†PēPrPē, C-PSPiC-P±C-C,PsCḡPē PiCḡPsC,PμP°P·Pē, P°P±Ps P·P°ClPsP±Pē, C¶PeC- ClPēP»CHPSPs C-PSPiC-P±CrCḡC,CH CYP2C19, PSP°PiCḡPēPeP»P°Pr PsPjPμPiCḡP°P·PsP» (PrPēPI. CḡPsP·PrC-P» B«P’P·P°C”PjPsPrC-C¶ P· C-PSC€PēPjPē P»C-PeP°CḡClCHPePēPjPē P·P°ClPsP±P°PjPē C,P° C-PSC€C- PIPēPrPē PIP·P°C”PjPsPrC-PNḡB»).

PμP°C†C-C”PSC,Pē P»C-C,PSCHPsPiPs PIC-PeCé

PkPμPjP°C” PSPμPsP±C...C-PrPSPsClC,C- Cr PePsCḡPμPeC†C-C— PrPsP·Pē PrP»C¶ C†C-C”C— PeP°C,PμPiPsCḡC-C— PiP°C†C-C”PSC,C-PI.

PμP°C†C-C”PSC,Pē P· PSPēCḡPePsPIPsCH PSPμPrPsClC,P°C,PSC-ClC,CH

P”P»C¶ PiP°C†C-C”PSC,C-PI C-P· PeP»C-CḡPμPSClPsPj PeCḡPμP°C,PēPSC-PSCr > 25 PjP»/C...PI ClPiPμC†C-P°P»CHPSP° PePsCḡPμPeC†C-C¶ PrPsP·CrPIP°PSPSC¶ PSPμ PīPsC,CḡC-P±PSP°. PīPēP»PsClC,P°P·PsP» PiCḡPsC,PēPiPsPeP°P·P°PSPēPNḡ PiP°C†C-C”PSC,P°Pj C-P· PeP»C-CḡPμPSClPsPj PeCḡPμP°C,PēPSC-PSCr ≤ 25 PjP»/C...PI.

PμP°C†C-C”PSC,Pē P· PiPμC†C-PSPePsPIPsCH PSPμPrPsClC,P°C,PSC-ClC,CH

P”P»C¶ PiP°C†C-C”PSC,C-PI P· P»PμPiPePsCH C,,PsCḡPjPsCH P·P°C...PIPsCḡCHPIP°PSPSC¶ PiPμC†C-PSPePē PrPsP·Cr PSPμ PiPsC,CḡC-P±PSPs P·PjC-PSCHPIP°C,Pē. P’C-PrClCrC,PSC- PrP°PSC- C%PsPrPs PiP°C†C-C”PSC,C-PI P· PiPsPjC-CḡPSPsCH P°P±Ps C,C¶P¶PePsCH PiPμC†C-PSPePsPIPsCH PSPμPrPsClC,P°C,PSC-ClC,CH. PhClPeC-P»CHPePē C†PēP»PsClC,P°P·PsP» P°PeC,PēPIPSs PjPμC,P°P±PsP»C-P·CrC”C,CHClC¶

C,,PμCḡPjPμPSC,P°PjPë PïPμC‡C-PSPePë, PIC-PS PïCḡPsC,PëPïPsPeP°P·P°PSPëPNë
PïP°C†C-C" PSC,P°Pj P· PïPsPjC-CḡPSPsCḡ P°P±Ps C,CïP¶PëPsCḡ PïPμC‡C-PSPePsPIPsCḡ
PSPμPrPsC†C,P°C,PSC-C†C,Cḡ.

PμP°C†C-C" PSC,Pë P»C-C,PSCḡPsPiPs PIC-PeCž

PḡPμPjP°C" PSPμPsP±C...C-PrPSPsC†C,C- PI PePsCḡPμPeC†C-C— PrPsP·Pë PrP»Cï C†C-C"C—
PeP°C,PμPiPsCḡC-C— PïP°C†C-C" PSC,C-PI.

P"C-C,Pë.

P>C-PeP°CḡC†CḡPePëPNë P·P°C†C-P± PSPμ CḡPμPePsPjPμPSPrC†C"C,CḡC†Cï
PïCḡPëP·PSP°C‡P°C,Pë PrC-C,CïPj C‡PμCḡPμP· PIC-PrC†C†C,PSC-C†C,Cḡ PrP°PSPëC...
C%oPsPrPs P±PμP·PïPμPePë C,P° PμC,,PμPeC,PëPIPsC†C,C- PNëPsPiPs
P·P°C†C,PSC†C†PIP°PSPSCï.

