

Р†РќРЎРЎР РЈРљРІР†РЇ

**PrP»CȚ PjPμPΓPëC‡PSPsPiPs P•P°CÍC,PsCÍCÍrPIP°PSPSCȚ P»C-PεP°CȚCÍCȚPεPsPiPs
P•P°CÍPsP±CÍ**

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:

$$\text{PeC}\bar{\eta}\text{PsC}\dots\text{PjP}^\circ\text{P}\gg\text{CH}\bar{\eta}\text{PeCr}\bar{\eta}\text{PeCr}\bar{\eta}\text{Cr}\bar{\eta}\text{PrP}\cdot\text{C}\bar{\eta}\text{PSP}\bar{\eta}\text{PN}_0,$$
$$\text{PiC-PrCH}_5\text{PsPeCl'}\text{PëPjP}\mu\text{C,PëP}\gg\text{PiCH}_5\text{PsPiC-P}\gg\text{C}\dagger\text{P}\mu\text{P}\gg\text{CH}_5\text{P}\gg\text{PsP}\cdot\text{P}^\circ\text{P}\cdot 5, \text{C}\dagger\text{P}\mu\text{P}\gg\text{CH}_5\text{P}\gg\text{PsP}\cdot\text{P}^\circ$$
$$\text{PjC-PeCHPsPeCHPëCfC, P°P} \gg \text{C-C} \ddagger \text{PSP}^\circ \text{ 101, PjP°PiPSC-CH CfC, P} \mu \text{P}^\circ \text{CHP}^\circ \text{C,, C} \ddagger \text{P} \mu \text{P} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ$$
$$\text{PjC-PeC}\bar{\text{H}}\text{PsPeC}\bar{\text{H}}\text{P}\bar{\text{e}}\text{C}\bar{\text{I}}\text{C,P}^\circ\text{P}\rangle\text{C-C}\bar{\text{I}}\text{PSP}^\circ \text{ 12, PeP}^\circ\text{P}\rangle\text{CHC}\bar{\text{I}}\text{C-C}\bar{\text{H}}\text{PeP}^\circ\text{C}\bar{\text{H}}\text{PjP}\bar{\text{u}}\text{P}\rangle\text{PsP}^\circ\text{P}^\circ;$$

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

$$\text{PeC}\overline{\text{T}}\text{P}\text{sC} \dots \text{PjP}^\circ \text{P} \gg \text{CH} \text{ PeC}\overline{\text{r}}\text{PeC}\overline{\text{r}}\text{C}\overline{\text{T}}\text{C}\overline{\text{r}}\text{PrP} \cdot \text{C}\overline{\text{L}}\text{PSP}\overline{\text{e}}\text{PN}_\circ,$$
$$\text{PiC-PrCHPsPeClPëPjPuC,PëP} \gg \text{PiCHPsPiC-P} \gg \text{C†PuP} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ \quad \text{P} \cdot 5, \text{C†PuP} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ$$
$$\text{PjC-PeCHPsPeCHPëCfC,P°P»C-C†PSP° 101, PiP°PiPSC-CH CfC,PuP°CHP°C,, PeP°P»CHC†C-CH}$$
$$P \in P^\circ \subset \mathcal{H} P \mid P \mu P \gg P_S P \cdot P^\circ.$$
$$\mathbf{P} \triangleright \mathbf{C} - \mathbf{P} \mathbf{e} \mathbf{P}^{\circ} \mathbf{C} \mathbf{f} \mathbf{C} \mathbf{f} \mathbf{C} \mathbf{h} \mathbf{P} \mathbf{e} \mathbf{P}^{\circ} \mathbf{C} \mathbf{,,} \mathbf{P} \mathbf{s} \mathbf{C} \mathbf{f} \mathbf{P} \mathbf{j} \mathbf{P}^{\circ} . \mathbf{P} \check{\mathbf{y}} \mathbf{P}^{\circ} \mathbf{P} \pm \mathbf{P} \gg \mathbf{P} \mu \mathbf{C} , \mathbf{P} \mathbf{e} \mathbf{P} \check{\mathbf{e}} .$$
$$PhCI\dot{P}SPsPIPSC-C_{\text{„}}C-P\cdot P\ddot{e}PePs-C...C-PjC-C\ddot{z}PSC-PIP\gg P^{\circ}CI\dot{C},P\ddot{e}PIPsCI\dot{C},C-:$$

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

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

PiChP°PIC-CHPIP°PSPSCIPj B«50B» P· PsPrPSPsPiPs P±PsPeCr;

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

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

PꝛP°CḥPjP°PePsC,PuCḥP°PiPuPIC,PëC±PSP° PiCḥCǵPiP°.

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

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”Cḡ PiCḡPë
PiPμCḡPμPjC-PḡPSC-PMë PeCfP»CHPiP°PiPsCfC,C- (P°P±Ps P·P° PjP°PeCfPëPjP°P»CHPSPsCḡ
PrPëCfC,P°PSC†C-C”Cḡ C...PsPrCHP±Pë (PḡP”Pḡ)) C,P° PiPsC±P°C,PePsPiPsCḡ
PrPëCfC,P°PSC†C-C”Cḡ PiPμCḡPμPjC-PḡPSPsC— PeCfP»CHPiP°PiPsCfC,C- (P°P±Ps P·P°
P±PμP·P±PsP»C-CfPSPsCḡ PrPëCfC,P°PSC†C-C”Cḡ C...PsPrCHP±Pë (P’P”Pḡ)) 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”Pḡ PiCḡPë
P·P°CfC,PscCfCfPiP°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,PsPeCf
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,PscCfCfPiP°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. P_hP°PeCfPëPjP°P»CHbPSP°
 PePsPSC†PμPSC,CfjP°C†C-Cj (P_Y_{max}) C†PëP»PsCfC,P°P·PsP»Cf C,P° P_NPsPiPs
 PjPμCfjPiPëPSPSPëC... PjPμC,P°P±PsP»C-C,C-PI PiC-PrPiPëC%Cr"C,CHCfCj PjPμPSC€
 PiCfjPsPiPsCfjC†C-P_NPsPs P· PiC-PrPiPëC%PμPSPSCjPj PrPsP·Pë, PiCfjPsC,Pμ PiP»PsC%P°
 PiC-Pr PeCfjPëPiPsCf B«PePsPSC†PμPSC,CfjP°C†C-Cj-C†P°CfB» (AUC)
 C†PëP»PsCfC,P°P·PsP»Cf C,P° P_NPsPiPs PjPμC,P°P±PsP»C-C,C-PI
 P·P±C-P»CHbC€CfC"C,CHCfCj PiCfjPëP±P»PëP·PSPs PiCfjPsPiPsCfjC†C-P_NPsPs PrPs
 PrPsP·CfPiP°PSPSCj. PjPiPSPëP_N PjPμCfjC-PsPr PSP°PiC-PIPiPëPiPμPrPμPSPSCj
 C†PëP»PsCfC,P°P·PsP»Cf CfPeP»P°PrP°C" 10,5 PiPsPrPëPSPë. P†CfPSCfC" PrPiP°
 PiPsP»PsPiPSPëC... PjPμC,P°P±PsP»C-C,Pë bñ" PrPμPiC-PrCfjPsC†PëP»PsCfC,P°P·PsP» C,P° 4'-
 C,CfjP°PSCf-PiC-PrCfjPsPeCfPëC†PëP»PsCfC,P°P·PsP», C%Ps PjP°CfC,CH P±P»PëP·CHbPeC-
 PiPsPeP°P·PSPëPePë PSP°PiC-PIPiPëPiPμPrPμPSPSCj. P" PμPiC-PrCfjPsPjPμC,P°P±PsP»C-C,
 PjP°C" Cf 4-7 CfjP°P·C-PI PiPëC%Cr P°PSC,PëC,CfjPsPjP±PsC,PëC†PSCf
 P°PeC,PëPiPSC-CfC,CH, PSC-P¶ PiPëC...C-PrPSP° CfjPμC†PsPiPëPSP°, P° 4'-C,CfjP°PSCf-
 PiC-PrCfjPsPeCfPëPjPμC,P°P±PsP»C-C, bñ" 1/5 PIC-Pr P°PeC,PëPiPSPsCfC,C-
 C†PëP»PsCfC,P°P·PsP»Cf. P_hPsPSC†PμPSC,CfjP°C†C-C— PI PiP»P°P·PjC- PeCfjPsPIC-
 (PsC,CfjPëPjP°PSC- P·P° PrPsPiPsPjPsPiPsCf AUC) PrPμPiC-PrCfjPs- C,P° 4'-C,CfjP°PSCf-
 PiC-PrCfjPsPeCfPëPjPμC,P°P±PsP»C-C,C-PI PiCfjPëP±P»PëP·PSPs CfPeP»P°PrP°CfC,CH 41 %
 C,P° 12 % PIC-Pr PePsPSC†PμPSC,CfjP°C†C-C— C†PëP»PsCfC,P°P·PsP»Cf PIC-PrPiPsPIC-PrPSPs.

P_hPμC,P°P±PsP»C-P·Pj

PiPëP»PsCfC,P°P·PsP» PiPëPiPsPrPëC,CHCfCj PiPμCfjPμPiP°P¶PSPs P·P° PrPsPiPsPjPsPiPsCf
 PjPμC,P°P±PsP»C-P·PjCf C,P° PiPsPrP°P»CHbC€PsPiPs PiPëPiPμPrPμPSPSCj P_NPsPiPs
 PjPμC,P°P±PsP»C-C,C-PI P·C- CfPμC†PμCf. PμPμCfjPiPëPSPSC- C-P·PsC,,PμCfjPjPμPSC,Pë
 C†PëC,PsC...CfjPsPjCf P 450, CjPeC- P±PμCfjCfC,CH CfC†P°CfC,CH Cf P_NPsPiPs
 PjPμC,P°P±PsP»C-P·PjC-, bñ" CYP3A4, PjPμPSC€PsCf PjC-CfjPsCf bñ" CYP2C19 C,P° C%Pμ
 PjPμPSC€PsCf PjC-CfjPsCf bñ" CYP1A2.

