

Р†РќРЎРЎР РЈРљРІР†РЇ

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

PᵤP₃P•PŷPhP₃

(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;

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

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:

$$\text{PeC}\bar{\text{T}}\text{P}\bar{\text{s}}\text{C}\dots\text{PjP}^\circ\text{P}\gg\text{CH}\bar{\text{b}}\text{PeC}\bar{\text{r}}\text{PeC}\bar{\text{r}}\text{C}\bar{\text{T}}\text{C}\bar{\text{r}}\text{P}\bar{\text{r}}\text{P}\cdot\text{C}\bar{\text{L}}\text{P}\text{S}\bar{\text{P}}\bar{\text{e}}\text{P}\bar{\text{N}}_0,$$
$$\text{PiC-PrCHPsPeClPëPjPuC,PëP} \gg \text{PiCHPsPiC-P} \gg \text{C†PuP} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ \quad \text{P} \cdot 5, \text{C†PuP} \gg \text{CHP} \gg \text{PsP} \cdot \text{P}^\circ$$
$$\text{PjC-PeCHPsPeCHPpPcTC,P}^{\circ}\text{P}\gg\text{C-C}\ddagger\text{PSP}^{\circ}\text{ 101, PiP}^{\circ}\text{PiPSC-CH TC, PuP}^{\circ}\text{CHP}^{\circ}\text{C,, PeP}^{\circ}\text{P}\gg\text{CHC}\ddagger\text{C-CH}$$
$$\text{PeP}^\circ\text{CHPjP}\mu\text{P}\gg\text{PsP}\cdot\text{P}^\circ.$$
$$\mathbf{P} \triangleright \mathbf{C} - \mathbf{P} \mathbf{e} \mathbf{P}^{\circ} \mathbf{C} \mathbf{f} \mathbf{C} \mathbf{f} \mathbf{C} \mathbf{h} \mathbf{P} \mathbf{e} \mathbf{P}^{\circ} \mathbf{C} \mathbf{,,} \mathbf{P} \mathbf{s} \mathbf{C} \mathbf{f} \mathbf{P} \mathbf{j} \mathbf{P}^{\circ} . \mathbf{P} \check{\mathbf{y}} \mathbf{P}^{\circ} \mathbf{P} \pm \mathbf{P} \gg \mathbf{P} \mu \mathbf{C} , \mathbf{P} \mathbf{e} \mathbf{P} \check{\mathbf{e}} .$$
$$PhCI\dot{P}SPsPIPSC-C_{\text{„}}C-P\cdot P\ddot{e}PePs-C...C-PjC-C\ddot{z}PSC-PIP\gg P^{\circ}CI\dot{C},P\ddot{e}PIPsCI\dot{C},C-:$$

C,P°P±P»PμC,PePë PïPs 50 PjPi: PeCĤCríPiP»C-, PïP»P°CĬPeC- 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°CĬPeC- 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°.

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

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. P_hP°PeCfPëPjP°P»CHbPSP°
 PePsPSC†PμPSC,CfjP°C†C-Cj (P_Y_{max}) C†PëP»PsCfC,P°P·PsP»Cf C,P° PN₂PsPiPs
 PjPμCfjPiPëPSPSPëC... PjPμC,P°P±PsP»C-C,C-PI PiC-PrPiPëC%Cr"C,CHCfCj PjPμPSC€
 PiCfjPsPiPsCfjC†C-PN₂PSPs 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° PN₂PsPiPs PjPμC,P°P±PsP»C-C,C-PI
 P·P±C-P»CHbC€CfC"C,CHCfCj PiCfjPëP±P»PëP·PSPs PiCfjPsPiPsCfjC†C-PN₂PSPs PrPs
 PrPsP·CfPiP°PSPSCj. PjPiPSPëPN₂ 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 PN₂PsPiPs
 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 PN₂PsPiPs
 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»PsPiPSPëPN₂ 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 % PN₂PsPiPs 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·PiPTM 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·PiPTM 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° PN₂PsPiPs

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-PrPİPsPIC-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-PrPİPsPIC-PrPSPs PSP° 41 % C,P° 47 % PSPeP¶C‡PëPjPë Cf PIP°C‡C-C”PSC,C-PI P· C,C¶P¶PePëPjPë PİPsC¶CfC¶PμPSPSC¶PjPë PSPeC¶PsPe PİPsC¶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-PrPİPsPIC-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· PİPsPjC-C¶PSPsC¶ C,P° C,C¶P¶PePsC¶ PİPμC‡C-PSPePsPIPsC¶ PSPμPrPsC¶C,P°C,PSC-C¶C,C¶.

