

1 PeP°PiCíCíP»P° PjC-CíC,PëC,CH PeP°CíPëPiCíP°P·PëPSCí 4,5 PjPi (Cí PIPëPiP»CЦPíC-

PeP°CḡPēPīCḡP°P·PēPSCř PiC–PrCḡPsC...P»PsCḡPēPrCř 4,905 PjPi).

P''PsPīPsPjC–PḡPSC– CḡPμC‡PsPIPēPSPē: PeCḡPsC...PjP°P»CH PeCřPeCřCḡCřPrP·CḡPSPēPNē
PīCḡPμPḡPμP»P°C,PēPSC–P·PsPIP°PSPēPNē, PjP°PiPSC–Cḡ CřC,PμP°CḡP°C,.

PμP°PīCřCžP»Pē C,PIPμCḡPrC–: C,PēC,P°PSCř PrC–PsPeCřPēPr, P• 171; PḡPμP»P°C,PēPS;
CřPiPμC†C–P°P»CHPSPēPNē C‡PμCḡPIPsPSPēPNē PhPŸ, P• 129; PrC–P°PjP°PSC,PsPIPēPNē
CřPēPSC–PNē FCF, P• 133; P·P°P»C–P·P° PsPeCřPēPr PḡPsPIC,PēPNē, P• 172; C‡PsCḡPSPēP»Ps
P±C–P»PsPiPs PePsP»CHPsCḡCř PrP»Cḡ PrCḡCřPeCř: PiP»P°P·CřCḡCH
C„P°CḡPjP°C†PμPIC,PēC‡PSP° (CēPμP»P°PeCř CḡPsP·C‡PēPS Pi PμC,P°PSPsP»C–); C,PēC,P°PSCř
PrC–PsPeCřPēPr, P• 171; C–P·PsPīCḡPsPīP°PSPsP»; P±CřC,P°PSPsP»; P°PjC–P°Pe PIPsPrPSPēPNē;
PīCḡPsPīC–P»PμPSPiP»C–PePsP»CH; CřPēPjPμC,PēPePsPS.

PμP°PīCřCřP»Pē C,PIPμCḡPrC– PiPs 6 PjPi

P''C–CḡC‡P° CḡPμC‡PsPIPēPSP°: PeP°CḡPēPīCḡP°P·PēPS;

1 PeP°PīCřCřP»P° PjC–CřC,PēC,CH PeP°CḡPēPīCḡP°P·PēPSCř 6 PjPi (Cř PIPēPiP»CḡPrC–
PeP°CḡPēPīCḡP°P·PēPSCř PiC–PrCḡPsC...P»PsCḡPēPrCř 6,540 PjPi).

P''PsPīPsPjC–PḡPSC– CḡPμC‡PsPIPēPSPē: PeCḡPsC...PjP°P»CH PeCřPeCřCḡCřPrP·CḡPSPēPNē
PīCḡPμPḡPμP»P°C,PēPSC–P·PsPIP°PSPēPNē, PjP°PiPSC–Cḡ CřC,PμP°CḡP°C,.

PμP°PīCřCžP»Pē C,PIPμCḡPrC–: C,PēC,P°PSCř PrC–PsPeCřPēPr, P• 171; PḡPμP»P°C,PēPS;
CřPiPμC†C–P°P»CHPSPēPNē C‡PμCḡPIPsPSPēPNē PhPŸ, P• 129; PrC–P°PjP°PSC,PsPIPēPNē
CřPēPSC–PNē FCF, P• 133; C‡PsCḡPSPēP»Ps C‡PsCḡPSPsPiPs PePsP»CHPsCḡCř PrP»Cḡ
PrCḡCřPeCř: P·P°P»C–P·P° PsPeCřPēPr C‡PsCḡPSPēPNē, P• 172; CēPμP»P°Pe; PμC,P°PSPsP»;
PIPsPrP°; PīCḡPsPīC–P»PμPSPiP»C–PePsP»CH; C–P·PsPīCḡPsPīP°PSPsP»; P±CřC,P°PSPsP»;
P°PjC–P°Pe PIPsPrPSPēPNē; PeP°P»C–Cḡ PiC–PrCḡPsPeCřPēPr.

P·C–PeP°CḡCřCHPeP° C„PsCḡPjP°. PμP°PīCřCřP»Pē C,PIPμCḡPrC–.

PhCřPSPsPIPSC– C„C–P·PēPePs–C...C–PjC–C‡PSC– PIP»P°CřC,PēPIPsCřC,C–:

PμP°PīCřCžP»Pē PiPs 1,5 PjPi. PŸPIPμCḡPrC– PḡPμP»P°C,PēPSPsPIC– PeP°PīCřCřP»Pē,
CḡPsP·PjC–Cḡ B„– 4. PμCḡPēCēPμC‡PeP° PeP°PīCřCřP»Pē Bḡ” P±C–P»P° PSPμPīCḡPsP·PsCḡP°,
PePsCḡPīCřCř PeP°PīCřCřP»Pē Bḡ” P±C–P»PēPNē PSPμPīCḡPsP·PsCḡPēPNē. PkP° PePsCḡPīCřCř
PeP°PīCřCřP»Pē PSP°PSPμCřPμPSPs PSP°PīPēCř B«GR 1.5B» C‡PsCḡPSPēPj PePsP»CHPsCḡPsPj.
P’PjC–CřC, PeP°PīCřCřP» Bḡ” PīPsCḡPsCēPsPe P±C–P»PsPiPs P°P±Ps PḡPsPIC,CřPIP°C,Ps–
P±C–P»PsPiPs PePsP»CHPsCḡCř.

PμP°PīCřCžP»Pē PiPs 3 PjPi. PŸPIPμCḡPrC– PḡPμP»P°C,PēPSPsPIC– PeP°PīCřCřP»Pē,
CḡPsP·PjC–Cḡ B„– 4. PμCḡPēCēPμC‡PeP° PeP°PīCřCřP»Pē Bḡ” P·PμP»PμPSP°
PSPμPīCḡPsP·PsCḡP°, PePsCḡPīCřCř PeP°PīCřCřP»Pē Bḡ” P±C–P»PēPNē
PSPμPīCḡPsP·PsCḡPēPNē. PkP° PePsCḡPīCřCř PeP°PīCřCřP»Pē PSP°PSPμCřPμPSPs PSP°PīPēCř
B«GR 3B» C‡PsCḡPSPēPj PePsP»CHPsCḡPsPj. P’PjC–CřC, PeP°PīCřCřP» Bḡ” PīPsCḡPsCēPsPe
P±C–P»PsPiPs P°P±Ps PḡPsPIC,CřPIP°C,Ps–P±C–P»PsPiPs PePsP»CHPsCḡCř.

PμP°PīCřCžP»Pē PiPs 4,5 PjPi. PŸPIPμCḡPrC– PḡPμP»P°C,PēPSPsPIC– PeP°PīCřCřP»Pē,
CḡPsP·PjC–Cḡ B„– 4. PμCḡPēCēPμC‡PeP° PeP°PīCřCřP»Pē Bḡ” P·PμP»PμPSP°
PSPμPīCḡPsP·PsCḡP°, PePsCḡPīCřCř PeP°PīCřCřP»Pē Bḡ” P·PμP»PμPSPēPNē

PSP_μPiC₇PsP·PsC₇PēPN₆. P_κP° PePsC₇PiC₇C₇ PeP°PiC₇C₇P»Pē PSP°PSP_μC₇P_μPSPs PSP°PiPēC₇ B«GR 4.5B» P±C-P»PēPj PePsP»CH₆PsC₇PsPj. P'PjC-C₇C, PeP°PiC₇C₇P» B₇" PiPsC₇PsC₆PsPe P±C-P»PsPiPs P°P±Ps P_¶PsPIC,C₇PIP°C,Ps-P±C-P»PsPiPs PePsP»CH₆PsC₇C₇.

P_λP°PiC₇C₇P»Pē PiPs 6 PjPi. P_¶PIP_μC₇PrC- P_¶P_μP»P°C,PēPSPsPIC- PeP°PiC₇C₇P»Pē, C₇PsP·PjC-C₇ B₇,- 3. P_λC₇PēC₆P_μC₇PeP° PeP°PiC₇C₇P»Pē B₇" C₇-PsP»P_μC,PsPIP° PSP_μPiC₇PsP·PsC₇P°, PePsC₇PiC₇C₇ PeP°PiC₇C₇P»Pē B₇" P±C-P»PēPN₆ PSP_μPiC₇PsP·PsC₇PēPN₆. P_κP° PePsC₇PiC₇C₇ PeP°PiC₇C₇P»Pē PSP°PSP_μC₇P_μPSPs PSP°PiPēC₇ B«GR 6B» C₇PsC₇PSPēPj PePsP»CH₆PsC₇PsPj. P'PjC-C₇C, PeP°PiC₇C₇P» B₇" PiPsC₇PsC₆PsPe P±C-P»PsPiPs P°P±Ps P_¶PsPIC,C₇PIP°C,Ps-P±C-P»PsPiPs PePsP»CH₆PsC₇C₇.

P_κP°C₇PjP°PePsC,P_μC₇P°PiP_μPIC,PēC₇PSP° PiC₇C₇PiP°. P_μC₇PēC...PsP»P_μPiC,PēC₇PSC- P·P°C₇PsP±Pē, C-PSC₆C- P°PSC,PēPiC₇PēC...PsC,PēC₇PSC- P·P°C₇PsP±Pē.

P_λPsPr P_hP_¶PI₇ N05A X15.

P_κP°C₇PjP°PePsP»PsPiC-C₇PSC- PIP»P°C₇C,PēPIPsC₇C,C-

P_κP°C₇PjP°PePsPrPēPSP°PjC-PeP°.

P_hP_μC...P°PSC-P·Pj PrC-C—

P_hP_μC...P°PSC-P·Pj PrC-C— PeP°C₇PēPiC₇P°P·PēPSC₇ C₇%₀P_μ PSP_μ PiPsPIPSC-C₇C,C₇ PIC-PrPsPjPēPN₆. P_μC₇PsC,P_μ C,P_μC₇P°PiP_μPIC,PēC₇PSPēPN₆ P_μC₇,P_μPeC, PeP°C₇PēPiC₇P°P·PēPSC₇ PjPsP_¶P_μ PsPiPsC₇P_μPrPePsPIC₇PIP°C,PēC₇C₇ C₇P_μC₇P_μP· PePsPjP±C-PSP°C₇C-C₇ PrC-C— C₇P°C₇C,PePsPIPsPiPs P°PiPsPSC-C₇C,P° PSP° D₃-, D₂- PrPsC₇,P°PjC-PSPsPIC- (P·PSP°C₇P_μPSPSC₇ Ki PIC-PrPiPsPIC-PrPSPs PI PjP_μP_¶P°C... 0,085B₇"0,3 PSP_h PiC₇PsC,Pē 0,49B₇"0,71 PSP_h) C,P° 5-HT_{1A}-C₇P_μC₇PsC,PsPSC-PSPsPIC- C₇P_μC₇P_μPiC,PsC₇Pē (P·PSP°C₇P_μPSPSC₇ Ki PI PjP_μP_¶P°C... 1,4B₇"2,6 PSP_h) C- PrC-C— P°PSC,P°PiPsPSC-C₇C,P° PSP° 5-HT_{2B}-, 5-HT_{2A}-C₇P_μC₇PsC,PsPSC-PSPsPIC- C,P° H₁- PiC-C₇C,P°PjC-PSPsPIC- C₇P_μC₇P_μPiC,PsC₇Pē (P·PSP°C₇P_μPSPSC₇ Ki PIC-PrPiPsPIC-PrPSPs PI PjP_μP_¶P°C... 0,58B₇"1,1 PSP_h, 18,8 PSP_h C,P° 23,3 PSP_h). P_λP°C₇PēPiC₇P°P·PēPS PjP°C" PSPēP·CH₆PeC₇ P°C₇,C-PSPSC-C₇C,CH₆ C₇%₀PsPrPs 5-HT_{2C}-C₇P_μC₇PsC,PsPSC-PSPsPIPēC... C,P° α₁-P°PrC₇P_μPSPsC₇P_μC₇PiC,PsC₇C-PI (P·PSP°C₇P_μPSPSC₇ Ki PIC-PrPiPsPIC-PrPSPs 134 PSP_h C,P° 155 PSP_h). P_λP°C₇PēPiC₇P°P·PēPS PSP_μ PjP°C" P·PSP°C₇PSPsC— P°C₇,C-PSPSPsC₇C,C- C₇%₀PsPrPs C...PsP»C-PSP_μC₇PiC-C₇PSPēC... PjC₇C₇PeP°C₇PēPSPsPIPēC... C₇P_μC₇P_μPiC,PsC₇C-PI (IC₅₀ > 1000 PSP_h). P"PIP° PsC₇PSPsPIPSPēC... P°PeC,PēPIPSPēC... PjP_μC,P°P±PsP»C-C,Pē B₇" PrP_μP·PjP_μC,PēP»-PeP°C₇PēPiC₇P°P·PēPS C,P° PrPēPrP_μP·PjP_μC,PēP»-PeP°C₇PēPiC₇P°P·PēPS B₇" P·PIB₇TM C₇IP·C₇CH₆,CH₆C₇C₇ P· C₇P_μC₇P_μPiC,PsC₇P°PjPē C,P° PjP°C₇C,CH₆ PiC₇PsC₇,C-P»CH₆ C₇,C₇PsP₆C₇C-PsPSP°P»CH₆PSPsC— P°PeC,PēPIPSPsC₇C,C- *in vitro*, P°PSP°P»PsPiC-C₇PSPēPN₆ PIPēC...C-PrPSC-PN₆ PrC-C₇C₇C-PN₆ C₇P_μC₇P_μPIPēPSC-.