P'PëPiPμPrPμPSPSCj

P"PsP»PsPiPSPëP_N C€P»CjC... PiPëPiPμPrPμPSPSCj bñ" P·C- CfPμC†PμCf (74 %),
 P·P°P»PëC€PePsPIC- PeC-P»CHbPePsCfC,C- PiPëPrC-P»CjCfC,CHCfCj P· PeP°P»PsPj.
 PkPμP·PSP°C†PSC- PeC-P»CHbPePsCfC,C- PSPμP·PjC-PSPμPSPsPiPs C†PëP»PsCfC,P°P·PsP»Cf
 PiPëPrC-P»CjCfC,CHCfCj P·C- CfPμC†PμCf, P° PjPμPSC€ PSC-P¶ 2 % P_NPsPiPs PrPsP·Pë
 PiPëPrC-P»CjC"C,CHCfCj Cf PiPëPiP»CjPrC- PrPμPiC-PrCfjPsC†PëP»PsCfC,P°P·PsP»Cf.
 PμCfjPëP±P»PëP·PSPs 30 % PIC-Pr PiPsC†P°C,PePsPiPsC— PrPsP·Pë PiPëPrC-P»CjC"C,CHCfCj
 P·C- CfPμC†PμCf CjPe 4'-C,CfjP°PSCf-PiC-PrCfjPsPeCfPëPjPμC,P°P±PsP»C-C.,
 P—P°P»PëC€PePsPiP° PeC-P»CHbPeC-CfC,CH PiPëPrC-P»CjC"C,CHCfCj CjPe CfCfPjP°
 PjPμC,P°P±PsP»C-C,C-PI, P¶PsPrPμPS P· CjPePëC... PSPμ PiPμCfjPμPiPëC%CrC" 5 % PIC-Pr
 P·P°PiP°P»CHbPSPsC— PeC-P»CHbPePsCfC,C-.

P PsP·PiPsPrC-P»

PiPëP»PsCfC,P°P·PsP» P·PiP_h™ CjP·CfC"C,CHCfCj P· P±C-P»PeP°PjPë PSP° 95-98 %,
 PiPμCfjPμPiP°P¶PSPs P· P°P»CHbP±CfPjC-PSPsPj. P" PμPiC-PrCfjPsPjPμC,P°P±PsP»C-C, C,P° 4'-
 C,CfjP°PSCf-PiC-PrCfjPsPeCfPëPjPμC,P°P±PsP»C-C, P·PiP_h™ CjP·CfCfC,CHCfCj P·
 P±C-P»PeP°PjPë PSP° 97,4 % C,P° 66 % PIC-PrPiPsPIC-PrPSPs.

PkPμPjP°C" PiC-PrC,PIPμCfjPrP¶PμPSPSCj P·PrP°C,PSPsCfC,C- C†PëP»PsCfC,P°P·PsP»Cf
 C-PSPrCfPeCfPiP°C,Pë PjC-PeCfjPsCfPsPjP°P»CHbPSC- C,,PμCfjPjPμPSC,Pë PiPμC†C-PSPëPë.
 PαP°CfjPjP°PePsPeC-PSPμC,PëPeP° C†PëP»PsCfC,P°P·PsP»Cf C,P° P_NPsPiPs

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†PëP»PsC¶C,P°P·PsP»Cf P±CfP»P° PSP° 27 % PIPeC%PsC¶, P° PŸ_{max} C,P° AUC P±CfP»Pë PIC-PrPipPsPIC-PrPSPs PSP° 29 % C,P° 39 % PSPeP¶C±PëPjPë, 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»Pë PIC-PrPipPsPIC-PrPSPs PSP° 41 % C,P° 47 % PSPeP¶C±PëPjPë Cf PIP°C†C-C”PSC,C-PI P· C,C¶P¶PePëPjPë PipsC¶CfCεPμPSPSC¶PjPë PSPeC¶PsPe PipsC¶C-PIPsC¶PSPs P· PIP°C†C-C”PSC,P°PjPë 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¶PëC†PëP»PsC¶C,P°P·PsP»Cf P±CfP»Pë PSP° 173 % C,P° 209 % PIC-PrPipPsPIC-PrPSPs PIPeC%PëPjPë 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· PipsPjC-C¶PSPsC¶ C,P° C,C¶P¶PePsC¶ PIPμC±C-PSPePsPIPsC¶ PSPμPrPsC¶C,P°C,PSC-C¶C,C¶.

РљР»С-РSC-С±РSC- С...Р°С¶Р°РеС,РμС¶РëС¶С,РëРеРë.

РμРsРeР°Р·Р°РSPSC¶.

P”P»C¶ P·P±C-P»CHCεPμPSPSC¶ PjP°PeC¶PëPjP°P»CHBPSPsC— P±PμP·P±PsP»C-C¶PSPsC— PrPëC¶C,P°PSC†C-C— C...PsPrCHBP±Pë Cf PIP°C†C-C”PSC,C-PI P· PIPμC¶PμPjC-P¶PSPsC¶ PeCfP»CHPiP°PIC-C¶C,C¶, C¶PeC- PSPμ PjP°C¶C,CH P±PsP»C¶ Cf C¶C,P°PSC- C¶PipsPePsC¶ C,P° PsP·PSP°Pe PSPμPeC¶PsP·Cf PIPμC¶PëC,,PμC¶PëC±PSPeC... C,PeP°PSPëPS (P·P°C...PIPsC¶PIP°PSPSC¶ PIPμC¶PëC,,PμC¶PëC±PSPeC... P°C¶C,PμC¶C-PNε, C¶C,P°PrC-C¶ II P·P° PαPsPSC,PμPNεPSPsPj).

P—P°C¶C,PsC¶PsPICfPIP°C,Pë C¶Pe C,PμC¶P°PiC-C¶ PrC¶CfPipsC— P»C-PSC-C— PrP»C¶ PIP°C†C-C”PSC,C-PI, Cf C¶PePëC... P·PjC-PSP° C¶C,PëP»C¶ P¶PëC,C,C¶ (PIPeP»C¶C±P°C¶C±Pë PIC-PrPjPsPICf PIC-Pr PeCfC¶C-PSPSC¶ C,P° PePsPSC,C¶PsP»CHBPSP°PSC- PïC¶PsPiC¶P°PjPë P·P°PSC¶C,CH C¶PipsC¶C,PsPj) C,P° C-PSCεC- PIC-PrPipPsPIC-PrPSC- P·P°C...PsPrPë PSPμ PïC¶PëP·PIPμP»Pë PrPs P·PSP°C±PSPsPips PipsC¶P»P°P±P»PμPSPSC¶ C¶PëPjPiC,PsPjC-PI PIPμC¶PμPjC-P¶PSPsC— PeCfP»CHPiP°PIPsC¶C,C-.

РμС¶РsС,РëРiРsРeР°Р·Р°РSPSC¶.

- P’C-PrPsPjP° PiC-PiPμC¶C±CfC,P»PëPIC-C¶C,CH PrPs C†PëP»PsC¶C,P°P·PsP»Cf P°P±Ps PrPs P±CfPrCH-C¶PePsPips PePsPjPipsPSPμPSC,P° PïC¶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,PëPSC-PSCf £ 25 PjP»/C...PI);
- PipsPjC-C¶PSP° P°P±Ps C,C¶P¶PeP° PIPμC±C-PSPePsPIP° PSPμPrPsC¶C,P°C,PSC-C¶C,CH;
- P·P°C¶C,C-PNεPSP° C¶PμC¶C†PμPIP° PSPμPrPsC¶C,P°C,PSC-C¶C,CH;
- PIP°PiC-C,PSC-C¶C,CH;