РљР»С-РSC-С‡РSC- С...Р°С¶Р°РєС,РμС¶РëС¶С,РëРєРë.

РμРsРєР°Р°Р°РSPSC¶.

P”P»C¶ P·P±C-P»CHbC¶PμPSPSC¶ 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· PİPμC¶PμPjC-P¶PSPsC¶ PeCfP»CHbPİP°PIC-C¶C,C¶, C¶PeC- PSPμ PjP°C¶C,CH P±PsP»C¶ Cf C¶C,P°PSC- C¶PİPsPePsC¶ C,P° PsP·PSP°Pe PSPμPeC¶PsP·Cf PİPμC¶PëC,,PμC¶PëC‡PSPeC... C,PeP°PSPëPS (P·P°C...PIPsC¶C¶PİP°PSPSC¶ PİPμC¶PëC,,PμC¶PëC‡PSPeC... P°C¶C,PμC¶C-PNë, C¶C,P°PrC-C¶ II P·P° PαPsPSC,PμPNëPSPsPj).

P—P°C¶C,PsC¶PsPICfPİP°C,Pë C¶Pe C,PμC¶P°PİC-C¶ PrC¶CfPİPsC— P»C-PSC-C— PrP»C¶ PİP°C‡C-C”PSC,C-PI, Cf C¶PePëC... P·PjC-PSP° C¶C,PëP»C¶ P¶PëC,C,C¶ (PİPeP»C¶C‡P°C¶Pë PIC-PrPjPsPICf PIC-Pr PeCfC¶C-PSPSC¶ C,P° PePsPSC,C¶PsP»CHbPsPIP°PSC- PİC¶PsPiC¶P°PjPë P·P°PSC¶C,CH C¶PİPsC¶C,PsPj) C,P° C-PSC€C- PIC-PrPİPsPIC-PrPSC- P·P°C...PsPrPë PSPμ PİC¶PëP·PİPμP»Pë PrPs P·PSP°C‡PSPsPiPs PİPsC¶P»P°P±P»PμPSPSC¶ C¶PëPjPİC,PsPjC-PI PİPμC¶PμPjC-P¶PSPsC— PeCfP»CHbPİP°PIPsC¶C,C-.

РμС¶РsС,РëРİРsРєР°Р°РSPSC¶.

- P’C-PrPsPjP° PiC-PİPμC¶C‡CfC,P»PëPIC-C¶C,CH PrPs C‡PëP»PsC¶C,P°P·PsP»Cf P°P±Ps PrPs P±CfPrCHb-C¶PePsPiPs PePsPjPİPsPSPμPSC,P° PİC¶PμPİP°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);
- PİPsPjC-C¶PSP° P°P±Ps C,C¶P¶PeP° PİPμC‡C-PSPePsPIP° PSPμPrPsC¶C,P°C,PSC-C¶C,CH;
- P·P°C¶C,C-PNëPSP° C¶PμC¶C‡PμPIP° PSPμPrPsC¶C,P°C,PSC-C¶C,CH;
- PIP°PiC-C,PSC-C¶C,CH;