P_κP°C₇PjP°PePsPrPēPSP°PjC-C₇PSC- P_μC₇,P_μPeC,Pē

P"PsPeP»C-PSC-C₇PSC- PrPsC₇P»C-PrP_¶P_μPSPSC₇ *in vivo* PiPsPeP°P·C₇CH₆,CH₆ C₇%₀Ps PeP°C₇PēPiC₇P°P·PēPS P·PIB₇TM C₇IP·C₇C" C,CH₆C₇C₇ P· D₃-C₇P_μC₇P_μPiC,PsC₇P°PjPē C,P°PePsC₇ P_¶ PjC-C₇PsC₇, C₇%₀Ps PN₆ C-P· D₂-C₇P_μC₇P_μPiC,PsC₇P°PjPē C₇

C,,P°CḡPjP°PePsP»PsPiC-C†PSPs PμC,,PμPeC,PëPIPSpëC... PrPsP·P°C.... P'PëCḡIPIP»CḡIP»PsCḡCḡ
P·P°P»PμP¶PSPμ PIC-Pr PrPsP·Pë P·PIBḡ™ CḡIP·CḡPIP°PSPSCḡ P· D₃- C,P° D₂-
PrPsC,,P°PjC-PSPsPIPëPjPë CḡPμC†PμPiC,PsCḡP°PjPë PiPsP»PsPIPSsPiPs PjPsP·PeCḡ (P·
PīPμCḡPμPIP°P¶PSPëPj P·PIBḡ™ CḡIP·CḡPIP°PSPSCḡPj PI PrC-P»CḡIPSPeP°C... P·
PiC-PrPIPëC%PμPSPëPj CḡPëPSC,PμP·PsPj D₃) Cḡ PiP°C†C-C"°PSC,C-PI P·
CëPëP·PsC,,CḡPμPSC-C"°Cḡ, CḡPeC- PiCḡPëPμPjP°P»Pë C,PμCḡP°PiPμPIC,PëC†PSC- PrPsP·Pë
PeP°CḡPëPiCḡP°P·PëPSCḡ PiCḡPsC,CḡPiPsPj 15 PrPSC-PI.

P'PiP»PëPI PeP°CḡPëPiCḡP°P·PëPSCḡ PSP° C-PSC,PμCḡPIP°P» QT P±CḡPI PsC†C-PSPμPSPëPμ
Cḡ PiP°C†C-C"°PSC,C-PI C-P· CëPëP·PsC,,CḡPμPSC-C"°Cḡ P°P±Ps CëPëP·PsP°C,,PμPeC,PëPIPSpëPj
CḡPsP·P»P°PrPsPj. P PμP·CḡP»CHC,P°C,Pë C...PsP»C,PμCḡC-PICḡCHPePsPiPs
PjPsPSC-C,PsCḡCḡPIP°PSPSCḡ B P·PḡP" B P±CḡP»Pë B P·C-P±CḡP°PSC- B Cḡ B 129
PiP°C†C-C"°PSC,C-PI PiCḡPsC,CḡPiPsPj 12-PiPsPrPëPSPSPsPiPs PiPμCḡC-PsPrCḡ PSP°
PIPëC...C-PrPSPsPjCḡ CḡC-PIPSC- C,P° CḡC-PIPSPsPIP°P¶PSPsPjCḡ CḡC,P°PSC-. PJ CḡP°P·C-
PIPëPePsCḡPëCḡC,P°PSPSCḡ CḡCḡP±C,PμCḡP°PiPμPIC,PëC†PSPëC... PrPsP· (9 PjPi/PrPsP±Cḡ
P°P±Ps 18 PjPi/PrPsP±Cḡ) PSPμ P±CḡP»Ps PIC-PrPjC-C†PμPSPs PiPsPrPsPIP¶PμPSPSCḡ
C-PSC,PμCḡPIP°P»Cḡ QT. PJ P¶PsPrPSPsPiPs P· PiP°C†C-C"°PSC,C-PI, CḡPeC-
P»C-PeCḡPIP°P»PëCḡCḡ PeP°CḡPëPiCḡP°P·PëPSPsPj, PSPμ PIC-PrPjC-C†P°P»PsCḡCḡ
PiPsPrPsPIP¶PμPSPSCḡ C-PSC,PμCḡPIP°P»Cḡ QT ≥ 60 PjCḡ PIC-Pr PIPëC...C-PrPSPsPiPs
CḡC-PIPSCḡ, C- P¶PsPrPμPS PiP°C†C-C"°PSC, PSPμ PjP°PI PiPsPrPsPIP¶PμPSPSCḡ
C-PSC,PμCḡPIP°P»Cḡ QT > 500 PjCḡ PiC-Pr C†P°Cḡ PrPsCḡP»C-PrP¶PμPSPSCḡ.

PḡP»C-PSC-C†PSP° PμC,,PμPeC,PëPIPSC-CḡC,CH C,P° P±PμP·PiPμPeP°

*P·C,,PμPeC,PëPIPSC-CḡC,CH PiCḡPë PePsCḡPsC,PePsC†P°CḡPSPsPjCḡ
P·P°CḡC,PsCḡCḡPIP°PSPSC-*

P·C,,PμPeC,PëPIPSC-CḡC,CH PeP°CḡPëPiCḡP°P·PëPSCḡ PI P»C-PeCḡPIP°PSPSC-
PiPsCḡC,CḡPsC— CëPëP·PsC,,CḡPμPSC-C— P±CḡP»P° PIPëPIC†PμPSP° PI C,CḡCHPsC...
P±P°PiP°C,PsC†PμPSC,CḡPsPIPëC...B B B B PjC-P¶PSP°CḡPsPrPSPëC...B B
B CḡP°PSPPrPsPjC-P·PsPIP°PSPëC...B B B PiPsPrPIC-PμPSPsB B B CḡP»C-PiPëC...
B B B PiP»P°C†PμP±PsPePsPSC,CḡPsP»CHPsPIP°PSPëC...B B B 6-C,PëP¶PSPμPIPëC...
PrPsCḡP»C-PrP¶PμPSPSCḡC..., PI CḡPePëC... P±CḡP°P»Pë CḡC†P°CḡC,CH 1 754
PiP°C†C-C"°PSC,Pë PIC-PePsPj PIC-Pr 18 PrPs 60 CḡPsPeC-PI. PJ PICḡC-C...
PrPsCḡP»C-PrP¶PμPSPSCḡC... PiPsCḡC,CḡPsC— CëPëP·PsC,,CḡPμPSC-C—
PiPμCḡPIPëPSPSPsCḡ PeC-PSC†PμPIPsCḡ C,PsC†PePsCḡ P±CḡP»P° P·PjC-PSP° PIC-Pr
PIPëC...C-PrPSPsPiPs CḡC-PIPSCḡ PrPs 6 C,PëP¶PSCḡ P·P° P·P°PiP°P»CHPSPëPjPë
PiPsPeP°P·PSPëPeP°PjPë CëPeP°P»Pë PsC†C-PSPePë PiPsP·PëC,PëPIPSpëC... C,P°
PSPμPiP°C,PëPIPSpëC... CḡPëPjPiC,PsPjC-PI (PANSS), P° PIC,PsCḡPëPSPSPsCḡ
PeC-PSC†PμPIPsCḡ C,PsC†PePsCḡ Bḡ" P·PjC-PSP° PIC-Pr PIPëC...C-PrPSPsPiPs CḡC-PIPSCḡ
PrPs 6 C,PëP¶PSCḡ P·P° PiPsPeP°P·PSPëPeP°PjPë CëPeP°P»Pë P·P°PiP°P»CHPSPsPiPs
PeP»C-PSC-C†PSPsPiPs PICḡP°P¶PμPSPSCḡ PiCḡPs C,CḡP¶PeC-CḡC,CH
P·P°C...PIPsCḡCḡPIP°PSPSCḡ (CGI-S). PJ PjC-P¶PSP°CḡPsPrPSPsPjCḡ
PiP»P°C†PμP±PsPePsPSC,CḡPsP»CHPsPIP°PSPsPjCḡ PrPsCḡP»C-PrP¶PμPSPSC-, PI CḡPePsPjCḡ
PrP»Cḡ C†CḡC,P»PëPIPsCḡC,C- P°PSP°P»C-P·Cḡ PIPëPePsCḡPëCḡC,PsPICḡPIP°P»PëCḡCḡ
C,,C-PeCḡPsPIP°PSC- PrPsP·Pë 1,5 PjPi, 3,0 PjPi C,P° 4,5 PjPi PeP°CḡPëPiCḡP°P·PëPSCḡ C- 4,0
PjPi CḡPëCḡPiPμCḡPëPrPsPSCḡ, PICḡC- PrPsP·Pë PeP°CḡPëPiCḡP°P·PëPSCḡ C,P°
P°PeC,PëPIPSpëPμ PePsPSC,CḡPsP»CH PiPsPeP°P·P°P»Pë CḡC,P°C,PëCḡC,PëC†PSPs
PrPsCḡC,PsPIC-CḡPSPμ PiPsPeCḡP°C%PμPSPSCḡ CḡPe PiPμCḡPIPëPSPSPsC—, C,P°Pe C-
PIC,PsCḡPëPSPSPsC— PeC-PSC†PμPIPëC... C,PsC†PsPe Cḡ PiPsCḡC-PIPSCḡPSPSC- P·
PiP»P°C†PμP±Ps. PJ PjC-P¶PSP°CḡPsPrPSPsPjCḡ
PiP»P°C†PμP±PsPePsPSC,CḡPsP»CHPsPIP°PSPsPjCḡ PrPsCḡP»C-PrP¶PμPSPSC-, PI CḡPePsPjCḡ

PrP»CЦ C†C†C,P»PëPIPsC†C,C- P°PSP°P»C-P·C† PIPëPePsC†PëC†C,PsPIC†PIP°P»PëC†CЦ C,,C-PeC†PsPIP°PSC- PrPsP·Pë 3,0 PjPi C,P° 6,0 PjPi PeP°C†PëP†C†P°P·PëPSC† C- 10 PjPi P°C†PëP†C-P†C†P°P·PsP»C†, CЦPe PrPsP·Pë PeP°C†PëP†C†P°P·PëPSC†, C,P°Pe C- P°PeC,PëPIPsPëP№ PePsPSC,C†PsP»C† P†PsPeP°P·P°P»Pë C†C,P°C,PëC†C,PëC†PSPs PrPsC†C,PsPIC-C†PSPµ P†PsPeC†P°C%PµPSPSCЦ P†PµC†PIPëPSPSPsC— C- PIC,PsC†PëPSPSPsC— PeC-PSC†PµPIPëC... C,PsC†PsPe C† P†PsC†C-PIPSCЦPSPSC- P· P†P»P°C†PµP±Ps. Pj C,C†PµC,C†PsPjC† PjC-P¶PSP°C†PsPrPSPsPjC† P†P»P°C†PµP±PsPePsPSC,C†PsP»C†PsPIP°PSPsPjC† PrPsC†P»C-PrP¶PµPSPSC-, PI CЦPePsPjC† PrP»CЦ C†C†C,P»PëPIPsC†C,C- P°PSP°P»C-P·C† PIPëPePsC†PëC†C,PsPIC†PIP°P»PëC†CЦ C,,C-PeC†PsPIP°PSC-/P°PrP°P†C,PsPIP°PSC- PrPsP·Pë 3,0B†”6,0 PjPi C,P° 6,0B†”9,0 PjPi PeP°C†PëP†C†P°P·PëPSC†, PsP±PëPrPIC- P†C†C†P†Pë PeP°C†PëP†C†P°P·PëPSC† P†PsPeP°P·P°P»Pë C†C,P°C,PëC†C,PëC†PSPs PrPsC†C,PsPIC-C†PSPµ P†PsPeC†P°C%PµPSPSCЦ CЦPe P†PµC†PIPëPSPSPsC—, C,P°Pe C- PIC,PsC†PëPSPSPsC— PeC-PSC†PµPIPëC... C,PsC†PsPe C† P†PsC†C-PIPSCЦPSPSC- P· P†P»P°C†PµP±Ps.

P PµP·C†P»C†C,P°C,Pë PIPëP·PSP°C†PµPSPSCЦ P†PµC†PIPëPSPSPsC— PeC-PSC†PµPIPSC— C,PsC†PePë PµC,,PµPeC,PëPIPsPSC†C,C- PSP°PIPµPrPµPSC- PI C,P°P±P»PëC†C- 1 PSPëP¶C†Pµ. P PµP·C†P»C†C,P°C,Pë PIPëP·PSP°C†PµPSPSCЦ PIC,PsC†PëPSPSPsC— PeC-PSC†PµPIPSC— C,PsC†PePë PµC,,PµPeC,PëPIPsPSC†C,C- (CGI) C,P° PrPsPrP°C,PePsPIPëC... PeC-PSC†PµPIPëC... C,PsC†PsPe P†C-PrC,PIPµC†PrP¶C†PIP°P»Pë P†PµC†PIPëPSPSC† PeC-PSC†PµPIC† C,PsC†PeC†.

PŷP°P±P»PëC†CЦ 1.B B B B P—PjC-PSPë PIC-Pr PIPëC...C-PrPSPsPiPs C†C-PIPSCЦ PrPs 6 C,PëP¶PSCЦ P·P° P·P°PiP°P»C†PSPëPj P†PsPeP°P·PSPëPePsPj PANSS C† PrPsC†P»C-PrP¶PµPSPSCЦC... P·P°PiPsC†C,C†PµPSPSCЦ C†PëP·PsC,,C†PµPSC-C— B†” P†C†C†P†P° ITT.