- $P \pm C \uparrow PrCH \cdot C \downarrow PeP^{\circ} PIC - PrPsPjP^{\circ} C \uparrow C \dots P \ddot{e}P \gg CH \cdot PSC - C \uparrow C, CH \cdot PrPs \cdot PeCH \cdot PsPIP sC, P_{\mu}C \uparrow C - (PSP^{\circ} \cdot P \ddot{e}CH \cdot P \ddot{e}PeP \gg P^{\circ} Pr, PIP \ddot{e}CH \cdot P^{\circ} P \cdot PeP^{\circ} C \ddot{e}P \gg C \uparrow PSPeP^{\circ} P^{\circ} P \pm Ps PrPIP^{\circ} PSP^{\circ} PrC \uparrow C \downarrow C, P \ddot{e}PiP^{\circ} P \gg PsC - PeP \ddot{e}C \ddot{e}PeP \ddot{e} C \uparrow C \uparrow C, P^{\circ} PrC - C - P^{\circ} P \cdot PiPsC \uparrow C, CH \cdot P_{\mu}PSPSC \downarrow, PSP_{\mu}C \% PsPrP^{\circ} PIPSC - PN_{\ddot{e}} PiP_{\mu}PjPsCH \cdot P^{\circ} PiC - C \uparrow PSP \ddot{e}PN_{\ddot{e}} C - PSC \uparrow C \uparrow P \gg CH \cdot C, (P \ddot{e}CH \cdot PsC, C \downarrow PiPsPj \cdot 6 PjC - C \uparrow C \downarrow C \uparrow C - PI), P \ddot{e}CH \cdot PsP \gg C - C, P_{\mu}CH \cdot P^{\circ} C, P \ddot{e}PIPSP^{\circ} C, PsCH \cdot PjP^{\circ} PrC - P^{\circ} P \pm P_{\mu}C, P \ddot{e}C \uparrow PSPsC - CH \cdot P_{\mu}C, P \ddot{e}PSPsPiP^{\circ} C, C - C - C \uparrow P \gg P^{\circ} P \pm PsPePsPSC, CH \cdot PsP \gg CH \cdot PsPIP^{\circ} PSP^{\circ} P^{\circ} CH \cdot C, P_{\mu}CH \cdot C - P^{\circ} P \gg CH \cdot PSP^{\circ} PiC - PiP_{\mu}CH \cdot C, P_{\mu}PSP \cdot C - C \downarrow);$
- $C \ddot{e}P \gg C \uparrow PSPsC \uparrow PePsPIP^{\circ} C, P^{\circ} C \dots C - PeP^{\circ} CH \cdot PrC - C \downarrow, C, C - P \pm CH \cdot P \ddot{e}P \gg C \downarrow C \uparrow C - C \downarrow C \ddot{e}P \gg C \uparrow PSPsC \uparrow PeC - PI P^{\circ} P \pm Ps PjC \uparrow P \gg CH \cdot C, P \ddot{e}P \gg PsPeC \uparrow P \gg C \downarrow C \uparrow CH \cdot PSP^{\circ} C \ddot{e}P \gg C \uparrow PSPsC \uparrow PePsPIP^{\circ} P_{\mu}PeC, PsPiC - C \downarrow PI P^{\circ} PSP^{\circ} PjPSP_{\mu}C - C \uparrow PiP^{\circ} C \uparrow C - C''PSC, C - PI, C \downarrow PeC - P \ddot{e}CH \cdot PsC \dots PsPrP \ddot{e}P \gg P \ddot{e} P^{\circ} P \pm Ps PSP_{\mu} P \ddot{e}CH \cdot PsC \dots PsPrP \ddot{e}P \gg P \ddot{e} PIC - PrPiPsPIC - PrPSC \uparrow C, P_{\mu}CH \cdot P^{\circ} PiC - CH, P^{\circ} C, P^{\circ} PePsP \uparrow PiPsPrPsPIP \uparrow P_{\mu}PSPSC \downarrow C - PSC, P_{\mu}CH \cdot PIP^{\circ} P \gg C \uparrow QT;$
- $C, C \downarrow P \uparrow PeP^{\circ} C, P^{\circ} C \dots C - P^{\circ} CH \cdot P \ddot{e}C, PjC - C \downarrow PI P^{\circ} PSP^{\circ} PjPSP_{\mu}C -;$
- $PsPrPSPsC \uparrow P^{\circ} C \uparrow PSP_{\mu} P \gg C - PeC \uparrow PIP^{\circ} PSPSC \downarrow PrPIP sPjP^{\circ} P^{\circ} P \pm Ps P \pm C - P \gg CH \cdot C \ddot{e}P_{\mu} PrPsPrP^{\circ} C, PePsPIP \ddot{e}PjP \ddot{e} P^{\circ} PSC, P \ddot{e}C, CH \cdot PsPjP \pm PsC \uparrow P \ddot{e}C, P^{\circ} CH \cdot PSP \ddot{e}PjP \ddot{e} P \cdot P^{\circ} C \uparrow PsP \pm P^{\circ} PjP \ddot{e} P^{\circ} P \pm Ps P^{\circ} PSC, P \ddot{e}PePsP^{\circ} PiC \uparrow P \gg C \downarrow PSC, P^{\circ} PjP \ddot{e} (PSP^{\circ} \cdot P \ddot{e}CH \cdot P \ddot{e}PeP \gg P^{\circ} Pr, P^{\circ} C \uparrow P_{\mu}C, P \ddot{e}P \gg C \uparrow P^{\circ} P \gg C - C \uparrow P \ddot{e}P \gg PsPIP^{\circ} PeP \ddot{e}C \uparrow P \gg PsC, P^{\circ}, PeP \gg PsPiC - PrPsPiCH \cdot P_{\mu}P \gg CH, PiP_{\mu}PiP^{\circ} CH \cdot P \ddot{e}PS, PIP^{\circ} CH \cdot C, P^{\circ} CH \cdot P \ddot{e}PS, P^{\circ} C \uparrow P_{\mu}PSPsPeC \uparrow PjP^{\circ} CH \cdot PsP \gg, PrP^{\circ} P \pm C - PiP^{\circ} C, CH \cdot P^{\circ} PS, CH \cdot P \ddot{e}PIP^{\circ} CH \cdot PsPeC \uparrow P^{\circ} P \pm P^{\circ} PS P^{\circ} P \pm Ps P^{\circ} PiC - PeC \uparrow P^{\circ} P \pm P^{\circ} PS);$
- $PSP_{\mu}C \uparrow C, P^{\circ} P \pm C - P \gg CH \cdot PSP^{\circ} C \uparrow C, P_{\mu}PSPsPeP^{\circ} CH \cdot PrC - C \downarrow, C - PSC, P^{\circ} CH \cdot PeC, PjC - PsPeP^{\circ} CH \cdot PrP^{\circ} P \ddot{e}CH \cdot PsC, C \downarrow PiPsPj PsC \uparrow C, P^{\circ} PSPSC - C \dots 6 PjC - C \uparrow C \downarrow C \uparrow C - PI P^{\circ} P \pm Ps PePsCH \cdot PsPSP^{\circ} CH \cdot PSP_{\mu} PIC, CH \cdot C \uparrow C \uparrow P^{\circ} PSPSC \downarrow P \ddot{e}CH \cdot PsC, C \downarrow PiPsPj PsC \uparrow C, P^{\circ} PSPSC - C \dots 6 PjC - C \uparrow C \downarrow C \uparrow C - PI.$

$P^{\circ} P \cdot P^{\circ} C'' PjPsPrC - C \downarrow P \cdot C - PSC \ddot{e}P \ddot{e}PjP \ddot{e} P \gg C - PeP^{\circ} CH \cdot C \uparrow CH \cdot PeP \ddot{e}PjP \ddot{e} P \cdot P^{\circ} C \uparrow PsP \pm P^{\circ} PjP \ddot{e} C, P^{\circ} C - PSC \ddot{e}C - PIP \ddot{e}PrP \ddot{e} PIP \cdot P^{\circ} C'' PjPsPrC - PN_{\ddot{e}}.$

$P \ddot{e}PSC, P \ddot{e}C, CH \cdot PsPjP \pm PsC, P \ddot{e}C \uparrow PSC - P \cdot P^{\circ} C \uparrow PsP \pm P \ddot{e}. P \downarrow P \ddot{e}P \gg PsC \uparrow C, P^{\circ} P \cdot PsP \gg C'' C - PSPiC - P \pm C - C, PsCH \cdot PsPj C, PsC \uparrow C, PsPrC - P_{\mu}C \uparrow C, P_{\mu}CH \cdot P^{\circ} P \cdot P \ddot{e} P \uparrow P \uparrow P \uparrow P^{\circ} PSC, P \ddot{e}C, CH \cdot PsPjP \pm PsC \uparrow P \ddot{e}C, P^{\circ} CH \cdot PSPsCH P^{\circ} PeC, P \ddot{e}PIPSC - C \uparrow C, CH. P^{\text{TM}} PsPiPs P \cdot P^{\circ} C \uparrow C, PsC \uparrow C \uparrow PIP^{\circ} PSPSC \downarrow P \cdot PrPsCH \cdot PsPIP \ddot{e}Pj PrPsP \pm CH \cdot PsPIP sP \gg CH \cdot C \uparrow C \downarrow Pj C \uparrow PrPsP \cdot C - 150 PjPi P \ddot{e}CH \cdot PsC, C \downarrow PiPsPj 5 PrPSC - PI PSP_{\mu} P \ddot{e}CH \cdot P \ddot{e}P \cdot PIPsPrP \ddot{e}P \gg Ps PrPs PiPsPrPsPIP \uparrow P_{\mu}PSPSC \downarrow C \uparrow P^{\circ} C \uparrow C \uparrow PeCH \cdot PsPIP sC, P_{\mu}C \uparrow C -.$

$P \ddot{e}C \uparrow P_{\mu}C, P \ddot{e}P \gg C \uparrow P^{\circ} P \gg C - C \uparrow P \ddot{e}P \gg PsPIP^{\circ} PeP \ddot{e}C \uparrow P \gg PsC, P^{\circ} (P \ddot{e}P \ddot{e}P). P \ddot{e}C \uparrow PjC - C \uparrow PSP_{\mu} P \cdot P^{\circ} C \uparrow C, PsC \uparrow C \uparrow PIP^{\circ} PSPSC \downarrow P \cdot P \ddot{e}P \ddot{e}P \ddot{e} P \ddot{e}CH \cdot PsC, C \downarrow PiPsPj PePsCH \cdot PsC, PePsPiPs C \uparrow P^{\circ} C \uparrow C \uparrow (PrPs 4 PrPSC - PI) P \pm C \uparrow P \gg Ps PiPsPi \ddot{e}P^{\text{TM}} C \downarrow P \cdot P^{\circ} PSP_{\mu} P \cdot PiC - PrPIP \ddot{e}C \% P_{\mu}PSPSC \downarrow Pj PSP^{\circ} 23-25 \% P \ddot{e}CH \cdot P \ddot{e}PiPSC - C \uparrow P_{\mu}PSPSC \downarrow P \ddot{e}P'' P \alpha - C - PSPrC \uparrow PePsPIP^{\circ} PSPsC - P^{\circ} PiCH \cdot P_{\mu}PiP^{\circ} C \uparrow C - C - C, CH \cdot PsPjP \pm PsC \uparrow P \ddot{e}C, C - PI PiPsCH \cdot PIPSC \downarrow PSPs P \cdot P \ddot{e}CH \cdot P \ddot{e}PN_{\ddot{e}} PsPjPsPj C, C - P \gg CH \cdot PeP \ddot{e} P \ddot{e}P \ddot{e}P \ddot{e}P. P \ddot{e}P_{\mu} C \uparrow PiPsC \uparrow C, P_{\mu}CH \cdot C - PiP^{\circ} P \gg PsC \uparrow C \downarrow PsC \uparrow P_{\mu}PIP \ddot{e}PrPSP \ddot{e}C \dots C, P_{\mu}PSPPrP_{\mu}PSC \uparrow C - PN_{\ddot{e}} PrPs P \cdot P \pm C - P \gg CH \cdot C \ddot{e}P_{\mu}PSPSC \downarrow CH \cdot C - PIPSC \downarrow PiP_{\mu}PjPsCH \cdot P^{\circ} PiC - C \uparrow PSP \ddot{e}C \dots PiPsP \pm C - C \uparrow PSP \ddot{e}C \dots P_{\mu}C, P_{\mu}PeC, C - PI C \uparrow PiP^{\circ} C \uparrow C - C''PSC, C - PI, C \downarrow PeC - P \ddot{e}CH \cdot P \ddot{e}PN_{\ddot{e}} PjP^{\circ} P \gg P \ddot{e} P \ddot{e}P \ddot{e}P \ddot{e}P C, P^{\circ} C \uparrow P \ddot{e}P \gg PsC \uparrow C, P^{\circ} P \cdot PsP \gg, PiPsCH \cdot PIPSC \downarrow PSPs P \cdot PiP^{\circ} C \uparrow C - C''PSC, P^{\circ} PjP \ddot{e}, C \downarrow PeC - P \ddot{e}CH \cdot P \ddot{e}PN_{\ddot{e}} PjP^{\circ} P \gg P \ddot{e} PiP \gg P^{\circ} C \uparrow P_{\mu}P \pm Ps C, P^{\circ} P_{\mu}PePIC - PIP^{\circ} P \gg P_{\mu}PSC, PSC - PrPsP \cdot P \ddot{e} P \ddot{e}P \ddot{e}P \ddot{e}P.$