- $P \pm C \uparrow PrCH \cdot C \downarrow PeP^{\circ} \text{ PIC} - PrPsPjP^{\circ} \text{ C} \uparrow C \dots P \ddot{e}P \gg CH \cdot PSC - C \uparrow C, CH \cdot PrPs \text{ Pe}C \uparrow PsPIP \cdot S, P_{\mu}C \uparrow C - (PSP^{\circ} \text{ P} \ddot{i}C \uparrow P \ddot{e}PeP \gg P^{\circ} Pr, PIP \ddot{e}C \uparrow P^{\circ} P \cdot PeP^{\circ} \text{ C} \epsilon P \gg C \uparrow PSPeP^{\circ} P^{\circ} P \pm Ps$
 $PrPIP^{\circ} PSP^{\circ} PrC \uparrow C \downarrow C, P \ddot{e}P \ddot{i}P^{\circ} P \gg PsC - PeP \ddot{e}C \epsilon PeP \ddot{e} \text{ C} \uparrow C \uparrow C, P^{\circ} PrC - C - P \cdot P^{\circ} P \ddot{i}PsC \uparrow C, C \uparrow P_{\mu}PSPSC \downarrow,$
 $PSP_{\mu}C \% PsPrP^{\circ} PIPSC - P \ddot{N}_{\epsilon} \text{ Pi}P_{\mu}PjPsC \uparrow P^{\circ} PiC - C \uparrow PSP \ddot{e}P \ddot{N}_{\epsilon} \text{ C} - PSC \uparrow C \uparrow P \gg CH \cdot C, (P \ddot{i}C \uparrow PsC, C \downarrow PiPsPj \text{ 6}$
 $PjC - C \uparrow C \downarrow C \uparrow C - PI), P \ddot{i}C \uparrow PsP \gg C - C, P_{\mu}C \uparrow P^{\circ} C, P \ddot{e}PIPSP^{\circ} \text{ C}, PsC \uparrow PjP^{\circ} PrC - P^{\circ} P \pm P_{\mu}C, P \ddot{e}C \uparrow PSPsC -$
 $C \uparrow P_{\mu}C, P \ddot{e}PSPsP \ddot{i}P^{\circ} C, C - C - , C \uparrow P \gg P^{\circ} P \pm PsPePsPSC, C \uparrow PsP \gg CH \cdot PsPIP^{\circ} PSP^{\circ}$
 $P^{\circ} C \uparrow C, P_{\mu}C \uparrow C - P^{\circ} P \gg CH \cdot PSP^{\circ} \text{ Pi}C - P \ddot{i}P_{\mu}C \uparrow C, P_{\mu}PSP \cdot C - C \downarrow);$
- $C \epsilon P \gg C \uparrow PSPsC \uparrow PePsPIP^{\circ} \text{ C}, P^{\circ} C \dots C - PeP^{\circ} C \uparrow PrC - C \downarrow, C, C - P \pm C \uparrow P \ddot{e}P \gg C \downarrow C \uparrow C - C \downarrow$
 $C \epsilon P \gg C \uparrow PSPsC \uparrow PeC - PI \text{ P}^{\circ} P \pm Ps \text{ Pj}C \uparrow P \gg CH \cdot C, P \ddot{e}P \gg PsPeC \uparrow P \gg C \downarrow C \uparrow C \uparrow PSP^{\circ} \text{ C} \epsilon P \gg C \uparrow PSPsC \uparrow PePsPIP^{\circ}$
 $P_{\mu}PeC, PsP \ddot{i}C - C \downarrow \text{ PI } P^{\circ} PSP^{\circ} PjPSP_{\mu}P \cdot C - \text{ C} \uparrow P \ddot{i}P^{\circ} C \uparrow C - C''PSC, C - PI, C \downarrow PeC - P \ddot{i}C \uparrow PsC \dots PsPrP \ddot{e}P \gg P \ddot{e}$
 $P^{\circ} P \pm Ps \text{ PSP}_{\mu} \text{ P} \ddot{i}C \uparrow PsC \dots PsPrP \ddot{e}P \gg P \ddot{e} \text{ PIC} - PrP \ddot{i}PsPIC - PrPSC \uparrow C, P_{\mu}C \uparrow P^{\circ} P \ddot{i}C - C \uparrow, P^{\circ} C, P^{\circ} PePsP \uparrow$
 $P \ddot{i}PsPrPsPIP \uparrow P_{\mu}PSPSC \downarrow \text{ C} - PSC, P_{\mu}C \uparrow PIP^{\circ} P \gg C \uparrow QT;$
- $C, C \downarrow P \uparrow PeP^{\circ} \text{ C}, P^{\circ} C \dots C - P^{\circ} C \uparrow P \ddot{e}C, PjC - C \downarrow \text{ PI } P^{\circ} PSP^{\circ} PjPSP_{\mu}P \cdot C - ;$
- $PsPrPSPsC \uparrow P^{\circ} C \uparrow PSP_{\mu} \text{ P} \gg C - PeC \uparrow PIP^{\circ} PSPSC \downarrow \text{ Pr}PIP \cdot PjP^{\circ} P^{\circ} P \pm Ps \text{ P} \pm C - P \gg CH \cdot C \epsilon P_{\mu}$
 $PrPsPrP^{\circ} C, PePsPIP \ddot{e}PjP \ddot{e} \text{ P}^{\circ} PSC, P \ddot{e}C, C \uparrow PsPjP \pm PsC \uparrow P \ddot{e}C, P^{\circ} C \uparrow PSP \ddot{e}PjP \ddot{e} \text{ P} \cdot P^{\circ} C \uparrow PsP \pm P^{\circ} PjP \ddot{e} \text{ P}^{\circ} P \pm Ps$
 $P^{\circ} PSC, P \ddot{e}PePsP^{\circ} PiC \uparrow P \gg C \downarrow PSC, P^{\circ} PjP \ddot{e} (PSP^{\circ} \text{ P} \ddot{i}C \uparrow P \ddot{e}PeP \gg P^{\circ} Pr,$
 $P^{\circ} C \uparrow P_{\mu}C, P \ddot{e}P \gg C \uparrow P^{\circ} P \gg C - C \uparrow P \ddot{e}P \gg PsPIP^{\circ} \text{ Pe}P \ddot{e}C \uparrow P \gg PsC, P^{\circ}, \text{ Pe}P \gg PsP \ddot{i}C - PrPsPiC \uparrow P_{\mu}P \gg CH,$
 $PiP_{\mu}P \ddot{i}P^{\circ} C \uparrow P \ddot{e}PS, PIP^{\circ} C \uparrow C, P^{\circ} C \uparrow P \ddot{e}PS, P^{\circ} C \uparrow P_{\mu}PSPsPeC \uparrow PjP^{\circ} C \uparrow PsP \gg, PrP^{\circ} P \pm C - PiP^{\circ} C, C \uparrow P^{\circ} PS,$
 $C \uparrow P \ddot{e}PIP^{\circ} C \uparrow PsPeC \uparrow P^{\circ} P \pm P^{\circ} PS \text{ P}^{\circ} P \pm Ps \text{ P}^{\circ} P \ddot{i}C - PeC \uparrow P^{\circ} P \pm P^{\circ} PS);$
- $PSP_{\mu}C \uparrow C, P^{\circ} P \pm C - P \gg CH \cdot PSP^{\circ} \text{ C} \uparrow C, P_{\mu}PSPsPeP^{\circ} C \uparrow PrC - C \downarrow, C - PSC, P^{\circ} C \uparrow PeC,$
 $PjC - PsPeP^{\circ} C \uparrow PrP^{\circ} \text{ P} \ddot{i}C \uparrow PsC, C \downarrow PiPsPj \text{ Ps}C \uparrow C, P^{\circ} PSPSC - C \dots \text{ 6 } PjC - C \uparrow C \downarrow C \uparrow C - PI \text{ P}^{\circ} P \pm Ps$
 $PePsC \uparrow PsPSP^{\circ} C \uparrow PSP_{\mu} \text{ PIC}, C \uparrow C \uparrow C \uparrow P^{\circ} PSPSC \downarrow \text{ P} \ddot{i}C \uparrow PsC, C \downarrow PiPsPj \text{ Ps}C \uparrow C, P^{\circ} PSPSC - C \dots \text{ 6}$
 $PjC - C \uparrow C \downarrow C \uparrow C - PI.$