<i>P'PëC...C-PrPSPëP№</i>	<i>P—PjC-PSP°</i>	<i>P C-P·PSPëC†CЦ PI</i>	<i>P -</i>
<i>C†C-PIPµPSC†</i>	<i>PŷPµC†PµPrPSC”</i>	<i>P»C-PeC†PIP°PSPSC-</i>	<i>P·PSP°C†PµPSPS</i>
<i>PŷPµC†PµPrPSC”</i>	<i>P·PSP°C†PµPSPSCЦ</i>	<i>PI</i>	<i>CЦ</i>
<i>P·PSP°C†PµPSPSCЦ</i>	<i>LS (PŷPµ)</i>	<i>P†PsC†C-PIPSCЦPSPS</i>	
<i>B± PŷP’</i>		<i>C- P· P†P»P°C†PµP±Ps</i>	
		<i>(95 % P”P†)</i>	

P—P°PiP°P»C†PSPëP№ P†PsPeP°P·PSPëPe PANSS (MMRM)

P”PsC†P»C-PrP¶PµPSPSCЦ RGH-MD-16 (n = 711)

PµP»P°C†PµP±Ps	97,3 B± 9,22	B†”13,29 (1,82)	B†”	B†”
PµP°C†PëP†C†P°P·Pë	97,1 B± 9,13	B†”21,27 (1,77)	B†”7,97 (B†”12,94, B†”3,01)	0,0017
PS 1,5 PjPi/PrPsP±C†			B†”8,16 (B†”13,09, B†”3,22)	0,0013
PµP°C†PëP†C†P°P·Pë	97,2 B± 8,66	B†”21,45 (1,74)	B†”10,48 (B†”15,41, B†”5,55)	< 0,0001
PS 3 PjPi/PrPsP±C†	96,7 B± 9,01	B†”23,77 (1,74)	B†”15,98 (B†”20,91, B†”11,04)	< 0,0001*
P PëC†P†PµC†PëPrPsP98,1	B± 9,50	B†”29,27 (1,74)		
S 4 PjPi/PrPsP±C†				

P”PsC†P»C-PrP¶PµPSPSCЦ RGH-MD-04 (n = 604)

PµP»P°C†PµP±Ps	96,5 B± 9,1	B†”14,3 (1,5)	B†”	B†”
PµP°C†PëP†C†P°P·Pë	96,1 B± 8,7	B†”20,2 (1,5)	B†”6,0 (B†”10,1, B†”1,9)	0,0044
PS 3 PjPi/PrPsP±C†			B†”8,8 (B†”12,9, B†”4,7)	< 0,0001
PµP°C†PëP†C†P°P·Pë	95,7 B± 9,4	B†”23,0 (1,5)	B†”7,0 (B†”11,0, B†”2,9)	0,0008*
PS 6 PjPi/PrPsP±C†	95,6 B± 9,0	B†”21,2 (1,4)		
P†C†PëP†C-P†C†P°P·P	95,6 B± 9,0	B†”21,2 (1,4)		
sP» 10 PjPi/PrPsP±C†				

P”PsC†P»C-PrP¶PµPSPSCЦ RGH-MD-05 (n = 439)

PµP»P°C†PµP±Ps	96,6 B± 9,3	B†”16,0 (1,6)	B†”	B†”
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PrPsCfP»C-PrP¶CfPIP°PICfC¶C¶ C¶ P¶PsC¶C-PIPSC¶PSPSC- P· C¶P¶CfP¶P¶C¶P¶P¶PrPsPSPsPj
(PrC-P°P¶P°P·PsPS PrPsP· 3b¶“6 PjPi, C¶C-P»CHbPsPIP° PrPsP·P° 4 PjPi) C¶ P¶P°C¶C-C”PSC,C-PI
C-P· P¶P¶C¶CfP¶CfC,C¶PIP°P»CHbPSP¶PjP¶ P¶P¶C¶P¶PIP°P¶PSPs PSP¶P¶P°C,P¶PIPSP¶PjP¶
CfP¶PjPiC,PsPjP°PjP¶ C¶P¶P·PsC,„C¶P¶PSC-C— (n = 461). 86 % P¶P°C¶C-C”PSC,C-PI P±CfP»P¶
PIC-PePsPj PrPs 55 C¶P¶PeC-PI, 54 % P· PSP¶C... P±CfP»P¶ C¶PsP»PsPIC-PeP°PjP¶.

P¶P¶C¶CfP¶CfC,C¶PIP°P»CHbPSC- P¶P¶C¶P¶PIP°P¶PSPs PSP¶P¶P°C,P¶PIPSC- CfP¶PjPiC,PsPjP¶
P±CfP»P¶ PIP¶P·PSP°C¶P¶PSC- C¶P¶ CfP¶PjPiC,PsPjP¶, C¶°Ps C,C¶P¶PIP°C¶C,CHb PSP¶
PjP¶PSC¶P¶ 6 PjC-CfC¶C¶C-PI C,P° C...P°C¶P°PeC,P¶C¶P¶P·CfC¶C,CHbCfC¶C PIP¶CfP¶PsPeP¶Pj
C¶C-PIPSP¶Pj PSP¶P¶P°C,P¶PIPSP¶C... CfP¶PjPiC,PsPjC-PI C- PSP¶P·CHbPeP¶Pj C¶C-PIPSP¶Pj
P¶PsP·P¶C,P¶PIPSP¶C... CfP¶PjPiC,PsPjC-PI [(P±P°P» P·P° P¶PsPeP°P·PSP¶PePsPj PANSS PrP»C¶
PSP¶P¶P°C,P¶PIPSP¶C... CfP¶PjPiC,PsPjC-PI ≥ 24, P±P°P» ≥ 4 C¶°PsPSP°P¶PjP¶PSC¶P¶ PI 2
C-P· 3 P¶PsPeP°P·PSP¶PeC-PI PANSS (N1: CfP¶P»PsC¶°P¶PSPSC¶ P¶PjPsC¶C-P¶, N4:
PIC-PrCfCfC,PSC-CfC,CHb PjPsC,P¶PIP°C¶C-C— C,P° N6: P±C-PrPSC-CfC,CHb PjPsPIP¶) C,P°
P·PSP°C¶P¶PSPSC¶ P¶PsPeP°P·PSP¶PeP° PANSS PrP»C¶ P¶PsP·P¶C,P¶PIPSP¶C...
CfP¶PjPiC,PsPjC-PI ≤ 19]. P¶P°C¶C-C”PSC,P¶ C-P· C,P°PeP¶PjP¶ PIC,PsC¶P¶PSPSP¶PjP¶
PSP¶P¶P°C,P¶PIPSP¶PjP¶ CfP¶PjPiC,PsPjP°PjP¶, C¶P¶ PrP¶P¶C¶P¶CfP¶PIPSC- CfP¶PjPiC,PsPjP¶
CfP¶C¶P¶PrPSCbPsPiPs C,P° C,C¶P¶¶PePsPiPs CfC,C¶P¶P¶PSC¶C¶ C,P° PeP»C-PSC-C¶PSPs
P·PSP°C¶CfC¶°P¶P¶ P¶P°C¶P¶C-PSCfP¶PSC-P·Pj (P¶PeCfC,C¶P°P¶C-C¶P°PjC-PrPSC-
CfP¶PjPiC,PsPjP¶ [P·P¶P¶]), P±CfP»P¶ PIP¶PeP»C¶C¶P¶PSC-.

P¶Pe P¶P°C¶C-C”PSC,P¶, C¶°Ps P»C-PeCfPIP°P»P¶CfC¶C¶ PeP°C¶P¶P¶C¶P°P·P¶PSPsPj, C,P°Pe C-
P¶P°C¶C-C”PSC,P¶, C¶°Ps P»C-PeCfPIP°P»P¶CfC¶C¶ C¶P¶CfP¶P¶C¶P¶P¶PrPsPSPsPj,
P¶PsPeP°P·P°P»P¶ CfC,P°C,P¶CfC,P¶C¶PSPs PrPsCfC,PsPIC-C¶PSP¶ P¶PsPeC¶P°C¶°P¶PSPSC¶
PI P·PjC-PSP°C... PIC-Pr PIP¶C...C-PrPSPsPiPs C¶C-PIPSC¶ PrPs P¶P°C¶P°PjP¶C,C¶P°
P¶P¶C¶PIP¶PSPSPsC— P¶C,„P¶PeC,P¶PIPSPsCfC,C- b¶” P±P°P» P¶PsPeP°P·PSP¶PeP° PANSS
PrP»C¶ PSP¶P¶P°C,P¶PIPSP¶C... CfP¶PjPiC,PsPjC-PI (PANSS-FSNS) (p < 0,001). P¶C¶PsC,P¶,
P¶PsC¶P¶PSP°C¶C¶P¶ P· 14 C,P¶P¶PSC¶, CfC,P°C,P¶CfC,P¶C¶PSPs PrPsCfC,PsPIC-C¶PSP°
C¶C-P·PSP¶C¶C¶ CfP¶PsCfC,P¶C¶C-P¶P°P»P°CfC¶C¶ PSP° PePsC¶P¶CfC,CHb
PeP°C¶P¶P¶C¶P°P·P¶PSCf P¶PsC¶C-PIPSC¶PSPs P· C¶P¶CfP¶P¶C¶P¶P¶PrPsPSPsPj (p = 0,002)
(C,P°P±P»P¶C¶C¶ 2). P¶Pe P¶P°C¶C-C”PSC,P¶, C¶°Ps P»C-PeCfPIP°P»P¶CfC¶C¶
PeP°C¶P¶P¶C¶P°P·P¶PSPsPj, C,P°Pe C- P¶P°C¶C-C”PSC,P¶, C¶°Ps P»C-PeCfPIP°P»P¶CfC¶C¶
C¶P¶CfP¶P¶C¶P¶P¶PrPsPSPsPj, P¶PsPeP°P·P°P»P¶ CfC,P°C,P¶CfC,P¶C¶PSPs
PrPsCfC,PsPIC-C¶PSP¶ P¶PsPeC¶P°C¶°P¶PSPSC¶ PI P·PjC-PSP°C... PIC-Pr
PIP¶C...C-PrPSPsPiPs C¶C-PIPSC¶ PrPs P¶P°C¶P°PjP¶C,C¶P° PIC,PsC¶P¶PSPSPsC—
P¶C,„P¶PeC,P¶PIPSPsCfC,C- b¶” P·P°P¶P°P»CHbPSP¶P¶ P¶PsPeP°P·PSP¶Pe P·P° C¶PeP°P»PsC¶
PsCfPsP±P¶CfC,C-CfPSPsPiPs C,P° CfPsC¶C-P°P»CHbPSPsPiPs
C,„CfPSPeC¶C-PsPSCfPIP°PSPSC¶ (PSP) (p < 0,001). P¶C¶PsC,P¶, P¶PsC¶P¶PSP°C¶C¶P¶ P· 10
C,P¶P¶PSC¶, CfC,P°C,P¶CfC,P¶C¶PSPs PrPsCfC,PsPIC-C¶PSP° C¶C-P·PSP¶C¶C¶
CfP¶PsCfC,P¶C¶C-P¶P°P»P°CfC¶C¶ PSP° PePsC¶P¶CfC,CHb PeP°C¶P¶P¶C¶P°P·P¶PSCf
P¶PsC¶C-PIPSC¶PSPs P· C¶P¶CfP¶P¶C¶P¶P¶PrPsPSPsPj (p = 0,001) (C,P°P±P»P¶C¶C¶ 2).

P¶Pe C¶C-P·PSP¶C¶C- P·P° C¶PeP°P»PsC¶ P·P°P¶P°P»CHbPSPsPiPs PeP»C-PSC-C¶PSPsPiPs
PIC¶P°P¶P¶PSPSC¶ P¶C¶Ps C,C¶P¶¶PeC-CfC,CHb P·P°C...PIPSC¶C¶PIP°PSPSC¶ (C¶ = 0,005)
C,P° P·P° C¶PeP°P»PsC¶ P¶PsPeC¶P°C¶°P¶PSPSC¶ (C¶ < 0,001), C,P°Pe C- C¶P°CfC,PsC,P°
PIC-PrP¶PsPIC-PrC- P·P° PANSS-FSNS (P¶PsPeC¶P°C¶°P¶PSPSC¶ PANSS FSNS ≥ 30 % PSP°
26 C,P¶P¶PSC-; C¶ = 0,003) P¶C-PrC,PIP¶C¶P¶P¶P¶P¶P¶ P¶ PIP¶CfPSPsPIPeP¶ CfC,PsCfPsPIPSPs
P¶P°C¶P°PjP¶C,C¶C-PI P¶P¶C¶PIP¶PSPSPsC— C,P° PIC,PsC¶P¶PSPSPsC—
P¶C,„P¶PeC,P¶PIPSPsCfC,C-.

$$\text{PhP} \pm \text{Cl}^+ \text{P} \text{S} \text{P} \gg \text{C} \text{H} \text{C}, \text{P} \text{S} \text{P}^\circ \quad \text{P} \pm \text{C} - \text{P} \text{S} \text{P} \gg \text{P} \text{S} \text{P} \text{I} \text{C} - \text{C} \pm \text{P} \text{S} \text{P}^\circ \quad \text{P} \text{r} \text{P} \text{S} \text{C} \text{I}^+ \text{C}, \text{C} \text{I}^+ \text{P} \text{I} \text{P} \text{S} \text{C} - \text{C} \text{I}^+ \text{C}, \text{C} \text{H}$$

PeP°CTHPePiCTHP°P·PēPSCr PSPμPIC-PrPsPjP°. PъP°CTHPePiCTHP°P·PēPS PrPsP±CTHPμ
PICrPjPsPeC,CrC"C,CHCCTCЦ PiC-CTP»CЦ PiPμCTHPsCTHP°P»CHPSPsPiPs PiCTHPePNēPsPjCr.
PμC-CTP»CЦ P±P°PiP°C,PsPeCTHP°C,PSPeC... PrPsP· PjP°PeCTrPēPjP°P»CHPSP°
PePsPSCtPμPSC,CTHP°CtC-CЦ PeP°CTHPePiCTHP°P·PēPSCr C,P° PNēPsPiPs PsCTrPSPsPIPSPeC...
P°PeC,PēPIPSPeC... PjPμC,P°P±PsP»C-C,C-PI Cr B PiP»P°P·PjC- B PeCTHPsPIC-
B P·P°P·PIPēCtP°PNē B PrPsCTrCЦPiP°C"C,CHCCTCЦ B PiCTHPeP±P»PēP·PSPs B CtPμCTHPμP·
B 3B7"8 PiPsPrPēPS PiC-CTP»CЦ P·P°CTrC,PsCTrCrPIP°PSPSCЦ.

PμCTHPePNēPsPj PsPrPSC-C"C— PrPsP·Pē PeP°CTHPePiCTHP°P·PēPSCr 1,5 PjPi CTHP°P·PsPj P·
PiCTHPsPrCrPeC,P°PjPē P· PIPēCTrPsPePēPj PIPjC-CTrC,PsPj P¶PēCTrCr (PIC-Pr 900 PrPs 1 000
PeP°P»PsCTHC-PNē) P·PSP°CtPSPs PSPμ PIPiP»PēPIP°PI PSP° PiPsPeP°P·PSPePe C_{max} P°P±Ps AUC
PeP°CTHPePiCTHP°P·PēPSCr (P·PSP°CtPμPSPSCЦ AUC_{0-∞} PiC-PrPIPēC%CrPIP°P»PsCTrCЦ PSP°
12 %, P·PSP°CtPμPSPSCЦ C_{max} P·PSPeP¶CrPIP°P»PsCTrCЦ PSP° 5 % PiCTHPē PiCTHPePNēPsPjC-
P»C-PeP°CTHCCTrCHPePsPiPs P·P°CTrPsP±Cr PiC-CTP»CЦ C—P¶C- PI PiPsCTHC-PIPSCЦPSC- P·
PiCTHPePNēPsPjPsPj PSP°C,C%oPμ). PtP¶P° C,P°PePsP¶ PjP°P»P° PjC-PSC-PjP°P»CHPSPePNē
PIPiP»PēPI PSP° PjPμC,P°P±PsP»C-C,Pē DCAR C,P° DDCAR.