$P \ddot{e}P \gg PsPiC - PrPsPiCH \cdot P_{\mu}P \gg CH \cdot C, P^{\circ} C - PSC \ddot{e}C - P^{\circ} PSC, P \ddot{e}C, CH \cdot PsPjP \pm PsC \uparrow P \ddot{e}C, P^{\circ} CH \cdot PSC -$

*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 (PµPš) P°P±Ps
P°PeC,PëPIPsPIP°PSPëPNë C†P°CÍC,PePsPIPëPNë C,CĤPsPjP±PsPíP»P°CÍC,PëPSPsPIPëPNë
C†P°CÍ (PĥPšPŸPš). 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°PiC¿P»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— (PµPš, PĥPšPŸPš,
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...CĤPsPjC¿ 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%CÍ, 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*

$P-P^{\circ}ClC$, $PsClC_rPIP^{\circ}PSPSC_{100}$ P_jPi $C_{\dagger}P_{\ddot{e}}P \gg PsClC$, $P^{\circ}P \cdot PsP \gg Cr$ 2 $C_{\ddot{H}}P^{\circ}P \cdot P_{\ddot{e}}PSP^{\circ}$ $PrPsP \pm Cr$ $P \cdot PrP_{\ddot{e}}P \gg C, C-P^{\circ}P \cdot P_{\mu}P_jPsP_j$ ($ClP \gg P^{\circ}P \pm PeP_{\ddot{e}}PN_{\infty}$ $C-PSPiC-P \pm C-C$, $PsC_{\ddot{H}}CYP3A4$) 180 P_jPi 1 $C_{\ddot{H}}P^{\circ}P \cdot PSP^{\circ}$ $PrPsP \pm Cr$ $PiC_{\ddot{H}}P_{\ddot{e}}P \cdot PIPsPrP_{\ddot{e}}P \gg Ps$ $PrPs$ $PiC-PrPIP_{\ddot{e}}C\%$ $P_{\mu}PSPSC_{100}$ AUC $C_{\dagger}P_{\ddot{e}}P \gg PsClC$, $P^{\circ}P \cdot PsP \gg Cr$ PSP° 44 %, $ClPeP_{\mu}$ $ClC_rPiC_{\ddot{H}}PsPIPsPrP_{\dagger}CrPIP^{\circ}P \gg PsClC_{100}$ $P \cdot P \pm C-P \gg CHC_{\ddot{e}}P_{\mu}PSPSC_{100}$ P_j AUC $PrP_{\mu}PiC-PrC_{\ddot{H}}PsP_jP_{\mu}C$, $P^{\circ}P \pm PsP \gg C-C$, Cr PSP° 4 % C, P° $P \cdot P \pm C-P \gg CHC_{\ddot{e}}P_{\mu}PSPSC_{100}$ P_j AUC 4'- $C, C_{\ddot{H}}P^{\circ}PSCl-PiC-PrC_{\ddot{H}}PsPeClP_{\ddot{e}}P_jP_{\mu}C$, $P^{\circ}P \pm PsP \gg C-C$, Cr PSP° 43 %. $P- CrC_{\ddot{H}}P^{\circ}C \dots CrPIP^{\circ}PSPSC_{100}$ P_j $P \cdot PSP^{\circ}C_{\dagger}P_{\mu}PSCH$ AUC $P \cdot P^{\circ}PiP^{\circ}P \gg CH_PSP^{\circ}$ $C, P^{\circ}C_{\ddot{H}}P_jP^{\circ}PePsP \gg PsPiC-C_{\dagger}PSP^{\circ}$ $P^{\circ}PeC$, $P_{\ddot{e}}PIPSC-ClC$, CH $C_{\dagger}P_{\ddot{e}}P \gg PsClC$, $P^{\circ}P \cdot PsP \gg Cr$ $P \cdot P \pm C-P \gg CHC_{\ddot{e}}CrC''C, CHClC_{100}$ PSP° 19 % $PiC_{\ddot{H}}P_{\ddot{e}}PsPrPSPsC_{\dagger}P^{\circ}ClPSPsP_jCr$ $PiC_{\ddot{H}}P_{\ddot{e}}PN_{\infty}PsP_jC- P \cdot$

PrPëP»C,C-P°P·PµPjPsPj. P°CḡCṛPSC,CṛCḡCṛPëCṛCḡ PSP° CṛPëC... PrP°PSPëC...,
PePsCḡPëPiCṛPIP°PSPSCḡ PrPsP·Pë PSPµ PṛPsC,CḡC-P±PSPs.

PµCḡPëPNḡPsPj PsPrPSPsCḡP°P·PsPIPSC— PrPsP·Pë 100 PjPi CṛPëP»PsCṛC,P°P·PsP»Cṛ P· 240 PjP»
PiCḡPµPNḡPṛC,,CḡCṛC,PsPIPSPiPs CṛPsPeCṛ (C-PSPiC-P±C-C,PsCḡ PePëCḡPePsPIPSPiPs CYP3A4)
PSPµ PIPëCḡPIP»CḡPI PṛPsPjC-C,PsPSPiPs PµC,,PµPeC,Cṛ PSP°
C,,P°CḡPjP°PePsPeC-PSPµC,PëPeCṛ CṛPëP»PsCṛC,P°P·PsP»Cṛ. Pj P·Piḡḡ™ CḡP·PeCṛ P· CṛPëPj
PePsCḡPëPiCṛPIP°PSPSCḡ PrPsP·Pë PSPµ PṛPsC,CḡC-P±PSPs. PµCḡPsC,Pµ PIPḡPëPIP°PSPSCḡ
PIPµP»PëPePëC... PsP±CṛCḡPiC-PI PiCḡPµPNḡPṛC,,CḡCṛC,PsPIPSPiPs CṛPsPeCṛ PjPsPḡPµ
PjP°C,Pë PeP»C-PSC-CṛPSPs P·PSP°CṛCṛC%PëPNḡ PIPṛP»PëPI PSP°
C,,P°CḡPjP°PePsPeC-PSPµC,PëPeCṛ CṛPëP»PsCṛC,P°P·PsP»Cṛ.

P—P°CṛC,PsCṛCṛPIP°PSPSCḡ CṛPëP»PsCṛC,P°P·PsP»Cṛ P· PsPjPµPiCḡP°P·PsP»PsPj
(C-PSPiC-P±C-C,PsCḡPsPj CYP2C19) PṛCḡPëP·PIPsPrPëP»Ps PrPs P·P±C-P»CḡCḡPµPSPSCḡ AUC
CṛPëP»PsCṛC,P°P·PsP»Cṛ PSP° 22 %, CḡPePµ CṛCṛPṛCḡPsPIPSPṛPḡCṛPIP°P»PsCṛCḡ
P·P±C-P»CḡCḡPµPSPSCḡPj AUC PrPµPiC-PrCḡPsPjPµC,P°P±PsP»C-C,Cṛ PSP° 68 % C-
P·PSPëPḡPµPSPSCḡPj AUC 4'C,CḡP°PSCṛ-PiC-PrCḡPsPeCṛPëPjPµC,P°P±PsP»C-C,Cṛ PSP° 36 %.
P— CṛCḡP°C...CṛPIP°PSPSCḡPj P·PSP°CṛPµPSCḡ AUC P·P°PiP°P»CḡPSP°
C,,P°CḡPjP°PePsP»PsPiC-CṛPSP° P°PeC,PëPIPSC-CṛC,Cḡ CṛPëP»PsCṛC,P°P·PsP»Cṛ
P·P±C-P»CḡCḡCṛC",CḡCṛCḡ PSP° 47 % PiCḡPë PsPrPSPsCṛP°CṛPSPsPjCṛ PiCḡPëPNḡPsPjC- P·
PsPjPµPiCḡP°P·PsP»PsPj. PḡP° PṛC-PrCṛC,P°PIC- CṛPëC... PrP°PSPëC...
CḡPµPePsPjPµPSPṛPsPIP°PSP° PrPsP·P° CṛPëP»PsCṛC,P°P·PsP»Cṛ CṛC,P°PSPsPIPëC,Cḡ 50 PjPi 2
CḡP°P·Pë PSP° PrPsP±Cṛ PiCḡPë PsPrPSPsCṛP°CṛPSPsPjCṛ PiCḡPëPNḡPsPjC- P·
PsPjPµPiCḡP°P·PsP»PsPj.