PμPμCḡPμPrPsP·CžPIP°PSPSCï.

P†PSC,,PsCḡPjP°C†C-Cï PïCḡPs PiPsC†C,CḡPμ PïPμCḡPμPrPsP·C†PIP°PSPSCï
PsP±PjPμP¶PμPSP°. PḡPsP¶P»PëPIC- C†PëP»CḡPSPëPNë PiPsP»PsPIPsPëPNë P±C-P»Cḡ,
PrC-P°CḡPμCï, C,P°C...C-PeP°CḡPrC-Cï C,P° C†PμCḡC†PμPIP° P°CḡPëC,PjC-Cï. P—P°
PïP°C†C-C" PSC,P°PjPë PSPμPsP±C...C-PrPSPs C†PiPsC†C,PμCḡC-PiP°C,Pë C,P°
PïCḡPsPIPsPrPëC,Pë PïC-PrC,CḡPëPjC†PIP°P»CḡPSC† C,PμCḡP°PïC-Cḡ. PḡPμPsP±C...C-PrPSPs
C†PiPsCḡPsP¶PSPëC,Pë CëP»C†PSPsPe CëP»CïC...PsPj C-PSPrC†PeC†C-C—
P±P»CḡPIP°PSPSCï P°P±Ps PïCḡPsPjPëPIP°PSPSCï CëP»C†PSPeP°.

PμPsP±C-C‡PSC- CḡPμP°PeC†C-C—.

PḡP°PNëP±C-P»CḡCë PïPsCëPëCḡPμPSC- PïPsP±C-C‡PSC- CḡPμP°PeC†C-C—, PïCḡPs CïPeC-
PïPsPIC-PrPsPjP»CïP»Pë C† PeP»C-PSC-C‡PSPëC... PrPsC†P»C-PrP¶PμPSPSCïC...
PïCḡPμPïP°CḡP°C,C†, P±C†P»Pë PiPsP»PsPIPsPëPNë P±C-P»Cḡ (>30 %), PrC-P°CḡPμCï (>15 %)
C,P° PïPsCḡC†CëPμPSPSCï CḡPsP±PsC,Pë PePëCëPμC‡PSPëPeC† (>15 %). PïC-
CḡPμP°PeC†C-C— P·P°P·PIPëC‡P°PNë PjP°P»Pë P»PμPiPeC† P°P±Ps PïPsPjC-CḡPSC†
C-PSC,PμPSC†PëPIPsC-C†C,Cḡ C,P° C-PSPsPrC- PïPsP»PμPiCëC†PIP°P»PëC†Cï P·P°
CḡP°C...C†PSPsPe P·PSPëP¶PμPSPSCï PrPsP·Pë.

PḡPμP±P°P¶P°PSC- PμC,,PμPeC,Pë, CïPeC- C-PSPsPrC- PjPsP¶C†C,Cḡ PIPëPSPëPePSC†C,Pë
PïC-Pr C‡P°C† P·P°C†C,PSC†C†PIP°PSPSCï C†PëP»PsC†C,P°P·PsP»C†, P·P°P·PSP°C‡PμPSC- C†
C,P°P±P»PëC†C- PSPëP¶C‡Pμ.

P§P°C†C,PSC,P° PïPsP±C-C‡PSPëC... CḡPμP°PeC†C-PNë: 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); CḡC-PrPePs (≥1/10000,
<1/1000); PrC†P¶Pμ CḡC-PrPePs (<1/10000); C‡P°C†C,PSC,P° PSPμPIC-PrPsPjP°
(PSPμPjPsP¶P»PëPIPs PsC†C-PSPëC,Pë PSP° PsC†PSPsPIC- PSP°CïPIPsPëC... PrP°PSPëC...).
P§P°C†C,PSC,P° PïPsP±C-C‡PSPëC... CḡPμP°PeC†C-PNë, CïPeC-
C†PiPsC†C,PμCḡC-PiP°P»PëC†Cï C† PïPμCḡC-PsPr
PïC-C†P»CïCḡPμC"C†C,CḡP°C†C-PNëPSPsPiPs P·P°C†C,PSC†C†PIP°PSPSCï,

PIPIP°P¶P°C”C,CHCÍCÍC PSpµPIC-PrPsPjPsCĤ (PSPµPjPsP¶P»PëPIPs PsC†C-PSPëC,Pë PSP°
PsCÍPSPsPIC- PSP°CÍPIPSPëC... PrP°PSPëC...).