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

$P \uparrow PSC, P \ddot{e}C, C \uparrow PsPjP \pm PsC, P \ddot{e}C \uparrow PSC - P \cdot P^{\circ} C \uparrow PsP \pm P \ddot{e}.$ $P \ddot{i}P \ddot{e}P \gg PsC \uparrow C, P^{\circ} P \cdot PsP \gg C''$
 $C - PSPiC - P \pm C - C, PsC \uparrow PsPj \text{ C}, PsC \uparrow C, PsPrC - P_{\mu}C \uparrow C, P_{\mu}C \uparrow P^{\circ} P \cdot P \ddot{e} \text{ P} \uparrow P \uparrow P \uparrow P \cdot$
 $P^{\circ} PSC, P \ddot{e}C, C \uparrow PsPjP \pm PsC \uparrow P \ddot{e}C, P^{\circ} C \uparrow PSPsC \uparrow P^{\circ} PeC, P \ddot{e}PIPSC - C \uparrow C, C \uparrow. P^{\text{TM}} \text{ PsPiPs}$
 $P \cdot P^{\circ} C \uparrow C, PsC \uparrow C \uparrow PIP^{\circ} PSPSC \downarrow \text{ P} \cdot PrPsC \uparrow PsPIP \ddot{e}Pj \text{ PrPsP} \pm C \uparrow PsPIP \cdot S \gg CH \cdot C \uparrow C \downarrow Pj \text{ C} \uparrow PrPsP \cdot C - 150$
 $PjPi \text{ P} \ddot{i}C \uparrow PsC, C \downarrow PiPsPj \text{ 5 } PrPSC - PI \text{ PSP}_{\mu} \text{ P} \ddot{i}C \uparrow P \ddot{e}P \cdot PIPsPrP \ddot{e}P \gg Ps \text{ PrPs } P \ddot{i}PsPrPsPIP \uparrow P_{\mu}PSPSC \downarrow$
 $C \uparrow P^{\circ} C \uparrow C \uparrow \text{ Pe}C \uparrow PsPIP \cdot S, P_{\mu}C \uparrow C -.$