PъP°CTHPePiCTHP°P·PēPS PjPsP¶PSP° P·P°CTrC,PsCTrPsPICrPIP°C,Pē PSPμP·P°P»PμP¶PSPs PIC-Pr
PiCTHPePNēPsPjCr C—P¶C-.

P PsP·PiPsPrC-P»

PkP° PsCTrPSPsPIC- PiPsPiCrP»CЦCtC-PNēPSPsPiPs P°PSP°P»C-P·Cr
C„P°CTHPjP°PePsPeC-PSPμC,PēPePē CrCЦPIPSPePNē PsP±B7™C"Pj CTHPsP·PiPsPrC-P»Cr (Ph/P)
CTrPeP»P°PrP°PI 916 P» PrP»CЦ PeP°CTHPePiCTHP°P·PēPSCr, 475 P» PrP»CЦ DCAR C,P° 1 568 P»
PrP»CЦ DDCAR, C%oPs PIPeP°P·CrC" PSP° P·PSP°CtPSPePNē CTHPsP·PiPsPrC-P»
PeP°CTHPePiCTHP°P·PēPSCr C,P° PNēPsPiPs PsCTrPSPsPIPSPeC... P°PeC,PēPIPSPeC...
PjPμC,P°P±PsP»C-C,C-PI. PъP°CTHPePiCTHP°P·PēPS C,P° PNēPsPiPs PsCTrPSPsPIPSC-
P°PeC,PēPIPSC- PjPμC,P°P±PsP»C-C,Pē P°PeC,PēPIPSPs P·PIB7™CЦP·CrCTHC,CHCCTCЦ
(PeP°CTHPePiCTHP°P·PēPS B7" PSP° 96B7"97 %, DCAR B7" PSP° 94B7"97 %, DDCAR B7" PSP°
92B7"97 %) P· P±C-P»PeP°PjPē PiP»P°P·PjPē.

P'C-PsC,CTHP°PSCrC„PsCTHPjP°CtC-CЦ

PъPμC,P°P±PsP»C-P·Pj PeP°CTHPePiCTHP°P·PēPSCr PIPeP»CTHCtP°C"
PrPμPjPμC,PēP»CTHIP°PSPSCЦ (DCAR C,P° DDCAR), PiC-PrCTHPsPeCTrPēP»CTHIP°PSPSCЦ
(PiC-PrCTHPsPeCTrPēPr PeP°CTHPePiCTHP°P·PēPSCr, HCAR) C,P° PePsPjP±C-PSP°CtC-CTHC
PrPμPjPμC,PēP»CTHIP°PSPSCЦ C,P° PiC-PrCTHPsPeCTrPēP»CTHIP°PSPSCЦ (PiC-PrCTHPsPeCTrPē-
PrPμP·PjPμC,PēP»-PeP°CTHPePiCTHP°P·PēPS, HDCAR, C,P° PiC-PrCTHPsPeCTrPē-
PrPēPrPμP·PjPμC,PēP»-PeP°CTHPePiCTHP°P·PēPS, HDDCAR). PkP°PrP°P»C- PjPμC,P°P±PsP»C-C,Pē
HCAR, HDCAR C,P° HDDCAR P±C-PsC,CTHP°PSCrC„PsCTHPjCrCTHC,CHCCTCЦ Cr
PIC-PrPiPsPIC-PrPSC- PePsPsB7™CTHPiP°C,Pē CTrCrP»CHC„P°C,Cr C,P°
PiP»CTHCCTrCTHPsPSC-PrCr. P"PsPrP°C,PePsPIPēPNē PjPμC,P°P±PsP»C-C, B7" PePēCTrP»PsC,P°
PrPμCTrPēC...P»PsCTHPsC„PμPSC-P»Cr-PiC-PiPμCTHP°P·PēPSCr-PeP°CTHPePiCTHP°P·PēPSCr
(DDCPPCAR) B7" CrC,PIPsCTHCCTHC,CHCCTCЦ PI PiCTHPsCtPμCTrC-
PrPμP·P°P»PeC-P»CrPIP°PSPSCЦ C,P° PSP°CTrC,CrPiPSPsPiPs PsPePēCTrPSPμPSPSCЦ
PeP°CTHPePiCTHP°P·PēPSCr.

PъP°CTHPePiCTHP°P·PēPS PjPμC,P°P±PsP»C-P·CrC"C,CHCCTCЦ CYP3A4 C,P° PjPμPSCePsCTHC
PjC-CTHPsCTHC CYP2D6 PrPs DCAR C,P° HCAR. PkP°PrP°P»C- DCAR
PjPμC,P°P±PsP»C-P·CrC"C,CHCCTCЦ CYP3A4 C,P° PjPμPSCePsCTHC PjC-CTHPsCTHC CYP2D6 PrPs
DDCAR C,P° HDCAR. PμPsC,C-Pj DDCAR PjPμC,P°P±PsP»C-P·CrC"C,CHCCTCЦ P·P°

$\text{P}_{\mu}\text{C}-\text{Cl}^{\text{I}}\text{P}\gg\text{Cl}_{\text{I}}\text{PiPsPIC}, \text{PsC}_{\text{H}}^{\text{I}}\text{PSPsPiPs P}\cdot\text{P}^{\circ}\text{Cl}^{\text{I}}\text{C}, \text{PsCl}^{\text{I}}\text{C}^{\text{I}}\text{PIP}^{\circ}\text{PSPSCl}_{\text{I}}\text{PePsPSC}^{\text{I}}\text{P}_{\mu}\text{PSC}, \text{C}_{\text{H}}^{\text{I}}\text{P}^{\circ}\text{C}^{\text{I}}\text{C}-\text{Cl}_{\text{I}}$
 $\text{PeP}^{\circ}\text{C}_{\text{H}}^{\text{I}}\text{P}^{\circ}\text{PiC}_{\text{H}}^{\text{I}}\text{P}^{\circ}\text{P}\cdot\text{P}^{\circ}\text{PSC}^{\text{I}}\text{C}, \text{P}^{\circ}\text{PN}_{\text{I}}\text{PsPiPs PrPIPsC}\dots \text{PsCl}^{\text{I}}\text{PSPsPIPS}^{\circ}\text{P}^{\circ}\text{C}\dots \text{P}^{\circ}\text{PeC}, \text{P}^{\circ}\text{PiPS}^{\circ}\text{P}^{\circ}\text{C}\dots$
 $\text{PjP}_{\mu}\text{C}, \text{P}^{\circ}\text{P}\pm\text{PsP}\gg\text{C}-\text{C}, \text{C}-\text{PI}, \text{PrP}_{\mu}\text{P}\cdot\text{PjP}_{\mu}\text{C}, \text{P}^{\circ}\text{P}\gg-\text{PeP}^{\circ}\text{C}_{\text{H}}^{\text{I}}\text{P}^{\circ}\text{PiC}_{\text{H}}^{\text{I}}\text{P}^{\circ}\text{P}\cdot\text{P}^{\circ}\text{PSC}^{\text{I}}\text{C} (\text{DCAR}) \text{C}, \text{P}^{\circ}$
 $\text{PrP}^{\circ}\text{PrP}_{\mu}\text{P}\cdot\text{PjP}_{\mu}\text{C}, \text{P}^{\circ}\text{P}\gg-\text{PeP}^{\circ}\text{C}_{\text{H}}^{\text{I}}\text{P}^{\circ}\text{PiC}_{\text{H}}^{\text{I}}\text{P}^{\circ}\text{P}\cdot\text{P}^{\circ}\text{PSC}^{\text{I}}\text{C} (\text{DDCAR}), \text{PI PiP}\gg\text{P}^{\circ}\text{P}\cdot\text{PjC}-$
 $\text{PiC}-\text{PrPIPS}^{\circ}\text{C}\% \text{C}^{\text{I}}\text{C}^{\text{I}}\text{C}, \text{CH}_{\text{I}}\text{Cl}^{\text{I}}\text{Cl}_{\text{I}}\text{PiC}_{\text{H}}^{\text{I}}\text{PsPiPsC}_{\text{H}}^{\text{I}}\text{C}^{\text{I}}\text{C}-\text{PN}_{\text{I}}\text{PSPs PrC}-\text{P}^{\circ}\text{PiP}^{\circ}\text{P}\cdot\text{PsPSC}^{\text{I}}\text{C}$

C, P_μCT_{HP}°P_iP_μPIC, P_{EC}±PSPsC— PrPsP·P_ē PIC-Pr 1,5 PjPi PrPs 6 PjPi.

P_hPeCT_{HP}P_μPjC- PiCT_{HC}CrP_iP_ē P_iP°CTC-C" PSC, C-PI

P_μPsCT_{HC}C_zCEP_μPSPSC_μ C,, C_zPSPeCTC-C— PSP_ēCT_{HP}PsPe

P_μPsP_iCrP»C_μCTC-PM_zPSP_μ C,, P°CT_{HP}JP°PePsPeC-PSP_μC, P_{EC}±PSP_μ PjPsPrP_μP»CT_{HP}IP°PSPSC_μ PIP_ēPePsPSCrPIP°P»PSC_μCTC P· PIP_ēPePsCT_{HP}P_ēCTC, P°PSPSC_μPj PrP°PSP_ēC... PIC-Pr P_iP°CTC-C" PSC, C-PI, C_μPeC- P±CrP»P_ē P·P°P»CrC±P_μPSC- PrPs PeP»C-PSC-C±PSPsPiPs PrPsCrP»C-PrP_μP_μPSPSC_μ CT_{HC}, PsCT_{HC}PsPIPSPs P»C-PeCrPIP°PSPSC_μ C_ēP_ēP·PsC,, CT_{HP}P_μPSC-C— PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSPsPj, P· CT_{HC}-P·PSP_ēPjP_ē P_iPsPeP°P·PSP_ēPeP°PjP_ē C,, CrPSPeCTC-C— PSP_ēCT_{HP}PsPe, PIPeP»CT_{HC}±PSPs P· PSPsCT_{HP}PjP°P»CH_zPSPsCT_{HC} C,, CrPSPeCTC-CT_{HC} PSP_ēCT_{HP}PsPe (PeP»C-CT_{HP}P_μPSC_μ PeCT_{HP}P_μP°C, P_ēPSC-PSC_μ (CrCl) ≥ 90 PjP»/C...PI) C- P_iPsCT_{HC}CrCEP_μPSPSC_μPjP_ē C,, CrPSPeCTC-C— PSP_ēCT_{HP}PsPe P»P_μPiPePsPiPs (CrCl 60B₇"89 PjP»/C...PI) C, P° CT_{HP}P_μCT_{HP}PrPSC_{HC}PsPiPs CT_{HC}, CrP_iP_μPSC_μ C, C_μP_μPePsCT_{HC}, C- (CrCl 30B₇"59 PjP»/C...PI). P_{HC}-P_μ PeP»C-CT_{HP}P_μPSC_μPsPj PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ PI P_iP»P°P·PjC- C, P° PeP»C-CT_{HP}P_μPSC_μPsPj PeCT_{HP}P_μP°C, P_ēPSC-PSC_μ PSP_μ P±CrP»Ps P·PSP°PM_zPrP_μPSPs P_μPsPrPSP_ēC... C-CT_{HC}, PsC, PSP_ēC... P·PIB₇TM C_μP·PeC-PI.

P" C-C_μ PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ PSP_μ PsCTC-PSC_{HC}IP°P»P°CT_{HC}CT_{HC} Cr P_iP°CTC-C" PSC, C-PI C-P· C, C_μP_μPeP_ēPjP_ē (CrCl < 30 PjP»/C...PI) P_iPsCT_{HC}CrCEP_μPSPSC_μPjP_ē C,, CrPSPeCTC-C— PSP_ēCT_{HP}PsPe (PrP_ēPI. CT_{HP}PsP·PrC-P» B«P_YP_iPsCT_{HC}-P± P·P°CT_{HC}, PsCT_{HC}CrPIP°PSPSC_μ C, P° PrPsP·P_ēB»).

P_μPsCT_{HC}C_zCEP_μPSPSC_μ C,, C_zPSPeCTC-C— P_iP_μC±C-PSPeP_ē

P"PsCT_{HC}P»C-PrP_μP_μPSPSC_μ PI PrPIPsC... C±P°CT_{HC}, P_ēPSP°C... (PsPrPSPsPeCT_{HP}P°C, PSP° PrPsP·P° PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ 1 PjPi [C±P°CT_{HC}, P_ēPSP° P_h] C, P° PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPS Cr PrPsP±PsPIC-PM_z PrPsP·C- 0,5 PjPi P_iCT_{HP}PsC, C_μPiPsPj 14 PrPSC-PI [C±P°CT_{HC}, P_ēPSP° P'] P_iCT_{HP}PsPiPsPrP_ēP»PSC_μCTC P·P° CrC±P°CT_{HC}, CT_{HC} P_iP°CTC-C" PSC, C-PI P· CT_{HC}-P·PSP_ēPjP_ē CT_{HC}, CrP_iP_μPSC_μPjP_ē P_iPsCT_{HC}CrCEP_μPSC_{HC} C,, CrPSPeCTC-C— P_iP_μC±C-PSPeP_ē (PeP»P°CT_{HC}P_ē P_h C, P° P' P·P° P_hP°PM_zP»PrPsPj B₇" P_μB₇TM CT_{HC}). P_μC-CT_{HC}P»C_μ P·P°CT_{HC}, PsCT_{HC}CrPIP°PSPSC_μ PsPrPSPsPeCT_{HP}P°C, PSPsC— PrPsP·P_ē PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ 1 PjPi P°P±Ps P_iCT_{HP}P_ēPM_zPsPjCr 0,5 PjPi PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ P_iCT_{HP}PsC, C_μPiPsPj 14 PrPSC-PI P_iP°CTC-C" PSC, P_ē P· P_iPsCT_{HC}CrCEP_μPSPSC_μPjP_ē C,, CrPSPeCTC-C— P_iP_μC±C-PSPeP_ē P»P_μPiPePsPiPs C±P_ē CT_{HC}P_μCT_{HP}PrPSC_{HC}PsPiPs CT_{HC}, CrP_iP_μPSC_μ Cr P_iPsCT_{HC}-PIPSC_μPSPSC- B P· P_iP°CTC-C" PSC, P°PjP_ē P· PSPsCT_{HP}PjP°P»CH_zPSPsCT_{HC} C,, CrPSPeCTC-C" CT_{HC} P_iP_μC±C-PSPeP_ē PjP°P»P_ē P_iCT_{HP}P_ēP±P»P_ēP·PSPs PSP° 25 % PIP_ēC%Cr PePsPSC±P_μPSC, CT_{HP}P°CTC-CT_{HC} PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ (C_{max} C, P° AUC) C, P° P_iCT_{HP}P_ēP±P»P_ēP·PSPs PSP° 45 % PSP_ēP_μCT_{HC}Cr PePsPSC±P_μPSC, CT_{HP}P°CTC-CT_{HC} PsCT_{HC}PSPsPIPSP_ēC... P°PeC, P_ēPIPS_ēC... PjP_μC, P°P±PsP»C-C, C-PI, PrP_μP·PjP_μC, P_ēP»-PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ C, P° PrP_ēPrP_μP·PjP_μC, P_ēP»-PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ.