PŸCṛP±CṛC,CḡP°C,Pë C,,PµCḡPjPµPSC,Cṛ CṛPëC,PsC...CḡPsPjCṛ P 450. P·CṛP»Ps
PIC-PrP·PSP°CṛPµPSPs PṛC-PrPIPëC%PµPSPSCḡ CṛPëP»PsCṛC,P°P·PsP»PsPj AUC
P»PsPIP°CṛC,P°C,PëPSCṛ (CṛCṛC,P»PëPIPëPNḡ CṛCṛP±CṛC,CḡP°C, CYP3A4) C,P° PNḡPsPiPs
β-PiC-PrCḡPsPeCṛPëPePëCṛP»PsC,Pë PrPs 70 %. PŸP»C-Pr PrPsC,CḡPëPjCṛPIP°C,PëCṛCḡ
PsP±PµCḡPµPḡPSPsCṛC,C- PiCḡPë CṛCṛPjC-CṛPSPsPjCṛ PiCḡPëPNḡPsPjC-
CṛPëP»PsCṛC,P°P·PsP»Cṛ P·C- CṛCṛP±CṛC,CḡP°C,P°PjPë CYP3A4 P· PICṛP·CḡPePëPj
C,PµCḡP°PiPµPIC,PëCṛPSPëPj C-PSPṛPµPeCṛPsPj (C,P°PePëPjPë CḡPe CṛPëP·P°PiCḡPëPr,
PiP°P»PsC,,P°PSC,CḡPëPS, PṛC-PjPsP·PëPr, PṛPsC...C-PrPSC- CḡC-PḡPeC-PI). PµPsC,CḡC-P±PSPs
PrPsC,CḡPëPjCṛPIP°C,PëCṛCḡ PsP±PµCḡPµPḡPSPsCṛC,C- PiCḡPë PsPrPSPsCṛP°CṛPSPsPjCṛ
PiCḡPëPNḡPsPjC- CṛPëP»PsCṛC,P°P·PsP»Cṛ P·C- CṛC,P°C,PëPSP°PjPë, C%Ps
PjPµC,P°P±PsP»C-P·CṛCḡC,CḡCṛCḡ C,,PµCḡPjPµPSC,P°PjPë CṛPëC,PsC...CḡPsPjCṛ CYP3A4,
PSP°PiCḡPëPeP»P°Pr P·C- CṛPëPjPIP°CṛC,P°C,PëPSPsPj, P°C,PsCḡPIP°CṛC,P°C,PëPSPsPj C-
P»PsPIP°CṛC,P°C,PëPSPsPj.

PṛPSPṛCṛPeC,PsCḡPë C,,PµCḡPjPµPSC,Cṛ CṛPëC,PsC...CḡPsPjCṛ P 450. P·PiP»PëPI
C-PSPṛCṛPeC,PsCḡC-PI CYP3A4 C,P° CYP2C19 (C,P°PePëC... CḡPe PeP°CḡP±P°PjP°P·PµPiC-PS,
C,,PµPSC-C,PsC—PS, CḡPëC,,P°PjPiC-CṛPëPS C,P° PiCḡPµPiP°CḡP°C,Pë P·PIC-CḡPsP±PsCḡ)
PSP° C,,P°CḡPjP°PePsPeC-PSPµC,PëPeCṛ CṛPëP»PsCṛC,P°P·PsP»Cṛ PSPµ P±CṛPI
PrPsCṛP»C-PrPḡPµPSPëPNḡ. PŸPµPsCḡPµC,PëCṛPSPs P°PSC,PëC,CḡPsPjP±PsC,PëCṛPSP° PrC-Cḡ
PjPsPḡPµ P±CṛC,Pë P·PjC-PSPµPSP°, C,PsPjCṛ PSPµPsP±C...C-PrPSPs PiCḡPsPIPSPṛPëC,Pë
PjPsPSC-C,PsCḡPëPSPi Cṛ CḡP°P·C- P·P°CṛC,PsCṛCṛPIP°PSPSCḡ CṛPëP»PsCṛC,P°P·PsP»Cṛ P·
C-PSPṛCṛPeC,PsCḡP°PjPë CYP3A4 C,P° CYP2C19.

PµC-Pr CṛP°Cṛ PrPsCṛP»C-PrPḡPµPSCḡ C,CḡC,CḡPSPsPṛP°P»C-PSPSCḡ (CḡPePµ
C-PSPṛCṛPeCṛC" CYP1A2) P·PSPëPḡCṛPIP°P»Ps PePsPSCṛPµPSC,CḡP°CṛC-Cḡ
CṛPëP»PsCṛC,P°P·PsP»Cṛ Cṛ PiP»P°P·PjC- PeCḡPsPIC- PSP° 18 %.

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

PŸP»C-Pr PrPsC, CħPēPjCrPIP°C, PēC†CΠ PsP±PμCħPμP¶PSPsC†C, C- PīCħPē
PsPrPSPsC†P°C†PSPsPjCr P·P°C†C, PsC†C†PIP°PSPSC- C†PēP»PsC†C, P°P·PsP»Cr P· P±CrPrCħ-
CΠPePēPj C-PSC€PēPj P·P°C†PsP±PsPj, P·PrP°C, PSPēPj P·PSPēP¶CrPIP°C, Pē
P°CħC, PμCħC-P°P»CħPSPēPNε C, PēC†Pe, C†PμCħPμP· PjPsP¶P»PēPIC-C†C, Cħ
CħPsP·PIPēC, PeCr P°PrPēC, PēPIPSPsPiPs PiC-PiPsC, PμPSP·PēPIPSPsPiPs PμC,, PμPeC, Cr, C%oPs
C†C†PiCħPsPIPsPrP¶CrC”C, CħC†CΠ CħPμC,, P»PμPeC, PsCħPSPsCħ C, P°C...C-PeP°CħPrC-C”Cħ.

PħC†PsP±P»PēPIPsC†C, C- P·P°C†C, PsC†CžPIP°PSPSCΠ.

PμCħPēPNεPSCΠC, PSC-C†C, Cħ P»C-PeCrPIP°PSPSCΠ C†PēP»PsC†C, P°P·PsP»PsPj
C†P»C-Pr CħPμC, PμP»CħPSPs PsC†C-PSCħPIP°C, Pē PīPsCħCΠPr P· C-PSC€PēPjPē
PIP°CħC-P°PSC, P°PjPē P»C-PeCrPIP°PSPSCΠ, C, P°PePēPjPē CΠPe
CħPμPIP°C†PeCrP»CΠCħPēP·P°C†C-CΠ.

P’ C†PēP»Cr C†PIPsPiPs PjPμC...P°PSC-P·PjCr PrC-C— C†PēP»PsC†C, P°P·PsP» PjPsP¶Pμ
C†PiCħPēC†PēPSPēC, Pē C, P°C...C-PeP°CħPrC-Cħ, PIC-PrC†CrC, C, CΠ C†PμCħC†PμP±PēC, C, CΠ,
C, P°C...C-P°CħPēC, PjC-Cħ C, P°/P°P±Ps P°CħC, PμCħC-P°P»CħPSC† PiC-PiPsC, PμPSP·C-Cħ.
P—P±C-P»CħC€PμPSPSCΠ C†P°C†C, PsC, Pē C†PμCħC†PμPIPēC... C†PePsCħPsC†PμPSCħ,
P°C†PsC†C-PNεPsPIP°PSPμ P· C†PēP»PsC†C, P°P·PsP»PsPj, C†C, P°PSPsPIPēC, Cħ
PīCħPēP±P»PēP·PSPs PIC-Pr 5 PrPs 7 CrPrP°CħC-PI PSP° C...PIPēP»PēPSC†, C, PsPjCr Cr
PīP°C†C-C”PSC, C-PI C-P· CħPēP·PēPePsPj PrP°PSPsPiPs CΠPIPēC%oP° PīCħPμPīP°CħP°C,
PjPsP¶Pμ C†PiCħPēC†PēPSCΠC, Pē C†C, PμPSPsPeP°CħPrC-Cħ.

P—P°B PīP°C†C-C”PSC, P°PjPē, CΠPeC- PjPsP¶CrC, Cħ P±CrC, Pē C†C...PēP»CħPSC- PrPs
PīC-PrPIPēC%oPμPSPsPiPs CħPēP·PēPeCr C†PμCħPNεPsP·PSPēC... PīPsP±C-C†PSPēC...
PμC,, PμPeC, C-PI P· P±PsPeCr C†PμCħC†CΠ PI CħPμP·CrP»CħC, P°C, C-
P·P±C-P»CħC€PμPSPSCΠ C†P°C†C, PsC, Pē C†PμCħC†PμPIPēC... C†PePsCħPsC†PμPSCħ,
PSP°PīCħPēPeP»P°Pr P·P° PīP°C†C-C”PSC, P°PjPē P·C- C†C, P°P±C-P»CħPSPsCħ
C-C€PμPjC-C†PSPsCħ C...PIPsCħPsP±PsCħ C†PμCħC†CΠ, C†P»C-Pr CħPμC, PμP»CħPSPs
C†PiPsC†C, PμCħC-PiP°C, Pē PīC-Pr C†P°C† P»C-PeCrPIP°PSPSCΠ C†PēP»PsC†C, P°P·PsP»PsPj;
PīPsC, CħC-P±PSPs PICħP°C...PsPIC†PIP°C, Pē, C%oPs C†PēP»PsC†C, P°P·PsP»
PīCħPsC, PēPīPsPeP°P·P°PSPēPNε PīP°C†C-C”PSC, P°Pj, CΠPeC- PīPμCħPμPSPμC†P»Pē
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°PSPSCΠ PīCħPsC, CΠPiPsPj
PsC†C, P°PSPSC-C... 6 PjC-C†CΠC†C-PI, C, P° PīP°C†C-C”PSC, P°Pj P· C, CΠP¶PePsCħ
C, P°C...C-P°CħPēC, PjC-C”Cħ PI P°PSP°PjPSPμP·C-.

PŸP»C-Pr PrPsC, CħPēPjCrPIP°C, PēC†CΠ PsP±PμCħPμP¶PSPsC†C, C- PīCħPē
PīCħPēP·PSP°C†PμPSPSC- C†PēP»PsC†C, P°P·PsP»Cr PīP°C†C-C”PSC, P°Pj P· PμPeC, PsPīC-C”Cħ
PīPμCħPμPrC†PμCħPrCΠ C- C€P»CrPSPsC†PeC-PI, P° C, P°PePsP¶ PīP°C†C-C”PSC, P°Pj C-P·
C,, C-P±CħPēP»CΠC†C-C”Cħ P°P±Ps C, CħC-PiPsC, C-PSPSCΠPj PīPμCħPμPrC†PμCħPrCΠ.