$P \uparrow C \uparrow P_{\mu}C, P \ddot{e}P \gg C \uparrow P^{\circ} P \gg C - C \uparrow P \ddot{e}P \gg PsPIP^{\circ} \text{ Pe}P \ddot{e}C \uparrow P \gg PsC, P^{\circ} (P \uparrow P \ddot{Y}P \uparrow).$ $P \ddot{Y}C \uparrow PjC - C \uparrow PSP_{\mu}$
 $P \cdot P^{\circ} C \uparrow C, PsC \uparrow C \uparrow PIP^{\circ} PSPSC \downarrow \text{ P} \cdot P \uparrow P \ddot{Y}P \uparrow \text{ P} \ddot{i}C \uparrow PsC, C \downarrow PiPsPj \text{ PePs}C \uparrow PsC, PePsPiPs \text{ C} \uparrow P^{\circ} C \uparrow C \uparrow (PrPs$
 $4 \text{ PrPSC} - PI) \text{ P} \pm C \uparrow P \gg Ps \text{ P} \ddot{i}PsPi \ddot{b} \uparrow \text{ C} \downarrow P \cdot P^{\circ} PSP_{\mu} \text{ P} \cdot P \ddot{i}C - PrPIP \ddot{e}C \% P_{\mu}PSPSC \downarrow Pj \text{ PSP}^{\circ} 23-25 \%$
 $P \ddot{i}C \uparrow P \ddot{e}PiPSC - C \uparrow P_{\mu}PSPSC \downarrow \text{ P} \uparrow P'' \text{ P} \alpha - C - PSPrC \uparrow PePsPIP^{\circ} PSPsC - P^{\circ} P \ddot{i}C \uparrow P_{\mu}PiP^{\circ} C \uparrow C - C -$
 $C, C \uparrow PsPjP \pm PsC \uparrow P \ddot{e}C, C - PI \text{ P} \ddot{i}PsC \uparrow C - PIPSC \downarrow PSPs \text{ P} \cdot P \ddot{i}C \uparrow P \ddot{e}P \ddot{N}_{\epsilon} \text{ PsPjPsPj } C, C - P \gg CH \cdot PeP \ddot{e} \text{ P} \uparrow P \ddot{Y}P \uparrow.$
 $P \uparrow P_{\mu} \text{ C} \uparrow P \ddot{i}PsC \uparrow C, P_{\mu}C \uparrow C - PiP^{\circ} P \gg PsC \uparrow C \downarrow \text{ Ps}C \uparrow P_{\mu}PIP \ddot{e}PrPSP \ddot{e}C \dots C, P_{\mu}PSPPrP_{\mu}PSC \uparrow C - P \ddot{N}_{\epsilon} \text{ PrPs}$
 $P \cdot P \pm C - P \gg CH \cdot C \epsilon P_{\mu}PSPSC \downarrow \text{ C} \uparrow C - PIPSC \downarrow \text{ Pi}P_{\mu}PjPsC \uparrow P^{\circ} PiC - C \uparrow PSP \ddot{e}C \dots P \ddot{i}PsP \pm C - C \uparrow PSP \ddot{e}C \dots$
 $P_{\mu}C, P_{\mu}PeC, C - PI \text{ C} \uparrow P \ddot{i}P^{\circ} C \uparrow C - C''PSC, C - PI, C \downarrow PeC - P \ddot{i}C \uparrow P \ddot{e}P \ddot{N}_{\epsilon} PjP^{\circ} P \gg P \ddot{e} \text{ P} \uparrow P \ddot{Y}P \uparrow \text{ C}, P^{\circ}$
 $C \uparrow P \ddot{e}P \gg PsC \uparrow C, P^{\circ} P \cdot PsP \gg, P \ddot{i}PsC \uparrow C - PIPSC \downarrow PSPs \text{ P} \cdot P \ddot{i}P^{\circ} C \uparrow C - C''PSC, P^{\circ} PjP \ddot{e}, C \downarrow PeC -$
 $P \ddot{i}C \uparrow P \ddot{e}P \ddot{N}_{\epsilon} PjP^{\circ} P \gg P \ddot{e} \text{ P} \ddot{i}P \gg P^{\circ} C \uparrow P_{\mu}P \pm Ps \text{ C}, P^{\circ} \text{ P}_{\mu}PePIC - PIP^{\circ} P \gg P_{\mu}PSC, PSC - PrPsP \cdot P \ddot{e} \text{ P} \uparrow P \ddot{Y}P \uparrow.$

$P \uparrow P \gg PsP \ddot{i}C - PrPsPiC \uparrow P_{\mu}P \gg CH \cdot C, P^{\circ} \text{ C} - PSC \epsilon C - P^{\circ} PSC, P \ddot{e}C, C \uparrow PsPjP \pm PsC \uparrow P \ddot{e}C, P^{\circ} C \uparrow PSC -$

*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%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 PiPsP±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° PiPμCḡPμPSPsCḡPēPjPsCḡC,C-.