P_μC-CT_{HC}P»C_μ P±P°PiP°C, PsCT_{HP}P°P·PsPiPsPiPs P_iCT_{HP}P_ēPM_zPsPjCr PeP°CT_{HP}P_ēP_iCT_{HP}P°P·P_ēPSC_μ PePsPSC±P_μPSC, CT_{HP}P°CTC-C_μ P·P°PiP°P»CH_zPSPsPiPs P°PeC, P_ēPIPS_ēPsPiPs PePsPjP_iPsPSP_μPSC, P° (CAR DCAR DD CAR) (AUC C, P° C_{max}) Cr P_iPsCT_{HC}-PIPSC_μPSPSC- B P· PIC-PrP_iPsPIC-PrPSP_ēPj P_iPsPeP°P·PSP_ēPePsPj CrB P_iP°CTC-C" PSC, C-PI P· PSPsCT_{HP}PjP°P»CH_zPSPsCT_{HC} C,, CrPSPeCTC-C" CT_{HC} P_iP_μC±C-PSPeP_ē P·PSP_ēP·P_ēP»P°CT_{HC}CT_{HC} PSP° 21B₇"22 % C, P° 13B₇"15 % PIC-PrP_iPsPIC-PrPSPs Cr B P_iP°CTC-C" PSC, C-PI P· P_iPsCT_{HC}CrCEP_μPSPSC_μPj C,, CrPSPeCTC-C— P_iP_μC±C-PSPeP_ē (P_μP_μP_μ) P»P_μPiPePsPiPs C±P_ē CT_{HC}P_μCT_{HP}PrPSC_{HC}PsPiPs CT_{HC}, CrP_iP_μPSC_μ C, C_μP_μPePsCT_{HC}, C-, C_μPeC%Ps PIC_{HP}P°C...PsPICrPIP°P»P_ēCT_{HC}CT_{HC} PSP_μP·PIB₇TM C_μP·P°PSC- P·PIB₇TM C_μP·P°PSC- PePsPSC±P_μPSC, CT_{HP}P°CTC-C—, B C, PsPrC- C_μPe PrP»C_μ PSP_μP·PIB₇TM C_μP·P°PSPsPiPs

P·P°PiP°P»CHbPSPsPiPs PePsPjPiPsPSPµPSC,P° P±CfP»Ps CḡPsP·CḡP°C...PsPIP°PSPs
P·PSPëP¶PµPSPSC¶PSP° 12bḡ“13 % C,P° PiC-PrPIPeC%oPµPSPSC¶PSP° 20bḡ“25 %
PIC-PrPiPsPIC-PrPSPs B Cf PiP°C†C-C”PSC,C-PI P· PµPαPµ P»PµPiPePsPiPs C,P°
C†PµCḡPµPrPSCHbPsPiPs C†C,CfPiPµPSC¶ C,C¶P¶PePsC†C,C-.

P”C-C¶ PeP°CḡPëPiCḡP°P·PëPSC† PSPµ PsC†C-PSCHPIP°P»P°C†C¶ Cf PiP°C†C-C”PSC,C-PI C-P·
C,C¶P¶PePëPjPë (PeP»P°C† PŸ P·P° P§P°PNëP»PrPsPj bḡ” Pµbḡ™ Cḡ) PiPsCḡCfCëPµPSPSC¶PjPë
C,,CfPSPeC†C-C— PiPµC†C-PSPePë (PrPëPI. CḡPsP·PrC-P» B«PŸPiPsC†C-P±
P·P°C†C,PsC†CfPIP°PSPSC¶ C,P° PrPsP·PëB»).

P’C-Pe, C†C,P°C,CH C,P° CḡP°C†P°

Pj PiPsPiCfP»C¶C†C-PNëPSPsPjCf C,,P°CḡPjP°PePsPeC-PSPµC,PëC†PSPsPjCf P°PSP°P»C-P·C-
PSPµ P±CfP»Ps PeP»C-PSC-C†PSPs P·PSP°C†PëPjPëC... PIC-PrPjC-PSPSPsC†C,PµPNë Cf
PiP°CḡP°PjPµC,CḡP°C... C,,P°CḡPjP°PePsPeC-PSPµC,PëPePë (AUC C,P° C_{max}B
PeP°CḡPëPiCḡP°P·PëPSC† C,P° PNëPsPiPs PsC†PSPsPIPSPëC... P°PeC,PëPIPSPëC...
PjPµC,P°P±PsP»C-C,C-PI) P·P°P»PµP¶PSPs PIC-Pr PIC-PeCf, C†C,P°C,C- C,P° CḡP°C†Pë
PiP°C†C-C”PSC,C-PI. PµC-Pr C†P°C† P°PSP°P»C-P·Cf B B PIPëPIC†P°P»Pë B PrP°PSC-
B C%oPsPrPs B 2 844 PiP°C†C-C”PSC,C-PI CḡC-P·PSPëC... CḡP°C†, P· C¶PePëC... 536
PiP°C†C-C”PSC,C-PI P±CfP»Pë PIC-PePsPj PIC-Pr 50 PrPs 65 CḡPsPeC-PI, 933 PsC†PsP±Pë
P±CfP»Pë P¶C-PSPeP°PjPë (PrPëPI. CḡPsP·PrC-P» B«PŸPiPsC†C-P± P·P°C†C,PsC†CfPIP°PSPSC¶
C,P° PrPsP·PëB»). P”P°PSC- C%oPsPrPs PiP°C†C-C”PSC,C-PI P»C-C,PSCHbPsPiPs PIC-PeCf
(PiPsPSP°Pr 65 CḡPsPeC-PI) PsP±PjPµP¶PµPSC-.

PµP°P»C-PSPSC¶

P§PµCḡPµP· C,Pµ, C%oPs PeP°CḡPëPiCḡP°P·PëPS PSPµ C” C†CfP±C†C,CḡP°C,PsPj PrP»C¶
CYP1A2, PSPµ PsC†C-PeCfC”C,CHbC†C¶ PIPiP»PëPIC† PiP°P»C-PSPSC¶PSP°
C,,P°CḡPjP°PePsPeC-PSPµC,PëPeCf PeP°CḡPëPiCḡP°P·PëPSC†.

PµPsC,PµPSC†C-PNëPSPëPNë PIPiP»PëPI PeP°CḡPëPiCḡP°P·PëPSC† PSP° C-PSCëC-
PiCḡPµPiP°CḡP°C,Pë

PḡP°CḡPëPiCḡP°P·PëPS C,P° PNëPsPiPs PsC†PSPsPIPSC- P°PeC,PëPIPSC- PjPµC,P°P±PsP»C-C,Pë
PSPµ C-PSPrCfPeCfPIP°P»Pë PµPSP·PëPjPë CYP1A2, CYP2B6 C,P° CYP3A4 C- PSPµ P±CfP»Pë
C-PSPiC-P±C-C,PsCḡP°PjPë CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP219, CYP2D6,
CYP2E1 C,P° CYP3A4 *in vitro*. PḡP°CḡPëPiCḡP°P·PëPS C,P° PNëPsPiPs PsC†PSPsPIPSC-
P°PeC,PëPIPSC- PjPµC,P°P±PsP»C-C,Pë PSPµ C” C-PSPiC-P±C-C,PsCḡP°PjPë
C,CḡP°PSC†PiPsCḡC,PSPëC... P±C-P»PeC-PI OATP1B1, OATP1B3, BCRP,
PsCḡPiP°PSC-C†PSPsPiPs PeP°C,C-PSPSPsPiPs C,CḡP°PSC†PiPsCḡC,PSPsPiPs P±C-P»PeP° 2
(OCT2) C,P° PsCḡPiP°PSC-C†PSPëC... P°PSC-PSPSPPëC... C,CḡP°PSC†PiPsCḡC,PSPëC...
P±C-P»PeC-PI 1 C,P° 3 (OAT1 C,P° OAT3) *in vitro*. DCAR C,P° DDCAR PSPµ P±CfP»Pë
C-PSPiC-P±C-C,PsCḡP°PjPë C,CḡP°PSC†PiPsCḡC,PSPsPiPs P±C-P»PeP° P-gp, C...PsC†P°
PeP°CḡPëPiCḡP°P·PëPS P±CfPI C-PSPiC-P±C-C,PsCḡPsPj P-gp PI PePëCëPµC†PSPëPeCf (PrPëPI.
CḡPsP·PrC-P» B«P’P·P°C”PjPsPrC-C¶ P· C-PSCëPëPjPë P»C-PeP°CḡC†CHbPePëPjPë
P·P°C†PsP±P°PjPë C,P° C-PSCëC- PIPëPrPë PIP·P°C”PjPsPrC-PNëB»).

P”P°PSC- PrPsPeP»C-PSC-C†PSPëC... PrPsC†P»C-PrP¶PµPSCHb P· P±PµP·PiPµPePë

PḡP°CḡPëPiCḡP°P·PëPS C†PiCḡPëC†PëPSC¶PI PrPIPsC†C,PsCḡPsPSPSCH PeP°C,P°CḡP°PeC,Cf
C,P° PIC,PsCḡPëPSPSC- P·PjC-PSPë C†C-C,PeC-PIPePë (PIC-PrCëP°CḡCfPIP°PSPSC¶ C,P°
PeC-C†C,PsPiPsPrC-P±PSC† PrPµPiPµPSPµCḡP°C†C-CH C†C-C,PeC-PIPePë) Cf C†PsP±P°Pe.

P—P°PiP°P»CHbPSP° PµPeCÍPíPsP·PëC†C—C¼ (AUC) PeP°CĤPëPíCĤP°P·PëPSCr,
B PrPsCÍC¼PiPSCrC,P° PíCĤPë P·P°CÍC,PsCÍCrPIP°PSPSC- PjP°PeCÍPëPjP°P»CHbPSPsC—
PrPsP·Pë, C°Ps PSPµ PíCĤPëP·PIPsPrPëC,CH PrPs CĤPsP·PIPëC,PeCÍ C¼PIPSPëC...
PSPµP±P°P¶P°PSPëC... PµC„PµPeC,C—PI (NOAEL) P· P±PsPeCÍ PsCĤPiP°PSC—PI P·PsCĤCr, Cr 4,2
CĤP°P·P° PíPµCĤPµPIPëC°CrC” PeP»C—PSC—C†PSCr AUC PíCĤPë PjP°PeCÍPëPjP°P»CHbPSC—PNë
CĤPµPePsPjPµPSPPrPsPIP°PSC—PNë PrPsP·C- PrP»C¼ P»CĤPrPëPSPë (PĥP P”P>) 6 PjPi PSP°
PrPsP±Cr. P—P±C—P»CHbCëPµPSPSC¼ C†P°CÍC,PsC,Pë
PrPµPiPµPSPµCĤP°C†C—C—/P°C,CĤPsC„C—C— CÍC—C,PeC—PIPePë
CÍPiPsCÍC,PµCĤC—PiP°P»PsCÍC¼ Cr C°CrCĤC—PI—P°P»CHbP±C—PSPsCÍC—PI Cr 2-
CĤC—C†PSPsPjCr PrPsCÍP»C—PrP¶PµPSPSC- PSP° C,P»C— PeP»C—PSC—C†PSPs
P·PSP°C†CrC°PsC— PµPeCÍPíPsP·PëC†C—C— PíCĤPµPíP°CĤP°C,Cr.

PαPsCÍC„PsP»C—PiC—PrPsP· CÍPiPsCÍC,PµCĤC—PiP°PICÍC¼ Cr P»PµPiPµPSC¼C... C°CrCĤC—PI,
CÍPsP±P°Pe C,P° PjPëCëPµPNë (P· P·P°PiP°P»PµPSPSC¼Pj P°P±Ps P±PµP· PSCĤPsPiPs) C,P° Cr
PePsCĤC— PSP°PrPSPëCĤPePsPIPëC... P·P°P»PsP· CÍPsP±P°Pe PSP° C„PsPSC—
PeP»C—PSC—C†PSPs P·PSP°C†CrC°PëC... PµPeCÍPíPsP·PëC†C—PNë PíCĤPµPíP°CĤP°C,Cr.
PŸPiPsCÍC,PµCĤC—PiP°P»PsCÍC¼ P·P°PiP°P»PµPSPSC¼ P»PµPiPµPSCĤ Cr CÍPsP±P°Pe, C¼PeC—
PsC,CĤPëPjCrPIP°P»Pë PeP°CĤPëPíCĤP°P·PëPS PíCĤPsC,C¼PiPsPj 1 CĤPsPeCÍ, PíCĤPë
C†CHbPsPjCr NOAEL C,P° PIC—PrPiPsPIC—PrPSC— PíPsPeP°P·PSPëPePë AUC
PíPµCĤPµPIPëC°CrPIP°P»Pë B C,P°PeC— Cr CĤP°P·C- P·P°CÍC,PsCÍCrPIP°PSPSC¼B PĥP P”P>
Cr 2,7 (CÍP°PjC†C-) C,P° 1,7 (CÍP°PjPePë) CĤP°P·P°. PĥP°PíCĤPëPeC—PSC†C— 2-
PjC—CÍC¼C†PSPsPiPs PíPµCĤC—PsPrCr P±PµP· PíCĤPëPNëPsPjCr PíCĤPµPíP°CĤP°C,Cr PíCĤPë
PµPeCÍPíPsP·PëC†C—C—, C¼PeP° PI 4,2 CĤP°P·P° B PíPµCĤPµPIPëC°CrC” PeP»C—PSC—C†PSCr
PµPeCÍPíPsP·PëC†C—CĤB PíCĤPë PĥP P”P>, P·P°PiP°P»PµPSPSC¼ PSPµ
CÍPiPsCÍC,PµCĤC—PiP°P»PsCÍC¼; PíCĤPsC,Pµ P·P°PiP°P»PµPSPSC¼ P·P±PµCĤC—PiP°P»PsCÍC¼
PíCĤPë P±C—P»CHbCë PIPëCÍPsPePëC... PrPsP·P°C....