PμP°C†C-C”PSC, C-PI PSPμPsP±C...C-PrPSPs PīPsPīPμCħPμPrPēC, Pē PīCħPs
PSPμPsP±C...C-PrPSC-C†C, Cħ P·PIPμCħPSC†C, PēC†CΠ PrPs P»C-PeP°CħCΠ Cr PIPēPīP°PrPeCr
PīPsCΠPIPē PeCħPsPIPsC, PμC† P°P±Ps C†PēPSC†C-PI PīC-Pr C†P°C† C, PμCħP°PīC-C—. Pj
CħP°P·C- PīPsCΠPIPē PsC†PSPēC... PeCħPsPIPsC, PμC† PīCħPēPNεPsPj C†PēP»PsC†C, P°P·PsP»Cr
PSPμPsP±C...C-PrPSPs PīCħPēPīPēPSPēC, Pē.

PhCTPec-P»CHPePe PictHpmPip°CTHP°C, P·PrP°C,PSPePN PictHpePipSC-C†CrPIP°C,Pē
P°PictHpmPip°C†C-CTH C,CTHpsPjP±PsC†PēC,C-PI, P·P±C-P»CHC€C†C”C,CHC†C† CTHPeP·PēPe
PeCTHpsPIPsC,PμC† PīC-Pr C†P°C† C...C-CTHCrCTHPiC-C†PSPeC... PIC,CTHCrC†P°PSCH
(PIPeP»CTHC†P°CTHC†Pē PSPμP·PSP°C†PSC- PIC,CTHCrC†P°PSPSC†, PSP°PictHpePeP»P°Pr
PIPePrP°P»PμPSPSC† P·CrP±P°). PīPeC%Ps PīP°C†C-C”PSC,C† PSPμPsP±C...C-PrPSPs
PictHpsPIPμC†C,Pē C...C-CTHCrCTHPiC-C†PSPμ PIC,CTHCrC†P°PSPSC† C-
P°PSC,PēP°PictHpmPip°C†C-PN PSPePN PμC,,PμPeC, C” PSPμP±P°P¶P°PSPePj, PictHpePN PsPj
C†PēP»PsC†C,P°P·PsP»C† C†P»C-Pr PictHpePipēPSPeC,Pē P·P° 5 PrPSC-PI PrPs
PsPīPμCTHP°C†C-C—.

PkP°PrC...PsPrPēP»Pē PīPsPsPrPēPSPsPeC- PīPsPIC-PrPsPjP»PμPSPSC† PictHps
PīPμPjP°C,PsP»PsPiC-C†PSC- PIC-PrC...PēP»PμPSPSC†, PIPeP»CTHC†P°CTHC†Pē
C,CTHpsPjP±PsC†PēC,PsPīPμPSC-CTH, P»PμPN PePsPīPμPSC-CTH, P°PictHP°PSC†P»PsC†PēC,PsP·,
PīP°PSC†PēC,PsPīPμPSC-CTH C,P° P°PīP»P°C†C,PēC†PSC† P°PSPμPjC-CTH. P’C-P»CHC€C-C†C,CH
PīP°C†C-C”PSC,C-PI PIPePrC†P¶C†PIP°P»Pē PīC-C†P»C† PictHpePipēPSPμPSPSC†
PictHpePN PsPjC† C†PēP»PsC†C,P°P·PsP»C†. PμCTHpsC,Pμ PrPμPeC-P»CHPeP° PIPePīP°PrPeC-PI
PīP°PSC†PēC,PsPīPμPSC-C— C,P° P°PīP»P°C†C,PēC†PSPsC— P°PSPμPjC-C— PjP°P»Pē
P»PμC,P°P»CHPSPePN PSP°C†P»C-PrPsPe.

PμP°C†C-C”PSC,C-PI C†P»C-Pr PīPsPīPμCTHPμPrPēC,Pē PictHps PSPμPsP±C...C-PrPSC-C†C,CH
PSPμPip°PN PSPs PīPsPIC-PrPsPjP»C†C,Pē PictHps P±C†PrCH-C†PeC- PsP·PSP°PePē, C†PeC-
PjPsP¶C†C,CH C†PIC-PrC†PēC,Pē PictHps CTHP°PSPSC-PN CTHpsP·PIPēC,PsPe
PīP°C,PsP»PsPiC-C†PSPeC... P·PjC-PS PeCTHpsPIC-, C,P°PePēC... C†Pe PiC-PīPμCTH,CμCTHPjC-C†
C,P° P±C-P»CH C† PīPsCTHP»C-. PkPμPsP±C...C-PrPSPs PictHpsPIPμC†C,Pē PīPsPIPSPePN
P°PSP°P»C-P· PeCTHpsPIC-, C†PeC%Ps C” PīC-PrPsP·CTHP° PSP° C-PSC,,PμPeC†C-CTH P°P±Ps
PSP°C†PIPSC- P±C†PrCH-C†PeC- C-PSC€C- PeP»C-PSC-C†PSC- PsP·PSP°PePē
PīP°C,PsP»PsPiC-C†PSPeC... P·PjC-PS PeCTHpsPIC-. PμCTHpePN PsPj C†PēP»PsC†C,P°P·PsP»C†
C†P»C-Pr PictHpePipēPSPeC,Pē, C†PeC%Ps C” PeP»C-PSC-C†PSC- P°P±Ps
P»P°P±PsCTHP°C,PsCTHpsC- PrPsPeP°P·Pē PīP°C,PsP»PsPiC-C†PSPeC... P·PjC-PS PeCTHpsPIC-.

Pj PīP°C†C-C”PSC,C-PI, C†PeC- PictHpePN PjP°P»Pē PīPsC,C†P¶PSC- C-PSPiC-P±C-C,PsCTHPē
CYP3A4 P°P±Ps CYP2C19, C†PīPsC†C,PμCTHC-PiP°P»PsC†C† P·P±C-P»CHC€PμPSPSC†
CTHC-PIPSC† C†PēP»PsC†C,P°P·PsP»C† C† PīP»P°P·PjC- PeCTHpsPIC-. Pj C,P°PePēC...
PIPePīP°PrPeP°C... CTHPμPePsPjPμPSPrPsPIP°PSP° PrPsP·P° C†PēP»PsC†C,P°P·PsP»C†
C†C,P°PSPsPIPeC,CH 50 PjPi 2 CTHP°P·Pē PSP° PrPsP±C†.

PkPμPsP±C...C-PrPSP° PsP±PμCTHPμP¶PSC-C†C,CH PictHpe C†C†PjC-C†PSPsPjC†
P·P°C†C,PsC†C†PIP°PSPSC- C†PēP»PsC†C,P°P·PsP»C† P· C-PSPiC-P±C-C,PsCTHP°PjPē P°P±Ps
C-PSPrC†PeC,PsCTHP°PjPē CYP 3A4, CYP 2C19 P°P±Ps C†C†P±C†C,CTHP°C,P°PjPē CYP 3A4.

PkPμPsP±C...C-PrPSPs P· PsP±PμCTHPμP¶PSC-C†C,CTH PictHpeP·PSP°C†P°C,Pē PictHpmPip°CTHP°C,
PīP°C†C-C”PSC,P°Pj C-P· PīPμCTHPμPrC†PμCTHPrPSPsCTH P°P±Ps C€P»C†PSPsC†PePsPIPsCTH
PμPeC,PsPiC-C”CTH, C,,C-P±CTHPeP»C†C†C-C”CTH P°P±Ps C,CTHC-PīPsC,C-PSPSC†Pj
PīPμCTHPμPrC†PμCTHPrCH.

PkPμPsP±C...C-PrPSP° PsP±PμCTHPμP¶PSC-C†C,CH PictHpe C†C†PjC-C†PSPsPjC†
PictHpePN PsPjC- C†PēP»PsC†C,P°P·PsP»C† P· P±C†PrCH-C†PePēPjPē C-PSC€PēPjPē
P»C-PeP°CTHC†CHPePēPjPē P·P°C†PsP±P°PjPē, C%Ps PjPsP¶C†C,CH P·PSPeP¶C†PIP°C,Pē
P°CTHC,PμCTHC-P°P»CHPSPePN C,PēC†Pe, PsC†PeC-P»CHPePē C-C†PSC†C” CTHPeP·PēPe
P°PrPēC,PēPIPSPsPiPs PiC-PīPsC,PμPSP·PēPIPSPsPiPs PμC,,PμPeC,C† P·
CTHPμC,,P»PμPeC,PsCTHpsPSC C,P°C...C-PeP°CTHPrC-C”CTH.

РҮР»С-Рr PrPsC,СҲРөРјСrPIP°С,РөСГCЦ PsP±PμCҲPμP¶PSPsCГC,С- PиCҲРө
PиCҲРөP·PSP°С±PμPSPSC- C†PөP»PsCГC,Р°P·PsP»Cр P· P±CрPrCH-СЦPePөPјPө C-PSC€PөPјPө
P°PSC,РөC,СҲPsPјP±PsC,РөC±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,PсPјP°C,РөC±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,Р°P·PsP»Cр PIP°PiC-C,PSPөPј,
PiPsC,PμPSC†C-PNөPSPөPNө CҲРөP·PөPe PSPμPIC-PrPsPјPөPNө. P"PsCГP»C-PrP¶PμPSPSCЦ PSP°
C,PIP°CҲРөPSP°С... 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,Р°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°С... PiPsPeP°P·P°P»Pө, C%oPs
C†PөP»PsCГC,Р°P·PsP» PјPsP¶Pμ PiCҲPsPSPөPeP°C,Pө Cр PiCҲCрPrPSPμ PјPsP»PsPePs.
PҮPsC±PSC- PrP°PSC- PiCҲPs PiCҲPsPSPөPePSPμPSPSCЦ C†PөP»PsCГC,Р°P·PsP»Cр Cр
PiCҲCрPrPSPμ PјPsP»PsPePs P¶C-PSPөPө PIC-PrCГCрC,PSC-. P'CҲP°С...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,Р°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°С... PiPsPeP°P·P°P»Pө, C%oPs
C†PөP»PsCГC,Р°P·PsP» PSPμ PIPiP»PөPIP°С" 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,CҲP°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

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¶¶PePsCḡ PïPμC‡C-PSPePsPIPsCḡ
PSPμPrPsCíC,P°C,PSC-CíC,Cḡ.