PμCḡPēPNēPsPj 100 PjPi C†PēP»PsCḡC,P°P·PsP»Cḡ PSP° 7-PNē PrPμPSCḡ
P·P°CḡC,PScḡCḡPiP°PSPSCḡ PμCḡPēC,CḡPsPjC-C†PēPSCr (PiPsPjC-CḡPSPēPNē
C-PSPiC-P±C-C,PScḡ CYP3A4) 500 PjPi 3 CḡP°P·Pē PSP° PrPsP±Cḡ PīCḡPēP·PiPsPrPēP»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· PiPsPjC-C,PSPēPj PiC-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... CḡPμPePsPjPμPSPrPsPiP°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·
PiPsPrC-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·PiPsPrPēPi 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...
CḡPμPePsPjPμPSPrPsPiP°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· PiPsPrC-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·PiPsPrPēP»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,PsiPisPiPs 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,PsiPisPiPs 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,PscfCfPIP°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-PSPrCfPeC,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-PSPrCfPeC,PsCḡP°PjPë CYP3A4 C,P° CYP2C19.

PμC-Pr C†P°Cf PrPsCfP»C-PrPḡPμPSCḡ C,CḡC,CḡPSPsPīP°P»C-PSPSCḡ (CḡPePμ
C-PSPrCfPeCfC" 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±C†PrCħ-
CıPePëPj C-PSC€PëPj P·P°C†PsP±PsPj, P·PrP°C, PSPëPj P·PSPëP¶C†PIP°C, Pë
P°CħC, PμCħC-P°P»CħPSPëPNε C, PëC†Pe, C†PμCħPμP· PjPsP¶P»PëPIC-C†C, Cħ
CħPsP·PIPëC, PeC† P°PrPëC, PëPIPSPsPiPs PiC-PiPsC, PμPSP·PëPIPSPsPiPs PμC,, PμPeC, Cr, C%oPs
C†C†PiCħPsPIPsPrP¶C†C”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†C¿PIP°PSPSCı.

PμCħPëPNεPSCıC, PSC-C†C, Cħ P»C-PeC†PIP°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-PeC†PIP°PSPSCı, C, P°PePëPjPë CıPe
CħPμPIP°C†PeC†P»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†PiCħPëC†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 C†PrP°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†PiCħPëC†PëPSCıC, Pë C†C, PμPSPsPeP°CħPrC-Cħ.

P—P°B PīP°C†C-C”PSC, P°PjPë, CıPeC- PjPsP¶C†C, Cħ P±C†C, Pë C†C...PëP»CħPSC- PrPs
PīC-PrPIPëC%oPμPSPsPiPs CħPëP·PëPeC† C†PμCħPNεPsP·PSPëC... PīPsP±C-C†PSPëC...
PμC,, PμPeC, C-PI P· P±PsPeC† C†PμCħC†Cı PI CħPμP·C†P»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†PiPsC†C, PμCħC-PiP°C, Pë PīC-Pr C†P°C† P»C-PeC†PIP°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, CħC†C†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»C†PSPsC†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°PrPeC†
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°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-PīPμCTHC,PμCTHPjC-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... CTHpmPePsPjPμPSPrPsPIP°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,CH 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,PsCTHPSPsCTH C,P°C...C-PeP°CTHPrC-C”CTH.

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

*P—P°CГC,PsCГCзPIP°PSPSCЦ Cз PiPμCҲC-PsPr PIP°PiC-C,PSPsCГC,C- 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° PиCҲРөPNөPјP°C,Pө Cр PiPμCҲC-PsPr
PIP°PiC-C,PSPsCГC,C-.

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- PиCҲPs PиCҲPsPSPөPePSPμPSPSCЦ 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 PиCҲPμPiP°CҲP°C,Cр Cр PiPμCҲC-PsPr PiPsPrCрPIP°PSPSCЦ
PiCҲCрPrPrCH PSPμ CҲPμPePsPјPμPSPPrCрC"C,CHCГCЦ. Pј CҲP°P·C-
PSPμPsP±C...C-PrPSPsCГC,C- P»C-PөCрPIP°PSPSCЦ C†PөP»PsCГC,P°P·PsP»PsPј CГP»C-Pr
PиCҲРөPiPөPSPөC,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—
PиCҲРө 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°C,РөСГCЦ PsP±PμCҲPμP¶PSPsCГC,C-, PsCГPeC-P»CHPePө
PиCҲРө PиCҲРөPNөPsPјC- PиCҲPμPiP°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
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,PëPIPSsCíC,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,PμPSCíPëPIPS-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.