P— P±PsPeCž PeCĤPsPIPsPSPsCÍPSPsC— C,P° P»C-PjC„P°C,PëC†PSPsC— CÍPëCÍC,PµPjPë	C†P°CÍC,Ps	PµPeC...C-PjPsP·
	PSPµC†P°CÍC,Ps	P°PSPµPjC-CÍ
	CĤC-PrPePs	PiCĤPsPrPsPIP¶PµPSPSCÍ C†P°CÍCí PeCĤPsPIPsC,PµC†C-, C,CĤPsPjP±PsC†PëC,PµPjC-CÍ
	C†P°CÍC,PsC,P° PSPµPIC-PrPsPjP°	C,PµPSPrPµPSC†C-CÍ PrPs PeCĤPsPIPsC,PµC†, C,CĤPsPjP±PsC†PëC,PsPiPµPSC-CÍ, PiCĤP°PSCíP»PsC†PëC,PsPiPµPSC-CÍ, P°PiCĤP°PSCíP»PsC†PëC,PsP·, P»PµPNëPePsPiPµPSC-CÍ, PiP°PSC†PëC,PsPiPµPSC-CÍ, P°PiP»P°CÍC,PëC†PSP° P°PSPµPjC-CÍ
P— P±PsPeCž C-PjCžPSPSPsC— CÍPëCÍC,PµPjPë	PSPµC†P°CÍC,Ps	P°P»PµCĤPiC-C†PSP° CĤPµP°PeC†C-CÍ
P— P±PsPeCž PsP±PjC-PSCž CĤPµC†PsPIPëPS C,P° C...P°CĤC†CžPIP°PSPSCÍ	C†P°CÍC,Ps	PiPµCĤPëC„PµCĤPëC†PSC- PSP°P±CĤCÍPePë, PSP°P±CĤCÍPePë PsP±P»PëC†C†CÍ, P°PSPsCĤPµPeCÍC-CÍ
	PSPµC†P°CÍC,Ps	PiC-PiPµCĤPiP»C-PePµPjC-CÍ, C†CíPeCĤPsPIPëPNë PrC-P°P±PµC,
P— P±PsPeCž PiCÍPëC...C-PePë	PSPµC†P°CÍC,Ps	C,CĤPëPIPsP¶PSC-CÍC,CH
P— P±PsPeCž PSPµCĤPIPsPIPsC— CÍPëCÍC,PµPjPë	PrCíP¶Pµ C†P°CÍC,Ps	PiPsP»PsPIPSPëPNë P±C-P»CH
	C†P°CÍC,Ps	P·P°PiP°PjPsCĤPsC†PµPSPSCÍ
	PSPµC†P°CÍC,Ps	P±PµP·CÍPsPSPSCÍ, PSC-C†PSC- P¶P°C...Pë
	C†P°CÍC,PsC,P° PSPµPIC-PrPsPjP°	PiP°CĤPµP·, PiC-PiPµCÍC,PµP·C-CÍ
P— P±PsPeCž PsCĤPiP°PSC-PI P·PsCĤCž	C†P°CÍC,PsC,P° PSPµPIC-PrPsPjP°	PePsPSBĤ™ CĤPSPeC,PëPIC-C,
P— P±PsPeCž PsCĤPiP°PSC-PI CÍP»CžC...Cž	C†P°CÍC,PsC,P° PSPµPIC-PrPsPjP°	PrP·PIC-PS C- CëCíPj Cí PICíC...P°C...
P— P±PsPeCž CÍPµCĤC†PµPIPsC— CÍPëCÍC,PµPjPë	C†P°CÍC,Ps	PIC-PrC†CíC,C,CÍ CÍPµCĤC†PµP±PëC,C,CÍ, C,P°C...C-PeP°CĤPrC-CÍ, CÍC,PµPSPsPeP°CĤPrC-CÍ, P°CĤPëC,PjC-CÍ, CëP»CíPSPsC†PePsPIP° PµPeCÍC,CĤP°CÍPëCÍC,PsP»C-CÍ
	PSPµC†P°CÍC,Ps	C-PSC„P°CĤPeC, PjC-PsPeP°CĤPrP°, C„C-P±CĤPëP»CÍC†C-CÍ PiPµCĤPµPrCÍPµCĤPrCH, P·P°CÍC,C-PNëPSP° CÍPµCĤC†PµPIP° PSPµPrPsCÍC,P°C,PSC-CÍC,CH, PSP°PrCëP»CíPSPsC†PePsPIP° C,P°C...C-PeP°CĤPrC-CÍ, CëP»CíPSPsC†PePsPIP° C,P°C...C-PeP°CĤPrC-CÍ, PSPµPiCĤPëC,PsPjPSC-CÍC,CH