P”C—PiPµCĤC,CĤPsC„C—C¼ PePsCĤPë PSP°PrPSPëCĤPePsPIPëC... P·P°P»PsP·
CÍPiPsCÍC,PµCĤC—PiP°P»P°CÍC¼ PSP° C,P»C— PePsPSC†PµPSC,CĤP°C†C—C—
PíCĤPµPíP°CĤP°C,Cr, C°Ps PI 4,1 CĤP°P·P° PíPµCĤPµPIPëC°CrC” B C,P°PeCÍ PíCĤPë
P·P°CÍC,PsCÍCrPIP°PSPSC- PĥP P”P>, Cr C°CrCĤC—PI (C,C—P»CHbPePë Cr CÍP°PjPsPe) C,P°
PíCĤPë PeP»C—PSC—C†PSPs P·PSP°C†CrC°PëC... P·P°PiP°P»CHbPSPëC...
PePsPSC†PµPSC,CĤP°C†C—C¼C... PeP°CĤPëPíCĤP°P·PëPSCr PI PíP»P°P·PjC- Cr PjPëCëPµPNë. Pj
CÍPsP±P°Pe CÍPiPsCÍC,PµCĤC—PiP°P»P°CÍC¼ PsP±PsCĤPsC,PSP°
PiC—PiPµCĤC,CĤPsC„C—C¼/PiC—PiPµCĤPíP»P°P·C—C¼ C,P°
PIP°PeCÍPsP»C—P·P°C†C—C¼/PIPµP·PëPeCÍP»C¼C†C—C¼ PePsCĤPë PSP°PrPSPëCĤPePsPIPëC...
P·P°P»PsP·, NOAEL Cr 4,2 CĤP°P·P° PíPµCĤPµPIPëC°CrPIP°P»P° B C,P°PeCÍ PíCĤPë PĥP P”P>.

Pj CÍP°PjPsPe C°CrCĤC—PI PIC—PrP·PSP°C†P°P»PsCÍC¼ P·PSPëP¶PµPSPSC¼
PíP»PsPrCĤC†PsCÍC,C- C,P° C—PSPPrPµPeCÍCr P·P°PiP»C—PrPSPµPSPSC¼ PíCĤPë
PeP»C—PSC—C†PSPs P·PSP°C†CrC°PëC... PµPeCÍPíPsP·PëC†C—C¼C... Cr
PíPµCĤPµCĤP°C...CrPSPeCÍ PSP° PjPi/Pj² PíP»PsC°C- PíPsPIPµCĤC...PSC- C,C—P»P°.
P’PíP»PëPICr PSP° C„PµCĤC,PëP»CHbPSC—CÍC,CH CÍP°PjC†C—PI PíCĤPë
PµPeCÍPíPsP·PëC†C—C¼C..., C°Ps PíPµCĤPµPIPëC°CrCĤC,CH PeP»C—PSC—C†PSCr
PµPeCÍPíPsP·PëC†C—CĤ PíCĤPë PĥP P”P> Cr 4,3 CĤP°P·P°, PSPµ
CÍPiPsCÍC,PµCĤC—PiP°P»PsCÍC¼.

P’PIPµPrPµPSPSC¼ PeP°CĤPëPíCĤP°P·PëPSCr C°CrCĤP°Pj Cr PíPµCĤC—PsPr
PsCĤPiP°PSPsPiPµPSPµP·Cr B CÍPíCĤPëC†PëPSC¼P»Ps PIP°PrPë CĤPsP·PIPëC,PeCÍ,
P·PSPëP¶PµPSPSC¼ PIPëP¶PëPIP°PSPSC¼ PíPsC,PsPjCÍC,PIP° C,P° P·P°C,CĤPëPjPeCÍ
CĤPsP·PIPëC,PeCÍ PíCĤPë PµPeCÍPíPsP·PëC†C—C¼C... PíCĤPµPíP°CĤP°C,Cr, PjPµPSCëPëC...,
PSC—P¶B PµPeCÍPíPsP·PëC†C—C¼ Cr P»CĤPrPëPSPë PíCĤPë PĥP P”P> 6 PjPi PSP° PrPsP±Cr. Pj

PeCḡPsP»C-PI PeP°CḡPëPīCḡP°P·PëPS B C‡PëPSPëPI C,PsPeCḡPëC‡PSCḡ PrC-Ḥ PSP°
PjP°C,PμCḡPëPSCḡḤPePëPNḡ PsCḡPiP°PSC-P·Pj, P°P»Pμ PSPμ CḡC,P°PSPsPiPëPI
PSPμP±PμP·PīPμPePë PrP»Cḡ PīP»PsPrP° PīCḡPë PμPeCḡPīPsP·PëC‡C-CḡC..., Cr 5,8 CḡP°P·P°
PiPëC%PëC... P·P° PeP»C-PSC-C‡PSCḡ PμPeCḡPīPsP·PëC‡C-Ḥ PīCḡPë PḥP P°P».

PḡP»C-PSC-C‡PSPs P·PSP°C‡CḡC%C- PμPeCḡPīPsP·PëC‡C-C— PeP°CḡPëPīCḡP°P·PëPSCḡ,
CḡPePëPNḡ PiPiPsPrPëP»Pë PiP°PiC-C,PSPëPj CḡP°PjPeP°Pj C%CrCḡC-PI Cr PīPμCḡC-PsPr
PsCḡPiP°PSPsPiPμPSPμP·Cḡ, PīCḡPsC,CḡPiPsPj CrCḡC-C°C— PiP°PiC-C,PSPsCḡC,C- C,P°
PīPμCḡC-PsPrCḡ PiCḡCḡPrPSPsPiPs PiPëPiPsPrPsPICḡPiP°PSPSCḡ,B P·PSPëPḡCḡPiP°P»Pë
PīPsCḡC,PSP°C,P°P»ḤPSPμ PiPëPḡPëPiP°PSPSCḡ, PjP°CḡCḡ C,C-P»P° PīCḡPë
PSP°CḡPsPrPḡPμPSPSC- C,P° PjP°CḡCḡ C,C-P»P° PīC-CḡP»Cḡ PIC-PrP»CḡC‡PμPSPSCḡ PIC-Pr
PiCḡCḡPrPμPNḡ PīPsC,PsPjCḡC,PiP°B PīPμCḡCḡPsPiPs PīPsPePsP»C-PSPSCḡ. PḡCḡC-Pj C,PsPiPs,
P·P° PIC-PrCḡCḡC,PSPsCḡC,C- C,PsPeCḡPëC‡PSPsC— PrC-C— PSP°
PjP°C,PμCḡPëPSCḡḤPePëPNḡ PsCḡPiP°PSC-P·Pj CḡPīPsCḡC,PμCḡC-PiP°P»P°CḡCḡ
P±P»C-PrC-CḡC,Ḥ,B P·PSPëPḡPμPSPSCḡ C,PμPjPiPμCḡP°C,CḡCḡPë C,C-P»P° C,P°
P·P°C,CḡPëPjPeP° CḡPsP·PiPëC,PeCḡ Cr PīP»PsPrP° (PSPμPrPsCḡPsP·PiPëC,PsPe
PSPëCḡPePsPiPëC... CḡPsCḡPsC‡PeC-PI C,P° P·PSPëPḡPμPSPSCḡ CḡP»CḡC...PsPiPsPiPs
CḡPμC,,P»PμPeCḡCḡ Cr CḡP°PjC‡C-PI). PḡPμCḡC,PëP»ḤPSC-CḡC,Ḥ B PīPsC,PsPjCḡC,PiP°
B PīPμCḡCḡPsPiPs PīPsPePsP»C-PSPSCḡ B PSPμ P·P°P·PSP°P»P° P·PjC-PS, PsPrPSP°Pe Cr
C%CrCḡC-PI PrCḡCḡPiPsPiPs PīPsPePsP»C-PSPSCḡ PIC-PrP·PSP°C‡P°P»PëCḡCḡ
P°PSP°P»PsPiC-C‡PSC- PeP»C-PSC-C‡PSC- PsP·PSP°PePë C,P° P·PSPëPḡPμPSPSCḡ PjP°CḡPë
C,C-P»P°.

PḡP°CḡPëPīCḡP°P·PëPS C,P° PNḡPsPiPs PjPμC,P°P±PsP»C-C,Pë PīCḡPsPSPëPeP°P»Pë Pi
PjPsP»PsPePs C%CrCḡC-PI Cr PīPμCḡC-PsPr PiCḡCḡPrPSPsPiPs PiPëPiPsPrPsPICḡPiP°PSPSCḡ.

PḡP»C-PSC-C‡PSC- C...P°CḡP°PeC,PμCḡPëCḡC,PëPePë.

PμPsPeP°P·P°PSPSCḡ.

P°P»Cḡ P»C-PeCḡPiP°PSPSCḡ CḡPëP·PsC,,CḡPμPSC-C— Cr PrPsCḡPsCḡP»PëC...
PīP°C‡C-C°PSC,C-PI.

PμCḡPsC,PëPīPsPeP°P·P°PSPSCḡ.

PḡC-PrPiPëC%PμPSP° C‡CḡC,P»PëPIC-CḡC,Ḥ PrPs PrC-ḤC‡PsC— CḡPμC‡PsPiPëPSPë P°P±Ps
PrPs P±CḡPrḤC-CḡPePsC— P· PrPsPīPsPjC-PḡPSPëC... CḡPμC‡PsPiPëPS.

PŸCḡPīCḡC,PSC° P·P°CḡC,PsCḡCḡPiP°PSPSCḡ PīPsC,CḡPḡPSPsPiPs C-PSPiC-P±C-C,PsCḡP°
CYP3A4 (PrPëPI. CḡPsP·PrC-P» B«P°P·P°C°PjPsPrC-Cḡ P· C-PSCḡPëPjPë
P»C-PeP°CḡCḡḤPePëPjPë P·P°CḡPsP±P°PjPë C,P° C-PSCḡC- PiPëPrPë PiP·P°C°PjPsPrC-PNḡB»).

PŸCḡPīCḡC,PSC° P·P°CḡC,PsCḡCḡPiP°PSPSCḡ PīPsC,CḡPḡPSPsPiPs P°P±Ps PīPsPjC-CḡPSPsPiPs
C-PSPrCḡPeC,PsCḡP° CYP3A4 (PrPëPI. CḡPsP·PrC-P» B«P°P·P°C°PjPsPrC-Cḡ P· C-PSCḡPëPjPë
P»C-PeP°CḡCḡḤPePëPjPë P·P°CḡPsP±P°PjPë C,P° C-PSCḡC- PiPëPrPë PiP·P°C°PjPsPrC-PNḡB»).

P°P·P°C°PjPsPrC-Cḡ P· C-PSCḡPëPjPë P»C-PeP°CḡCḡḤPePëPjPë P·P°CḡPsP±P°PjPë C,P°

C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PN.

PµPsC,PµPSC†C-PNëPSPëPNë PIPiP»PëPI C-PSC€PëC... PïCḡPµPïP°CḡP°C,C-PI PSP°
PeP°CḡPëPïCḡP°P·PëPS

PḡPµC,P°P±PsP»C-P·Pj PeP°CḡPëPïCḡP°P·PëPSCr C,P° PNëPsPiPs PsC†PSPsPIPSPëC...
P°PeC,PëPIPSPëC... PjPµC,P°P±PsP»C-C,C-PI, PrPµP·PjPµC,PëP»C†-PeP°CḡPëPïCḡP°P·PëPSCr
(DCAR) C,P° PrPëPrPµP·PjPµC,PëP»C†-PeP°CḡPëPïCḡP°P·PëPSCr (DDCAR), PïPµCḡPµPIP°P¶PSPs
PsPiPsC†PµCḡPµPrPePsPICrC" C,CHC†C† CYP3A4 P· PjC-PSC-PjP°P»CHPSPëPj PIPiP»PëPIPsPj
CYP2D6.

P†PSPiC-P±C-C,PsCḡPë CYP3A4

PḡPµC,PsPePsPSP°P·PsP», C†PëP»CHPSPëPNë C-PSPiC-P±C-C,PsCḡ CYP3A4,
C†PïCḡPëC†PëPSCḡC" PïC-PrPIPëC%oPµPSPSC† PIPjC-C†C,C† P·P°PiP°P»CHPSPsPiPs
PeP°CḡPëPïCḡP°P·PëPSCr (PeP°CḡPëPïCḡP°P·PëPSCr C,P° PNëPsPiPs P°PeC,PëPIPSPëC...
PjPµC,P°P±PsP»C-C,C-PI) PI PïP»P°P·PjC- PI 2 CḡP°P·Pë PïCḡPsC,C†PiPsPj
PSPµC,CḡPëPIP°P»PsPiPs (4 PrPSC-) C†C†PïC†C,PSCHPsPiPs P·P°C†C,PsC†C†PIP°PSPSC†,
C†PeC%oPs PICḡP°C...PsPICrCḡC,CHC†C† PSPµP·PïBḡ™ C†P·P°PSC- P°P±Ps
PSPµP·PïBḡ™ C†P·P°PSC- P·PïBḡ™ C†P·P°PSC- PePsPjPiPsPSPµPSC,Pë.