PḡP°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...).
PḡP°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,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

$P - P \pm PsPeC \acute{e} C \acute{I} C \acute{a} PrP \ddot{e} PSPSPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e}$	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P_{\mu} C \ddagger PsPIPSPiP \ddot{e} P \gg P \ddot{e} P_i P_i PsPePs, PSPsC \acute{I} PsPIC - PeC \ddagger PsPSPsC, P_{\mu} C \ddagger C -, C \acute{e} P \gg C \acute{r} PSPePsPSPs - PeP \ddot{e} C \acute{e} PePsPIC - PeC \ddagger PsPSPsC, P_{\mu} C \ddagger C -, PSP_{\mu} P \cdot \mathfrak{B} \ddot{e}^{\text{TM}} C \ddagger C \acute{I} C \acute{I} PsPIP^{\circ} PSC - PeC \ddagger PsPSPsC, P_{\mu} C \ddagger C -, PsC \ddagger C, PsC \acute{I} C, P^{\circ} C, P \ddot{e} C \ddagger PSP^{\circ} P_i C - P_i PsC, P_{\mu} PSP \cdot C - C \ddagger$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P_i C \ddagger P \ddot{e} P_i P \gg P \ddot{e} P_i P \ddot{e}, P_i C - P_i P_{\mu} C \ddagger C, P_{\mu} PSP \cdot C - C \ddagger, P_i C - P_i PsC, P_{\mu} PSP \cdot C - C \ddagger, PeC \ddagger PsPSPsPIP \ddot{e} P \gg P \ddot{e} P_i P \ddot{e} P_i P_j PsP \cdot PsPe, P \gg P_{\mu} P_i P_{\mu} PSC -, P_j \mathfrak{B} \ddot{e}^{\text{TM}} C \ddagger P \cdot P \ddot{e}, PrP \ddot{e} C \dots P^{\circ} P \gg CH \ddagger PSC - C \acute{e} P \gg C \ddagger C \dots P \ddot{e}; P_i C - PrC \acute{e} PeC - C \ddagger PSC - PeC \ddagger PsPSPsPIP \ddot{e} P \gg P \ddot{e} P_i P \ddot{e}$
$P - P \pm PsPeC \acute{e} PrP \ddot{e} C \dots P^{\circ} P \gg CH \ddagger PSPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e}$	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$C \ddagger P \ddot{e} PSC - C, C, P^{\circ} C \ddagger P \ddot{e} PSP_i C - C,$
	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P \cdot P^{\circ} PrP \ddot{e} C \acute{e} PeP^{\circ}, P_i PSP_{\mu} P_i P_j PsPSC - C \ddagger, PeP^{\circ} C \acute{e} P_{\mu} P \gg CH$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$C - PSC, P_{\mu} C \ddagger C \acute{I} C, P \ddot{e} C \ddagger C - P^{\circ} P \gg CH \ddagger PSP^{\circ} P_i PSP_{\mu} P_i P_j PsPSC - C \ddagger$
$P - P \pm PsPeC \acute{e} C \acute{e} P \gg C \acute{a} PSPePsPSPs - PeP \ddot{e} C \acute{e} PePsPSPsP_i Ps C, C \ddagger P^{\circ} PeC, C \acute{e}$	$PrC \acute{r} P \ddagger P_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$PrC - P^{\circ} C \ddagger P_{\mu} C \ddagger, P_i PsC \ddagger C \acute{r} C \acute{e} P_{\mu} PSPSC \ddagger P_i P \ddot{e} P_i PsC \ddagger PsP \ddagger PSP_{\mu} PSPSC \ddagger$
	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$PSC \acute{r} PrPsC, P^{\circ} C - P \pm P \gg CH \ddagger PIP^{\circ} PSPSC \ddagger, PrP \ddot{e} C \acute{I} P_i P_i C \acute{I} C - C \ddagger, P_j P_{\mu} C, P_{\mu} PsC \ddagger P \ddot{e} P \cdot P_j, P \pm C - P \gg CH C \acute{r} P \ddagger P \ddot{e} P_i PsC, C -$
	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P_i P^{\circ} C \acute{I} C, C \ddagger P \ddot{e} C,$
$P - P \pm PsPeC \acute{e} P_i P_{\mu} P_i P^{\circ} C, PsP \pm C - P \gg C - P^{\circ} C \ddagger PSPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e}$	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P_i P_{\mu} P_i P^{\circ} C, P \ddot{e} C, P^{\circ} PSPsP_j P^{\circ} P \gg C - C - P_i P_{\mu} C \ddagger C - PSPePsPSPsC - C, C \acute{r} PSPeC \ddagger C - C -, P \ddagger PsPIC, C \ddagger PSP \ddot{e} C \ddagger C \ddagger$