P— P±PsPeCž CÍCžPrPëPSPSPsC— CÍPëCÍC,PμPjPë	PSPμC‡P°CÍC,Ps	PлCђPsPIPsPIPëP»PëPI PI PsPePs, PSPsCÍPsPIC- PeCђPsPIPsC,PμC‡C-, CєP»CрPSPePsPIPs-PePëCєPePsPIC- PeCђPsPIPsC,PμC‡C-, PSPμP·бђ™ CІCІPsPIP°PSC- PeCђPsPIPsC,PμC‡C-, PsCђC,PsCÍC,P°C,PëC‡PSP° PiC-PiPsC,PμPSP·C-CІ
	C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP°	PiCђPëPiP»PëPIPë, PiC-PiPμCђC,PμPSP·C-CІ, PiC-PiPsC,PμPSP·C-CІ, PeCђPsPIPsPIPëP»PëPIPë PI PjPsP·PsPe, P»PμPiPμPSC-, Pjбђ™ CІP·Pë, PrPëC...P°P»CHбPSC- CєP»CІC...Pë; PiC-PrCєPeC-CђPSC- PeCђPsPIPsPIPëP»PëPIPë
P— P±PsPeCž PrPëC...P°P»CHбPSPsC— CÍPëCÍC,PμPjPë	C‡P°CÍC,Ps	CђPëPSC-C,, C,,P°CђPëPSPiC-C,
	PSPμC‡P°CÍC,Ps	P·P°PrPëCєPeP°, PiPSPμPIPjPsPSC-CІ, PeP°CєPμP»CHб
	C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP°	C-PSC,PμCђCÍC,PëC‡C-P°P»CHбPSP° PiPSPμPIPjPsPSC-CІ
P— P±PsPeCž CєP»CžPSPePsPIPs- PePëCєPePsPIPsPiPs C,CђP°PeC,Cž	PrCрP¶Pμ C‡P°CÍC,Ps	PrC-P°CђPμCІ, PiPsCђCрCєPμPSPSCІ PIPëPiPsCђPsP¶PSPμPSPSCІ
	C‡P°CÍC,Ps	PSCрPrPsC,P° C- P±P»CђPIP°PSPSCІ, PrPëCІPiPμPiCÍC-CІ, PjPμC,PμPsCђPëP·Pj, P±C-P»CHб Cр P¶PëPIPsC,C-
	PSPμC‡P°CÍC,Ps	PiP°CÍC,CђPëC,
P— P±PsPeCž PiPμPiP°C,PsP±C-P»C-P°CђPSPsC— CÍPëCÍC,PμPjPë	C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP°	PiPμPiP°C,PëC,, P°PSPsPjP°P»C-C— PiPμC‡C-PSPePsPIPsC— C,,CрPSPeC‡C-C—, P¶PsPIC,CІPSPëC‡CІ
P— P±PsPeCž CєPeC-CђPë C- PiC-PrCєPeC-CђPSPëC... C,PeP°PSPëPS	C‡P°CÍC,Ps	PIPëCІPëPiP°PSPSCІ, CІPIPμCђP±C-P¶
	C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP°	PμPeP·PμPjP°, CєPeC-CђPSC- PIPëCІPëPiP°PSPSCІ, CІPëPSPPrCђPsPj PŸC,C-PIPμPSCІP°-P°P¶PsPSCІPsPSP°, C,PsPeCІPëC‡PSPëP№ PμPiC-PrPμCђPjP°P»CHбPSPëP№ PSPμPeCђPsP»C-P·, PeCђPsPiPëPiбђ™ CІPSPeP°
P— P±PsPeCž CІPePμP»PμC,PSPs- Pjеђ™ CІP·PsPIPsC— CÍPëCÍC,PμPjPë C,P° CІPiPsP»CžC‡PSPsC— C,PeP°PSPëPSPë	PSPμC‡P°CÍC,Ps	PjC-P°P»PiC-CІ
P— P±PsPeCž PSPëCђPsPe C,P° CІPμC‡PsPIPëPIC-PrPSPëC... CєP»CІC...C-PI	CђC-PrPePs	PSPëCђPePsPIP° PSPμPrPsCÍC,P°C,PSC-CÍC,CHб, PiPsCђCрCєPμPSPSCІ C,,CрPSPeC‡C-C— PSPëCђPsPe
	C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP°	PiPμPjP°C,CрCђC-CІ, PiPsP»P°PeC-CрCђC-CІ
P—P°PiP°P»CHбPSC- CђPsP·P»P°PrPë	C‡P°CÍC,Ps	P±C-P»CHб Cр PiCђCрCІC..., P°CÍC,PμPSC-CІ
	PSPμC‡P°CÍC,Ps	PsP·PSPsP±, PSPμP·PrCрP¶P°PSPSCІ
	C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP°	PiC-CђPμPeCÍC-CІ, P±C-P»CHб
P»P°P±PsCђP°C,PsCђPSC- PrPsCІP»C-PrP¶PμPSPSCІ	C‡P°CÍC,PsC,P° PSPμPIC-PrPsPjP°	PiC-PrPIPëC%PμPSPSCІ CђC-PIPSCІ CІPμC‡PsPIPsC— PePëCІP»PsC,Pë, CІPμC‡PsPIPëPSPë Cр PeCђPsPIC-, PeCђPμP°C,PëPSC-PSCр PI PeCђPsPIC-