PḡPµCḡPµP· PrPsPIPiPëPNë PïPµCḡC-PsPr PSP°PïC-PIPIPëPIPµPrPµPSPSC† P°PeC,PëPIPSPëC...
PePsPjPiPsPSPµPSC,C-PI PeP°CḡPëPïCḡP°P·PëPSCr PïPsPrP°P»CHC€Pµ
PïC-PrPIPëC%oPµPSPSC† PIPjC-C†C,C† P·P°PiP°P»CHPSPsPiPs PeP°CḡPëPïCḡP°P·PëPSCr PI
PïP»P°P·PjC- PjPsP¶Pµ PsC†C-PeC†PIP°C,PëC†C† PïC-Pr C†P°C† P±C-P»CHC€
C,CḡPëPIP°P»PsPiPs PePsPjP±C-PSPsPIP°PSPsPiPs PïCḡPëPNëPsPjC†. PḡPsPjC†
PePsPjP±C-PSPsPIP°PSPëPNë PïCḡPëPNëPsPj PeP°CḡPëPïCḡP°P·PëPSCr P· PïPsC,C†P¶PSPëPjPë
C-PSPiC-P±C-C,PsCḡP°PjPë CYP3A4 (PSP°PïCḡPëPeP»P°Pr, P±PsC†PµPïCḡPµPIC-Cḡ,
PeP»P°CḡPëC,CḡPsPjC-C†PëPS, PePsP±C-C†PëC†C,P°C,, C-PSPrPëPSP°PIC-Cḡ,
C-C,CḡP°PePsPSP°P·PsP», PePµC,PsPePsPSP°P·PsP», PSPµC,,P°P·PsPrPsPS,
PSPµP»C,,C-PSP°PIC-Cḡ, PïPsP·P°PePsPSP°P·PsP», CḡPëC,PsPSP°PIC-Cḡ,
C†P°PePIC-PSP°PIC-Cḡ, C,PµP»P°PïCḡPµPIC-Cḡ, C,PµP»C-C,CḡPsPjC-C†PëPS,
PIPSCḡPëPePsPSP°P·PsP») PïCḡPsC,PëPïPsPeP°P·P°PSPëPNë (PrPëPI. CḡPsP·PrC-P»
B«PµCḡPsC,PëPïPsPeP°P·P°PSPSC†B»).

P·CḡPëC,CḡPsPjC-C†PëPS (500 PjPi PrPIC-C†C- PSP° PrPsP±C†), PïPsPjC-CḡPSPëPNë
C-PSPiC-P±C-C,PsCḡ CYP3A4, PIPëPeP»PëPeP°PI C† C†PµCḡPµPrPSCḡPsPjC† 1,4-
PeCḡP°C,PSPµ (PrC-P°PiP°P·PsPS 1,03Bḡ"2,32 CḡP°P·P°) P·P±C-P»CHC€PµPSPSC†
PµPeC†PïPsP·PëC†C-C— P·P°PiP°P»CHPSPsPiPs PeP°CḡPëPïCḡP°P·PëPSCr PI PïP»P°P·PjC-
PeCḡPsPIC- PïC-C†P»C† 3 C,PëP¶PSC-PI PsPrPSPsC†P°C†PSPsPiPs P·P°C†C,PsC†C†PIP°PSPSC†.
PḡP°PePëPj C†PëPSPsPj, PïCḡPsC,C†PiPsPj PïPµCḡC-PsPrC† PsPrPSPsC†P°C†PSPsPiPs
P·P°C†C,PsC†C†PIP°PSPSC† PeP°CḡPëPïCḡP°P·PëPSCr P· PïPsPjC-CḡPSPëPj
C-PSPiC-P±C-C,PsCḡPsPj CYP3A4 (PSP°PïCḡPëPeP»P°Pr, PµCḡPëC,CḡPsPjC-C†PëPSPsPj,
C,,P»C†PePsPSP°P·PsP»PsPj, PrPëP»C,C-P°P·PµPjPsPj, PIPµCḡP°PïP°PjC-P»PsPj)
CḡPµPePsPjPµPSPrC†C" C,CHC†C† PePsPSC,CḡPsP»CHPIP°C,Pë C-PSPrPëPIC-PrC†P°P»CHPSCr
CḡPµP°PeC†C-Cḡ C,P° PïPµCḡPµPSPsC†PëPjC-C†C,CH C-, C†PeC%oPs PSPµPsP±C...C-PrPSPs,
PrPsP·C† PeP°CḡPëPïCḡP°P·PëPSCr C†P»C-Pr (C,PëPjC†P°C†PsPIPs) P·PjPµPSC€PëC,Pë,
PICḡP°C...PsPICrCḡC†Pë PïPsC,PµPSC†C-PNëPSPsPiPµ P·P±C-P»CHC€PµPSPSC†
PµPeC†PïPsP·PëC†C-C—. P°PSP°C†P»C-PrPsPe C,CḡPëPIP°P»PsPiPs PïPµCḡC-PsPrC†
PSP°PïC-PIPIPëPIPµPrPµPSPSC† PeP°CḡPëPïCḡP°P·PëPSCr C,P° PNëPsPiPs P°PeC,PëPIPSPëC...
PjPµC,P°P±PsP»C-C,C-PI PïPsC†P°C,PsPe, PïCḡPëPïPëPSPµPSPSC† P»C-PeC†PIP°PSPSC†
PïPsPjC-CḡPSPëPj C-PSPiC-P±C-C,PsCḡPsPj CYP3A4 P°P±Ps P·PjC-PSP° PrPsP·Pë

PiPsPIPSC-ClC,Ch PSPu PIC-PrPsP±CtjP°P·PëC,ChClCtCt PSP° CtjC-PIPsCtC...
 PiCtjPµPiP°CtjP°C,Cr PI PiP»P°P·PjC- PeCtjPsPIC- PiCtjPsC,CtjPiPsPj PiPµCtjCëPëC...
 PrPµPeC-P»CHPePsC... C,PëP¶PSC-PI. PµCtjPsC,CtjPiPsPj PrPµPeC-P»CHPePsC... C,PëP¶PSC-PI
 PiC-ClP»CtCt PiPsCtP°C,PeCr P°P±Ps PiCtjPëPiPëPSPµPSPSCtCt ClCtPjC-ClPSPsPiPs
 PiCtjPëPNëPsPjCr PiCtjPµPiP°CtjP°C,C-PI P°P±Ps PiC-ClP»CtCt PePsP¶PSPsC— P·PjC-PSPë
 PrPsP·Pë PeP°CtjPëPiCtjP°P·PëPSCr ClP»C-Pr PePsPSC,CtjPsP»CHPiP°C,Pë PiP°CtC-C”PSC,C-PI
 PSP° PSP°CtjPiPSC-ClC,Ch PiPsP±C-CtPSPëC... CtjPµP°PeCtC-PNë C,P° PIC-PrPiPsPIC-PrC-
 PSP° P»C-PeCrPiP°PSPSCtCt.

PŸP»C-Pr CrPSPëPeP°C,Pë PiP¶PëPiP°PSPSCtCt PiCtjPµPNëPiC,,CtjCrC,PsPiPsPiPs ClPsPeCr.

P†PSPrCzPeC,PsCtjPë CYP3A4

PµPsPjP±C-PSPsPiP°PSPëPNë PiCtjPëPNëPsPj PeP°CtjPëPiCtjP°P·PëPSCr P· PiPsC,CrP¶PSPëPjPë
 P°P±Ps PiPsPjC-CtjPSPëPjPë C-PSPrCrPeC,PsCtjP°PjPë CYP3A4 PjPsP¶Pµ
 ClPiCtjPëCtPëPSCtCt,Pë P·PSP°CtPSPµ PiC-PrPiPëC%oPµPSPSCtCt PiP¶P»PëPICr
 P·P°PiP°P»CHPSPsPiPs PeP°CtjPëPiCtjP°P·PëPSCr, C,PsPjCr PePsPjP±C-PSPsPiP°PSPëPNë
 PiCtjPëPNëPsPj PeP°CtjPëPiCtjP°P·PëPSCr C,P° PiPsC,CrP¶PSPëC... P°P±Ps PiPsPjC-CtjPSPëC...
 C-PSPrCrPeC,PsCtjC-PI CYP3A4 (PSP°PiCtjPëPeP»P°Pr, PeP°CtjP±P°PjP°P·PµPiC-PS,
 C,,PµPSPsP±P°CtjP±C-C,P°P», C,,PµPSC-C,PsC—PS, CtjPëC,,P°PjPiC-CtPëPS, P·PIC-CtjPsP±C-PNë
 P·PiPëCtP°PNëPSPëPNë (*Hypericum perforatum*), P±PsP·PµPSC,P°PS, PµC,,P°PIC-CtjPµPSCt,
 PµC,CtjP°PIC-CtjPëPS, PjPsPrP°C,,C-PSC-P», PSP°C,,CtPëP»C-PS)
 PiCtjPsC,PëPiPsPeP°P·P°PSPëPNë (PrPëPI. CtjPsP·PrC-P» B«PµCtjPsC,PëPiPsPeP°P·P°PSPSCtB»).

P†PSPiC-P±C-C,PsCtjPë CYP2D6

PµPiPsClPµCtjPµPrPePsPiP°PSC- CYP2D6 CëP»CtCt...Pë PIC-PrC-PiCtjP°CtC,Ch
 PSPµP·PSP°CtPSCr CtjPsP»CH Cr PjPµC,P°P±PsP»C-P·PjC- PeP°CtjPëPiCtjP°P·PëPSCr,
 PiPsP»PsPiPSPëPNë CëP»CtCt... Btj” CtPµCtjPµP· CYP3A4 (PrPëPI. CtjPsP·PrC-P»
 B«PαP°CtjPjP°PePsPeC-PSPrC,PëPeP°B»). PŸPsPjCr PjP°P»PsPNëPjPsPIC-CtjPSPs, C%oPs
 C-PSPiC-P±C-C,PsCtjPë CYP2D6 PjP°C,PëPjCrC,Ch PeP»C-PSC-CtPSPs P·PSP°CtCrC%oPëPNë
 PiP¶P»PëPI PSP° PjPµC,P°P±PsP»C-P·Pj PeP°CtjPëPiCtjP°P·PëPSCr.

PµPsC,PµPSCtC-PNëPSPëPNë PiP¶P»PëPI PeP°CtjPëPiCtjP°P·PëPSCr PSP° C-PSCëC-
PiCtjPµPiP°CtjP°C,Pë

PŸCzP±ClC,CtjP°C,Pë P-PiP»C-PePsPiCtjPsC,PµC—PSCz (P-gp)

PµP°CtjPëPiCtjP°P·PëPS Btj” CtPµ C-PSPiC-P±C-C,PsCtj P-gp *in vitro* PI PNëPsPiPs
 C,PµPsCtjPµC,PëCtPSPs PSP°PNëP±C-P»CHCëC-PNë PePëCëPePsPIC-PNë
 PePsPSCtPµPSC,CtjP°CtC-C—. PµP»C-PSC-CtPSC- PSP°ClP»C-PrPePë CtCHPsPiPs
 PµC,,PµPeC,Cr C%oPµ PSPµ PiPsPiPSC-ClC,Ch P·CtjPsP·CrPjC-P»C-, PiCtjPsC,Pµ PrP»CtCt
 PiPëPePsCtjPëClC,P°PSPSCtCt C,P°PePëC... ClCtP±ClC,CtjP°C,C-PI P-gp C-P· PICrP·CHPePëPjPë
 C,PµCtjP°PiPµPIC,PëCtPSPëPj C-PSPrPµPeClPsPj, CtjPe PrP°P±C-PiP°C,CtjP°PS C,P°
 PrPëPiPsPeClPëPS, PjPsP¶Pµ B P±CrC,Pë PiPsC,CtjC-P±PSPëPNë PiPsClPëP»PµPSPëPNë
 PjPsPSC-C,PsCtjPëPSPi C,P° PePsCtjPëPiCrPiP°PSPSCtCt PrPsP·Pë.

P”PsCtjPjPsPSP°P»CHPSC- PePsPSC,CtjP°CtPµPiC,PëPiPë

Pj PrPsClP»C-PrP¶PµPSPSC- PiP·P°C”PjPsPrC-C— P»C-PeP°CtjClCHPePëC... P·P°ClPsP±C-PI
 28-PrPµPSPSPµ P»C-PeCrPiP°PSPSCtCt PeP°CtjPëPiCtjP°P·PëPSPsPj Cr PrPsP·C- 6 PjPi PSP°
 PrPsP±Cr PSPµ PjP°P»Ps PeP»C-PSC-CtPSPs P·PSP°CtCrC%oPsPiPs PiP¶P»PëPICr PSP°
 C,,P°CtjPjP°PePsPeC-PSPrC,PëPeCr PiPµCtjPsCtjP°P»CHPSPëC... PePsPSC,CtjP°CtPµPiC,PëPIC-PI

(P_μC,PēPSC-P»P_μC[†]C,C_ḡP°PrC-PsP»C[†] C,P° P»P_μPIP_sPSP_sC_ḡPiP_μC[†]C,C_ḡP_μP»C[†]).

P_αP°C_ḡPjP°PePsPrPēPSP°PjC-C_‡PSC- PIP·P°C°PjPsPrC-C—

B P— PsPiP»C_‡PrC[†] PSP° PīP_μC_ḡPIPēPSPSPēPN_ε PIPiP»PēPI B PSP° C[†]P_μPSC,C_ḡP°P»C_ḡPSC[†]
PSP_μC_ḡPIPsPIC[†] C[†]PēC[†]C,P_μPjC[†] PiC_ḡP_μPiP°C_ḡP°C, P P_μP°PiC-P»P° PSP_μPsP±C...C-PrPSP_s
PsP±P_μC_ḡP_μP_ḡPSP_s P·P°C[†]C,PsC[†]PsPIC[†]PIP°C,Pē PI PePsPjP±C-PSP°C[†]C-C— P·C-PSCēPēPjPē
P»C-PeP°C_ḡC_ḡCHPePēPjPē P·P°C[†]PsP±P°PjPē C[†]P_μPSC,C_ḡP°P»C_ḡPSP_sC— PrC-C— C,P°
P°P»PePsPiPsP»P_μPj.

P_hC[†]PsP±P»PēPIP_sC[†]C,C- P·P°C[†]C,PsC[†]C_‡PIP°PSPSC_‡.

P_ŸC[†]C—C[†]PēPrP°P»C_ḡPSC- PrC[†]PjPePē C,P° PīPsPIP_μPrC-PSPeP°

P_ḡPsP_ḡP»PēPIC-C[†]C,CH B C[†]C[†]C—C[†]PēPrP°P»C_ḡPSP_sC[†]C,C- (C[†]C[†]C—C[†]PēPrP°P»C_ḡPSC-
PrC[†]PjPePē, C[†]PiC_ḡPsP±Pē C[†]PePsC°PSPSC_‡ C[†]P°PjPsPiC[†]P±C[†]C,PIP° C,P° C[†]PePsC°PSP_μ
C[†]P°PjPsPiC[†]P±C[†]C,PIPs) C° C...P°C_ḡP°PeC,P_μC_ḡPSPēPj C_‡PIPēC°P_μPj PrP»C_‡
PiC[†]PēC...C-C_‡PSPēC... P·P°C...PIP_sC_ḡCHPIP°PSC_ḡ C-B P·P°PiP°P»PsPj
C[†]PiPsC[†]C,P_μC_ḡC-PiP°C°C,CHC[†]C_‡ PsPrC_ḡP°P·C[†] PiC-C[†]P»C_‡ PīPsC[†]P°C,PeC[†] C_‡Pē
P·PjC-PSPē P°PSC,PēPiC[†]PēC...PsC,PēC_‡PSP_sC— C,P_μC_ḡP°PiC-C—. P_ŸP_μC_ḡP°PiC-C_‡
P°PSC,PēPiC[†]PēC...PsC,PēPeP°PjPē PjP°C° C[†]C[†]PiC_ḡPsPIPsPrP_ḡC[†]PIP°C,PēC[†]C_‡
PīPēP»C_ḡPSPēPj PSP°PiP»C_‡PrPsPj P·P° PīP°C[†]C-C°PSC,P°PjPē PiC_ḡC[†]PiPē PIPēC[†]PsPePsPiPs
C_ḡPēP·PēPeC[†].