	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$PIP \ddot{e} C \acute{I} P \ddot{e} P_i P^{\circ} PSPSC \ddagger, C \acute{I} P_i P_{\mu} C \ddagger P \pm C - P \ddagger$
$P - P \pm PsPeC \acute{e} C \acute{e} PeC - C \ddagger P \ddot{e} C - P_i C - PrC \acute{e} PeC - C \ddagger PSP \ddot{e} C \dots C, PeP^{\circ} PSP \ddot{e} PS$	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$P_{\mu} PeP \cdot P_{\mu} P_j P^{\circ}, C \acute{e} PeC - C \ddagger PSC - P_i P \ddot{e} C \acute{I} P \ddot{e} P_i P^{\circ} PSPSC \ddagger, C \acute{I} P \ddot{e} PSPPrC \ddagger PsP_j P \ddot{Y} C, C - P_i P_{\mu} PSC \acute{I} P^{\circ} - P^{\circ} P \ddagger PsPSC \acute{I} PsPSP^{\circ}, C, PsPeC \acute{I} P \ddot{e} C \ddagger PSP \ddot{e} P_{\mu} P_{\mu} P_i C - PrP_{\mu} C \ddagger P_j P^{\circ} P \gg CH \ddagger PSP \ddot{e} P_{\mu} PSP_{\mu} PeC \ddagger PsP \gg C - P \cdot, PeC \ddagger PsP_i P \ddot{e} P_i \mathfrak{B} \ddot{e}^{\text{TM}} C \ddagger PSPeP^{\circ}$
	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$P_j C - P^{\circ} P \gg P_i C - C \ddagger$
$P - P \pm PsPeC \acute{e} C \acute{I} PeP_{\mu} P \gg P_{\mu} C, PSPs - P_j \mathfrak{B} \ddot{e}^{\text{TM}} C \ddagger P \cdot PsPSPsC - C \acute{I} P \ddot{e} C \acute{I} C, P_{\mu} P_j P \ddot{e} C, P^{\circ} C \acute{I} P_i PsP \gg C \acute{a} C \ddagger PSPsC - C, PeP^{\circ} PSP \ddot{e} PSP \ddot{e}$	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P_i P_{\mu} P_j P^{\circ} C, C \acute{r} C \ddagger C - C \ddagger, P_i PsP \gg P^{\circ} PeC - C \acute{r} C \ddagger C - C \ddagger$
	$C \ddagger P^{\circ} C \acute{I} C, Ps$	$P \pm C - P \gg CH C \acute{r} P_i C \ddagger C \acute{r} PrC \ddagger C \dots, P^{\circ} C \acute{I} C, P_{\mu} PSC - C \ddagger$
$P - P^{\circ} P_i P^{\circ} P \gg CH \ddagger PSC - C \ddagger PsP \cdot P \gg P^{\circ} PrP \ddot{e}$	$PSP_{\mu} C \ddagger P^{\circ} C \acute{I} C, Ps$	$PsP \cdot PSPsP \pm, PSP_{\mu} P \cdot PrC \acute{r} P \ddagger P^{\circ} PSPSC \ddagger$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P_i C - C \ddagger P_{\mu} PeC \acute{I} C - C \ddagger, P \pm C - P \gg CH$
	$C \ddagger P^{\circ} C \acute{I} C, PsC, P^{\circ} PSP_{\mu} PIC - PrPsP_j P^{\circ}$	$P_i C - PrPIP \ddot{e} C \% P_{\mu} PSPSC \ddagger C \ddagger C - PIPSC \ddagger C \acute{I} P_{\mu} C \ddagger PsPSPsC - PeP \ddot{e} C \acute{I} P \gg PsC, P \ddot{e}, C \acute{I} P_{\mu} C \ddagger PsPIP \ddot{e} PSP \ddot{e} C \acute{r} PeC \ddagger PsPIC -, PeC \ddagger P_{\mu} P^{\circ} C, P \ddot{e} PSC - PSC \acute{r} P_i PeC \ddagger PsPIC -$

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

$P-P \pm P_{\mu} C_7 C - P_i P^{\circ} C, P_{\bar{e}} P_i C_7 P_{\bar{e}} C, P_{\mu} P_j P_i P_{\mu} C_7 P^{\circ} C, C_r C_7 C -$ $PSP_{\mu} PIP_{\bar{e}} C \% P_{\mu} 25 B^{\circ} P_{\bar{Y}} PI$
 $PsC_7 P_{\bar{e}} P_i C - PSP^{\circ} P \gg CHbPSC - PN_{\bar{e}} C_r P_i P^{\circ} P_e PsPIC \dagger C -.$

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

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

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

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

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

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

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

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

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

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

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

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