PμP°C‡C-C''PSC,Pë P»C-C,PSCḡPsPiPs PIC-PeCž

PḡPμPjP°C'' PSPμPsP±C...C-PrPSPsCíC,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°CḡCíCḡPePëPNë P·P°CíC-P± PSPμ CḡPμPePsPjPμPSPrCíC''C,CḡCíCï
PïCḡPëP·PSP°C‡P°C,Pë PrC-C,CïPj C‡PμCḡPμP· PIC-PrCíCíC,PSC-CíC,Cḡ PrP°PSPëC...
C%oPsPrPs P±PμP·PïPμPePë C,P° PμC,,PμPeC,PëPIPsCíC,C- PNëPsPiPs
P·P°CíC,PsCíCíPIP°PSPSCï.

PμPμCḡPμPrPsP·CžPIP°PSPSCï.

P‡PSC,,PsCḡPjP°C‡C-Cï PïCḡPs PiPsCíC,CḡPμ PïPμCḡPμPrPsP·CíPIP°PSPSCï
PsP±PjPμP¶PμPSP°. PḡPsP¶P»PëPIC- CíPëP»CḡPSPëPNë PiPsP»PsPIPsPëPNë P±C-P»Cḡ,
PrC-P°CḡPμCï, C,P°C...C-PeP°CḡPrC-Cï C,P° CíPμCḡC‡PμPIP° P°CḡPëC,PjC-Cï. P—P°
PïP°C‡C-C''PSC,P°PjPë PSPμPsP±C...C-PrPSPs CíPïPsCíC,PμCḡC-PiP°C,Pë C,P°
PïCḡPsPIPsPrPëC,Pë PïC-PrC,CḡPëPjCíPIP°P»CḡPSCí C,PμCḡP°PïC-Cḡ. PḡPμPsP±C...C-PrPSPs
CíPïPsCḡPsP¶PSPëC,Pë CëP»CíPSPsPe CëP»CïC...PsPj C-PSPrCíPeC‡C-C—
P±P»CḡPIP°PSPSCï P°P±Ps PïCḡPsPjPëPIP°PSPSCï CëP»CíPSPeP°.

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 Cí PeP»C-PSC-C‡PSPëC... PrPsCíP»C-PrP¶PμPSPSCïC...
PïCḡPμPïP°CḡP°C,Cí, P±CíP»Pë PiPsP»PsPIPsPëPNë P±C-P»Cḡ (>30 %), PrC-P°CḡPμCï (>15 %)
C,P° PïPsCḡCíCëPμPSPSCï CḡPsP±PsC,Pë PePëCëPμC‡PSPëPeCí (>15 %). PïC-
CḡPμP°PeC‡C-C— P·P°P·PIPëC‡P°PNë PjP°P»Pë P»PμPiPeCí P°P±Ps PïPsPjC-CḡPSCí
C-PSC,PμPSCíPëPIPsC-CíC,Cḡ C,P° C-PSPsPrC- PïPsP»PμPiCëCíPIP°P»PëCíCï P·P°
CḡP°C...CíPSPsPe P·PSPëP¶PμPSPSCï PrPsP·Pë.

PḡPμP±P°P¶P°PSC- PμC,,PμPeC,Pë, CïPeC- C-PSPsPrC- PjPsP¶CíC,Cḡ PIPëPSPëPePSCíC,Pë
PïC-Pr C‡P°Cí P·P°CíC,PsCíCíPIP°PSPSCï C‡PëP»PsCíC,P°P·PsP»Cí, P·P°P·PSP°C‡PμPSC- Cí
C,P°P±P»PëC‡C- PSPëP¶C‡Pμ.

P§P°CíC,PsC,P° PïPsP±C-C‡PSPëC... CḡPμP°PeC‡C-PNë: PrCíP¶Pμ C‡P°CíC,Ps (≥1/10);
C‡P°CíC,Ps (≥1/100, <1/10); PSPμC‡P°CíC,Ps (≥1/1000, <1/100); CḡC-PrPePs (≥1/10000,
<1/1000); PrCíP¶Pμ CḡC-PrPePs (<1/10000); C‡P°CíC,PsC,P° PSPμPIC-PrPsPjP°
(PSPμPjPsP¶P»PëPIPs PsC‡C-PSPëC,Pë PSP° PsCíPSPsPIC- PSP°CïPIPsPëC... PrP°PSPëC...).

P§P°CíC,PsC,P° PïPsP±C-C‡PSPëC... CḡPμP°PeC‡C-PNë, CïPeC-
CíPïPsCíC,PμCḡC-PiP°P»PëCíCï Cí PïPμCḡC-PsPr
PïC-CíP»CïCḡPμC''CíC,CḡP°C‡C-PNëPSPsPiPs P·P°CíC,PsCíCíPIP°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,PµPSPPrµPSC†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

$P - P \pm PsPeC \acute{z} C \acute{I} C \acute{z} PrP \ddot{e} PSPSPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e}$	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P_{\mu} C \ddot{H} PsPIP sPIP \ddot{e} P \gg P \ddot{e} PI PI PsPePs, PSPsC \acute{I} PsPIC - PeC \ddot{H} PsPIPsC, P_{\mu} C \ddagger C -, C \acute{e} P \gg C \acute{r} PSPePsPIPs - PeP \ddot{e} C \acute{e} PePsPIC - PeC \ddot{H} PsPIPsC, P_{\mu} C \ddagger C -, PSP_{\mu} P \cdot \mathfrak{B} \ddot{H}^{\text{TM}} C \ddot{I} C \acute{I} PsPIP^{\circ} PSC - PeC \ddot{H} PsPIPsC, P_{\mu} C \ddagger C -, PsC \ddot{H} C, PsC \acute{I} C, P^{\circ} C, P \ddot{e} C \ddagger PSP^{\circ} P \ddot{I} C - P \ddot{I} PsC, P_{\mu} PSP \cdot C - C \ddot{I}$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P \ddot{I} C \ddot{H} P \ddot{e} P \ddot{I} P \gg P \ddot{e} P \ddot{I} P \ddot{e}, P \ddot{I} C - P \ddot{I} P_{\mu} C \ddot{H} C, P_{\mu} PSP \cdot C - C \ddot{I}, P \ddot{I} C - P \ddot{I} PsC, P_{\mu} PSP \cdot C - C \ddot{I}, PeC \ddot{H} PsPIPsPIP \ddot{e} P \gg P \ddot{e} P \ddot{I} P \ddot{e} PI P_j PsP \cdot PsPe, P \gg P_{\mu} P \ddot{I} P_{\mu} PSC -, P_j \mathfrak{B} \ddot{H}^{\text{TM}} C \ddot{I} P \cdot P \ddot{e}, PrP \ddot{e} C \dots P^{\circ} P \gg CH \ddot{H} PSC - C \acute{e} P \gg C \ddot{I} C \dots P \ddot{e}; P \ddot{I} C - PrC \acute{e} PeC - C \ddot{H} PSC - PeC \ddot{H} PsPIPsPIP \ddot{e} P \gg P \ddot{e} P \ddot{I} P \ddot{e}$
$P - P \pm PsPeC \acute{z} PrP \ddot{e} C \dots P^{\circ} P \gg CH \ddot{H} PSPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e}$	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$C \ddot{H} P \ddot{e} PSC - C, C, P^{\circ} C \ddot{H} P \ddot{e} PSP \ddot{I} C - C,$
	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P \cdot P^{\circ} PrP \ddot{e} C \acute{e} PeP^{\circ}, P \ddot{I} PSP_{\mu} P \ddot{I} P_j PsPSC - C \ddot{I}, PeP^{\circ} C \acute{e} P_{\mu} P \gg CH$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$C - PSC, P_{\mu} C \ddot{H} C \acute{I} C, P \ddot{e} C \ddagger C - P^{\circ} P \gg CH \ddot{H} PSP^{\circ} P \ddot{I} PSP_{\mu} P \ddot{I} P_j PsPSC - C \ddot{I}$
$P - P \pm PsPeC \acute{z} C \acute{e} P \gg C \acute{z} PSPePsPIPs - PeP \ddot{e} C \acute{e} PePsPIPsP \ddot{I} Ps C, C \ddot{H} P^{\circ} PeC, C \acute{z}$	$PrC \acute{r} P \ddot{I} P_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$PrC - P^{\circ} C \ddot{H} P_{\mu} C \ddot{I}, P \ddot{I} PsC \ddot{H} C \acute{r} C \acute{e} P_{\mu} PSPSC \ddot{I} P \ddot{I} P \ddot{e} P \ddot{I} PsC \ddot{H} PsP \ddot{I} PSP_{\mu} PSPSC \ddot{I}$
	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$PSC \acute{r} PrPsC, P^{\circ} C - P \pm P \gg CH \ddot{H} P \ddot{I} P^{\circ} PSPSC \ddot{I}, PrP \ddot{e} C \acute{I} P \ddot{I} P_{\mu} P \ddot{I} C \acute{I} C - C \ddot{I}, P_j P_{\mu} C, P_{\mu} PsC \ddot{H} P \ddot{e} P \cdot P_j, P \pm C - P \gg CH C \acute{r} P \ddot{I} P \ddot{e} P \ddot{I} PsC, C -$
	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P \ddot{I} P^{\circ} C \acute{I} C, C \ddot{H} P \ddot{e} C,$
$P - P \pm PsPeC \acute{z} P \ddot{I} P_{\mu} P \ddot{I} P^{\circ} C, PsP \pm C - P \gg C - P^{\circ} C \ddot{H} PSPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e}$	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P \ddot{I} P_{\mu} P \ddot{I} P^{\circ} C, P \ddot{e} C, P^{\circ} PSPsP_j P^{\circ} P \gg C - C - P \ddot{I} P_{\mu} C \ddagger C - PSPePsPIPsC - C, C \acute{r} PSPeC \ddagger C - C -, P \ddot{I} PsPIC, C \ddot{I} PSP \ddot{e} C \ddagger C \ddot{I}$
	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$P \ddot{I} P \ddot{e} C \acute{I} P \ddot{e} P \ddot{I} P^{\circ} PSPSC \ddot{I}, C \acute{I} P \ddot{I} P_{\mu} C \ddot{H} P \pm C - P \ddot{I}$
$P - P \pm PsPeC \acute{z} C \acute{e} PeC - C \ddot{H} P \ddot{e} C - P \ddot{I} C - PrC \acute{e} PeC - C \ddot{H} PSP \ddot{e} C \dots C, PeP^{\circ} PSP \ddot{e} Ps$	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P_{\mu} PeP \cdot P_{\mu} P_j P^{\circ}, C \acute{e} PeC - C \ddot{H} PSC - P \ddot{I} P \ddot{e} C \acute{I} P \ddot{e} P \ddot{I} P^{\circ} PSPSC \ddot{I}, C \acute{I} P \ddot{e} PSP \ddot{r} C \ddot{H} PsP_j P \ddot{Y} C, C - P \ddot{I} P_{\mu} PSC \acute{I} P^{\circ} - P^{\circ} P \ddot{I} PsPSC \acute{I} PsPSP^{\circ}, C, PsPeC \acute{I} P \ddot{e} C \ddagger PSP \ddot{e} P \mathfrak{N} P_{\mu} P \ddot{I} C - PrP_{\mu} C \ddot{H} P_j P^{\circ} P \gg CH \ddot{H} PSP \ddot{e} P \mathfrak{N} PSP_{\mu} PeC \ddot{H} PsP \gg C - P \cdot, PeC \ddot{H} PsP \ddot{I} P \ddot{e} P \mathfrak{I} \mathfrak{B} \ddot{H}^{\text{TM}} C \ddot{I} P SPeP^{\circ}$
	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P_j C - P^{\circ} P \gg P \ddot{I} C - C \ddot{I}$
$P - P \pm PsPeC \acute{z} C \acute{I} PeP_{\mu} P \gg P_{\mu} C, PSPs - P_j \mathfrak{B} \ddot{H}^{\text{TM}} C \ddot{I} P \cdot PsPIPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e} C, P^{\circ} C \acute{I} P \ddot{I} PsP \gg C \acute{z} C \ddagger PSPsC - C, PeP^{\circ} PSP \ddot{e} PSP \ddot{e}$	$C \ddot{H} C - PrPePs$	$PSP \ddot{e} C \ddot{H} PePsPIP^{\circ} PSP_{\mu} PrPsC \acute{I} C, P^{\circ} C, PSC - C \acute{I} C, CH, P \ddot{I} PsC \ddot{H} C \acute{r} C \acute{e} P_{\mu} PSPSC \ddot{I} C, C \acute{r} PSPeC \ddagger C - C - PSP \ddot{e} C \ddot{H} PsPe$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P \ddot{I} P_{\mu} P_j P^{\circ} C, C \acute{r} C \ddot{H} C - C \ddot{I}, P \ddot{I} PsP \gg P^{\circ} PeC - C \acute{r} C \ddot{H} C - C \ddot{I}$
$P - P^{\circ} P \ddot{I} P^{\circ} P \gg CH \ddot{H} PSC - C \ddot{H} PsP \cdot P \gg P^{\circ} PrP \ddot{e}$	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$P \pm C - P \gg CH C \acute{r} P \ddot{I} C \ddot{H} C \acute{r} PrC \ddot{I} C \dots, P^{\circ} C \acute{I} C, P_{\mu} PSC - C \ddot{I}$
	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$PsP \cdot PSPsP \pm, PSP_{\mu} P \cdot PrC \acute{r} P \ddot{I} P^{\circ} PSPSC \ddot{I}$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P \ddot{I} C - C \ddot{H} P_{\mu} PeC \acute{I} C - C \ddot{I}, P \pm C - P \gg CH$
$P \cdot P^{\circ} P \pm PsC \ddot{H} P^{\circ} C, PsC \ddot{H} PSC - PrPsC \acute{I} P \gg C - PrP \ddot{I} P_{\mu} PSPSC \ddot{I}$	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P \ddot{I} C - PrP \ddot{I} P \ddot{e} C \% P_{\mu} PSPSC \ddot{I} C \ddot{H} C - P \ddot{I} PSC \ddot{I} C \acute{I} P_{\mu} C \ddagger PsPIPsC - PeP \ddot{e} C \acute{I} P \gg PsC, P \ddot{e}, C \acute{I} P_{\mu} C \ddagger PsPIP \ddot{e} PSP \ddot{e} C \acute{r} PeC \ddot{H} PsPIC -, PeC \ddot{H} P_{\mu} P^{\circ} C, P \ddot{e} PSC - PSC \acute{r} P \ddot{I} PeC \ddot{H} PsPIC -$