P—P±C-P»CHбCєPμPSPSCІ PeC-P»CHбPePsCÍC,C- PIPëPiP°PrPeC-PI PIC-PrC‡CрC,C,CІ

P—P±PμCḡC-PiP°C,Pë Cḡ PSPμPrPsCḡC,CḡPḡPSPsPjCḡ PrP»Cḡ PrC-C,PμPNḡ PjC-CḡC†C-.

PJPḡP°PePsPIPeP°.

PμPs 10 C,P°P±P»PμC,PsPe Cḡ P±P»C-CḡC,PμCḡC-; PḡPs 3 P°P±Ps 6 P±P»C-CḡC,PμCḡC-PI Cḡ PeP°CḡC,PsPSPSC-PNḡ CḡPḡP°PePsPIC†C-.

PḡP°C,PμPiPsCḡC-Cḡ PIC-PrPḡCḡCḡPeCḡ. P—P° CḡPμC†PμPḡC,PsPj.

P’PëCḡPsP±PSPëPe.

PḡPḡ B«PḡPrP°PjPμPr PḡP°CḡPjP°B».

PḡC-CḡC†PμP·PSP°C...PsPrPḡPμPSPSCḡ PIPëCḡPsP±PSPëPeP° C,P° P°PrCḡPμCḡP° PjC-CḡC†Cḡ PḡCḡPsPIP°PrPḡPμPSPSCḡ PNḡPsPiPs PrC-CḡP»CḡPSPsCḡC,C-.

P’CḡP». PḡP°CḡC€. P”Pḡ. PμC-P»CḡCḡPrCḡCḡPePsPiPs 5, 95-200, PμP°P±Bḡ™ CḡPSC-C†Pμ, PμPsP»CḡC%P°.

P—P°CḡPIIPSPëPe.

PḡP·Pḡ PḡP°CḡPjP°CḡCḡCḡC,C-PeP°P»Cḡ P>C-PjC-C,PμPr.

PḡC-CḡC†PμP·PSP°C...PsPrPḡPμPSPSCḡ P·P°CḡPIIPSPëPeP°.

PḡPμPSPSPμPrC- PḡPIPμPSCḡ 89/201, 1077 PḡC-PePsCḡC-Cḡ, PḡC-PḡCḡ.