$P - P \pm C - P \gg CH \ddot{H} C \acute{e} P_{\mu} PSPSC \ddot{I} PeC - P \gg CH \ddot{H} PePsC \acute{I} C, C - P \ddot{I} P \ddot{e} P \ddot{I} P^{\circ} PrPeC - P \ddot{I} PIC - PrC \ddagger C \acute{r} C, C, C \ddot{I}$

$P-P\pm P_{\mu}C_{\overline{H}}C-PiP^{\circ}C, P\ddot{e} \text{ } C\acute{r} \text{ } PSP_{\mu}PrPsC\acute{I}C, C\acute{r}P\ddot{i}PSPsPjC\acute{r} \text{ } PrP\gg C\overline{I} \text{ } PrC-C, P_{\mu}PN_{\mathbb{N}} \text{ } PjC-C\acute{I}C\ddagger C-.$

$PjP\ddot{i}P^{\circ}PePsPIPeP^{\circ}.$

$P_{\overline{I}}Ps \text{ } 10 \text{ } C, P^{\circ}P\pm P\gg P_{\mu}C, PsPe \text{ } C\acute{r} \text{ } P\pm P\gg C-C\acute{I}C, P_{\mu}C_{\overline{H}}C-; \text{ } P\ddot{i}Ps \text{ } 3 \text{ } P^{\circ}P\pm Ps \text{ } 6 \text{ } P\pm P\gg C-C\acute{I}C, P_{\mu}C_{\overline{H}}C-PI \text{ } C\acute{r} \text{ } PeP^{\circ}C_{\overline{H}}C, PsPSPSC-PN_{\mathbb{N}} \text{ } C\acute{r}P\ddot{i}P^{\circ}PePsPIC\ddagger C-.$

$P_{\overline{L}}P^{\circ}C, P_{\mu}PiPsC_{\overline{H}}C-C\overline{I} \text{ } PIC-PrP\ddot{i}C\acute{r}C\acute{I}PeC\acute{r}.$ $P-P^{\circ} \text{ } C_{\overline{H}}P_{\mu}C\ddagger P_{\mu}P\ddot{i}C, PsPj.$

$P'P\ddot{e}C_{\overline{H}}PsP\pm PSP\ddot{e}Pe.$

$P_{\overline{h}}P_{\overline{y}} \text{ } B\langle P_{\overline{h}}PrP^{\circ}PjP_{\mu}Pr \text{ } P\propto P^{\circ}C_{\overline{H}}PjP^{\circ}B\rangle.$

$P_{\overline{H}}C-C\acute{I}C\ddagger P_{\mu}P\cdot PSP^{\circ}C...PsPrP\overline{I}P_{\mu}PSPSC\overline{I} \text{ } PIP\ddot{e}C_{\overline{H}}PsP\pm PSP\ddot{e}PeP^{\circ} \text{ } C, P^{\circ} \text{ } P^{\circ}PrC_{\overline{H}}P_{\mu}C\acute{I}P^{\circ} \text{ } PjC-C\acute{I}C\ddagger C\overline{I} \text{ } P\ddot{i}C_{\overline{H}}PsPIP^{\circ}PrP\overline{I}P_{\mu}PSPSC\overline{I} \text{ } PN_{\mathbb{N}}PsPiPs \text{ } PrC-C\overline{I}P\gg C_{\overline{H}}PSPsC\acute{I}C, C-.$

$P'C\acute{r}P\gg. \text{ } P_{\overline{H}}P^{\circ}C_{\overline{H}}C\mathbb{E}. \text{ } P''P\overline{I}. \text{ } P_{\overline{I}}C-P\gg C\acute{I}C\acute{r}PrC\acute{I}C_{\overline{H}}PePsPiPs \text{ } 5, \text{ } 95-200, \text{ } P_{\overline{I}}P^{\circ}P\pm B_{\overline{H}}^{\text{TM}} \text{ } C\overline{I}PSC-C\ddagger P_{\mu}, \text{ } P_{\overline{I}}PsP\gg C_{\overline{H}}C\%_{\circ}P^{\circ}.$

$P-P^{\circ}C\overline{I}PIPSP\ddot{e}Pe.$

$P_{\overline{Y}}P\cdot P_{\overline{H}} \text{ } P\propto P^{\circ}C_{\overline{H}}PjP^{\circ}C\acute{I}C_{\overline{H}}C_{\overline{H}}C, C-PeP^{\circ}P\gg C\acute{I} \text{ } P\triangleright C-PjC-C, P_{\mu}Pr.$

$P_{\overline{H}}C-C\acute{I}C\ddagger P_{\mu}P\cdot PSP^{\circ}C...PsPrP\overline{I}P_{\mu}PSPSC\overline{I} \text{ } P\cdot P^{\circ}C\overline{I}PIPSP\ddot{e}PeP^{\circ}.$

$P_{\overline{L}}P_{\mu}PSPSP_{\mu}PrC- \text{ } P_{\overline{h}}PIP_{\mu}PSC_{\overline{H}} \text{ } 89/201, \text{ } 1077 \text{ } P\acute{K}C-PePsC\acute{I}C-C\overline{I}, \text{ } P_{\overline{L}}C-P\ddot{i}C_{\overline{H}}.$