P_ḡPeP°C,PēP·C-C_‡, P·P±C[†]PrP_ḡP_μPSPSC_‡

P_ḡPeP°C,PēP·C-C_‡ C,P° P·P±C[†]PrP_ḡP_μPSPSC_‡ B_ḡ C[†]P_μ PīPsP±C-C_‡PSC- P_μC,,P_μPeC,Pē
P°PSC,PēPiC[†]PēC...PsC,PēPeC-PI, C°P_s PIPēPSPēPeP°C_ḡC,CH PrPsC[†]C,P°C,PSCH_sPs
C_‡P°C[†]C,Ps. P_ḡPeP°C,PēP·C-C_‡ B_ḡ C[†]P_μ C_ḡPsP·P»P°Pr C_ḡC[†]C...C[†], C°P_s
C...P°C_ḡP°PeC,P_μC_ḡPēP·C[†]C°C,CHC[†]C_‡ PīPsC_‡C[†]C,C,C_‡Pj PIPSC[†]C,C_ḡC-ēPSC_ḡPsC—
P·P±C[†]PrP_ḡP_μPSP_sC[†]C,C- C,P° PSP_μPiP_μC_ḡP_μP±PsC_ḡPSP_sC_ḡ PīPsC,C_ḡP_μP±PsC_ḡ
PīPsC[†]C,C-PN_εPSP_s PīP_μC_ḡP_μP±C[†]PIP°C,Pē PI C_ḡC[†]C[†]C-, P° C,P°PePsP_ḡ C,P°PePēPjPē
PrC-C_‡PjPē, C_‡Pe PīPsC...PēC,C[†]PIP°PSPSC_‡ PiC-Pr C_‡P°C[†] C[†]C,PsC_‡IPSPSC_‡ C_‡Pē
C[†]PēPrC-PSPSC_‡, PiC-PrC-PN_εPjP°PSPSC_‡ PSP_sPiPē C_‡Pe PiC_ḡPē PjP°C_ḡCēPēC_ḡC[†]PIP°PSPSC-
PSP° PjC-C[†]C[†]C-, PīP_μC_ḡP_μC...C_ḡP_μC°C[†]PIP°PSPSC_‡ C,P° C_ḡPsP·PiC_ḡC_‡PjP»C_‡IPSPSC_‡
PSC-Pi PiC-Pr C_‡P°C[†] C[†]PēPrC-PSPSC_‡. P_hC[†]PeC-P»C_ḡPePē PeP°C_ḡPēPiC_ḡP°P·PēPS
C[†]PiC_ḡPēC_‡PēPSC_ḡC° P°PeP°C,PēP·C-C_ḡ C,P° P·P±C[†]PrP_ḡP_μPSPSC_‡, PīP°C[†]C-C°PSC,P°Pj,
C_‡PeC- C[†]C...PēP»C_ḡPSC- C_‡Pē PIP_ḡP_μ PiC_ḡPsC_‡PIP»C_‡C_ḡC,CH C[†]PēPjPiC,PsPjPē
P°PeP°C,PēP·C-C—, PīPsC,C_ḡC-P±PSP_s P·P°C[†]C,PsC[†]PsPIC[†]PIP°C,Pē PN_εPsPiPs P·
PsP±P_μC_ḡP_μP_ḡPSC-C[†]C,C_ḡ. P_ḡPeP°C,PēP·C-C_‡ C_ḡPsP·PIPēPIP°C°C,CHC[†]C_‡ PSP°
C_ḡP°PSPSC-C... P_μC,P°PīP°C... P»C-PeC[†]PIP°PSPSC_‡. P_ŸPsPjC[†] PIP°P_ḡP»PēPIPs
PiC_ḡPsPIPsPrPēC,Pē C_ḡP_μC,P_μP»C_ḡPSPēPN_ε PjPsPSC-C,PsC_ḡPēPSPi PSP° PīP_μC_ḡCēPsPjC[†]
P_μC,P°PiC- P»C-PeC[†]PIP°PSPSC_‡. P_μC_ḡPsC,,C-P»P°PeC,PēPeP° PIPeP»C_ḡC_‡P°C°
PīPsPIC-P»C_ḡPSP_μ PiC-PrPIPēC°P_μPSPSC_‡ PrPsP·Pē; C,P_μC_ḡP°PīP_μPIC,PēC_‡PSC-
P·P°C...PsPrPē PIPeP»C_ḡC_‡P°C_ḡC,CH PSP_μP·PSP°C_‡PSP_μ P·PSPēP_ḡP_μPSPSC_‡ PrPsP·Pē
PeP°C_ḡPēPiC_ḡP°P·PēPSC[†] C_‡Pē P»C-PeP°C_ḡC_ḡCHPePēC... P·P°C[†]PsP±C-PI PrP»C_‡
P»C-PeC[†]PIP°PSPSC_‡ P_μPeC[†]C,C_ḡP°PiC-C_ḡP°PjC-PrPSPēC... C[†]PēPjPiC,PsPjC-PI. P°PsP·P°
PjPsP_ḡP_μ P·PjC-PSC_ḡPIP°C,PēC[†]C_‡ P·P°P»P_μP_ḡPSP_s PIC-Pr C-PSP_ḡPēPIC-PrC[†]P°P»C_ḡPSP_sC—
PIC-PrPīPsPIC-PrC- C,P° PīP_μC_ḡP_μPSP_sC[†]PēPjPsC[†]C,C- (PrPēPI. C_ḡPsP·PrC-P»
B«P_μPsP±C-C_‡PSC- C_ḡP_μP°PeC[†]C-C—B»).

РѹС-Р·PSCЇ РrРёСГРёС-PSРµР·С-СЇ

РѹС-Р·PSCЇ РrРёСГРёС-PSРµР·С-СЇ вѢ” С†Рµ СГРёPSРrСѢPsPj, С%Ps
РiСѢPsСЇPIР»СЇС”С,СѢСГРёСЇ СѢРёС,РjС-С†PSРёРjРё РjРёРjPsPIC-Р»СѢPSРёРjРё
СѢСрС...Р°РjРё РiРµСѢРµPIР°Р¶PSРs СЇР·РёРёР° С,Р°/Р°Р±Ps PsР±Р»РёС†С†СЇ С- РjPsР¶Рµ
СѢPsР·PIРёPIР°С,РёСГРёСЇ Ср РiР°С†С-С”PSC,С-PI, СЇРёС- Р»С-РёСрСѢС,СѢСГРёСЇ
Р°PSC,РёРiСГРёС...PsС,РёРёР°РjРё. РiРёС%Ps СГРёРjРiС,PsРjРё РiС-Р·PSCѢPsС—
РrРёСГРёС-PSРµР·С-С— Р·вѢ”™ СЇPIР»СЇСѢС,СѢСГРёСЇ Ср РiР°С†С-С”PSC,Р°, СЇРёРёРµ
Р»С-РёСрС”С,СѢСГРёСЇ РёР°СѢРёРiСѢР°Р·РёPSРsPj, РiPsС,СѢС-Р±PSРs СѢPsР·РiР»СЇPSCрС,Рё
PSРµPsР±С...С-РrPSC-СГРёС,СѢ РiСѢРёРiРёPSРµPSPSCЇ В Р·Р°СГРёС,PsСГРёСРiР°PSPSCЇ
С†СѢPsРiPs РiСѢРµРiР°СѢР°С,Ср.

РГРiPsСѢPsР±Р° РµР°СѢРёС-PSСГРёPsPSP°

РiРёС%Ps Р°PSC,РёРiСГРёС...PsС,РёС†PSC- Р·Р°СГРёPsР±Рё РiСѢРёР·PSP°С†Р°СѢС,СѢСГРёСЇ
РiР°С†С-С”PSC,Р°Рj С-Р· С...PIPsСѢPsР±PsСѢ РµР°СѢРёС-PSСГРёPsPSP°, С,Ps РjPsР¶РµР»РёРiРµ
Р·Р°РiPsСГРёС,СѢРµPSPSCЇ С,,PsPSPsPIPsРiPs Р·Р°С...PIPsСѢСѢPIР°PSPSCЇ С,Р°
РiPsРiС-СѢСёРµPSPSCЇ РiРµСѢРµР±С-РiСр С...PIPsСѢPsР±Рё РµР°СѢРёС-PSСГРёPsPSP°.
РъPsРjСр, РiСѢРёР·PSP°С†Р°СѢРё РёР°СѢРёРiСѢР°Р·РёPS РiР°С†С-С”PSC,Р°Рj С-Р·
С...PIPsСѢPsР±PsСѢ РµР°СѢРёС-PSСГРёPsPSP°, Р»С-РёР°СѢС- РjР°СѢС,СѢ Р·PIР°Р¶СрРiР°С,Рё
СГРёРiС-PIPIC-РrPSPsСёРµPSPSCЇ РёPsСѢРёСГРёС,СѢ/СѢРёР·РёРё.

РъРёРjРiС,PsРjРё Р· Р±PsРёСр PsС†РµРµ/ РёР°С,Р°СѢР°РёС,Р°

Рj РrPsРёР»С-PSC-С†PSРёС... РrPsСГР»С-РrР¶РµPSPSCЇС... РёР°СѢРёРiСѢР°Р·РёPSCр PI
СГРёPsР±Р°Рё Р±СрР»Ps РiPsРjС-С†РµPSPs РiPsРjСрС,PSC-PSPSCЇ РёСѢРёСёС,Р°Р»РёРёР°/
РёР°С,Р°СѢР°РёС,Р° (РrРёPI. СѢPsР·РrС-Р»Рё В«РµPsР±С-С†PSC- СѢРµР°С†С-С—В» С,Р°
В«Р”Р°PSC- РrPsРёР»С-PSC-С†PSРёС... РrPsСГР»С-РrР¶РµPSCѢ Р· Р±РµР·РiРµРёВ»).

РµСѢРёС†РёPSРsPSP°СГР»С-РrРёPsPIРёРµ Р·РiвѢ”™ СЇР·Р·Рё РjС-Р¶ Р·РjС-PSP°РjРё PI
РёСѢРёСёС,Р°Р»РёРёРёРё/ РёР°С,Р°СѢР°РёС,PsСѢ, С%Ps СГРiРiPsСГРёС,РµСѢС-РiР°Р»РёРёСГРёСЇ
РiС-Рr С†Р°СГР РrPsСГР»С-РrР¶РµPSCѢ Ср Р»СѢРrРµРµ, С- Р·Р°СГРёС,PsСГРёСРiР°PSPSCЇРj
РёР°СѢРёРiСѢР°Р·РёPSCр PSРµ Р±СрPI СрСГРёС,Р°PSPsPIР»РµPSPёРµ. РµСѢPsС,Рµ
РiР°С†С-С”PSC,Р°Рj, Ср СЇРёРёС... РjPsР¶СрС,СѢ СѢPsР·PIРёPSCрС,РёСГРёСЇ СГРёРjРiС,PsРjРё,
С%Ps РiPsС,РµPSC†С-РµPSPs РjР°СѢС,СѢ PIC-РrPSPsСёРµPSPSCЇ РrPs РёР°С,Р°СѢР°РёС,Рё,
РiPsС,СѢС-Р±PSРs РiPsСѢР°РrРёС,Рё РiСѢPsРµС,Рё PsС,,С,Р°Р»РёРjPsР»PsРiС-С†PSРµ
PsР±СГРёС,РµР¶РµPSPSCЇ, Р° РiPsС,С-Рj СГР»С-Рr РiPsPIC,PsСѢPSPs В СѢPsР·РiР»СЇPSCрС,Рё
РiРёС,Р°PSPSCЇ РiСѢPs РiСѢPsРrPsPIР¶РµPSPSCЇ Р»С-РёСрРiР°PSPSCЇ.

Р—Р»PsСЇРёС-СГРPSРёРµ PSPµРµСѢPsР»РµРiС,РёС†PSРёРµ СГРёPSРrСѢPsPj
РµPsС,РµPSC†С-РµPSPs Р»РµС,Р°Р»РёР»РёPSРёРµPsРjРiР»РµРёСГР СГРёРjРiС,PsРjС-PI, С%Ps
РjР°С” PSP°Р·PICр Р·Р»PsСЇРёС-СГРPSРёРµ PSPµРµСѢPsР»РµРiС,РёС†PSРёРµ СГРёPSРrСѢPsPj
(Р—РќРъ), PIC-РrР·PSP°С†Р°С”С,СѢСГРёСЇ РiСѢРё Р»С-РёСрРiР°PSPSC-
Р°PSC,РёРiСГРёС...PsС,РёРёР°РjРё. РъР»С-PSC-С†PSРёРjРё РiСѢPsСЇPIР°РjРё Р—РќРъ С”
РiС-РiРµСѢРiС-СѢРµРёСГРёС-СЇ, РjвѢ”™ СЇР·Р·РёР° СѢРёРiС-РrPSC-СГРёС,СѢ,
РiС-РrPIРёС%РµPSPёРµ СѢС-PIРµPSCѢ РёСѢРµР°С,РёPSC-PSC,,PsСГРёС,,PsРёС-PSP°Р·Рё PI
СГРёСѢPsPIР°С,С†С-, Р·РjС-PSPµPSPёРµ РiСГРёС...С-С†PSРёРµ СГРёС,Р°PS С,Р° PsР·PSP°РёРё
СѢPsР·Р»Р°РrС РiРµРiРµС,Р°С,РёPIPsРs— PSРµСѢPIPsРs— СГРёСГРёС,РµРjРё
(PSРµСѢРµРiСр»СЇСѢPSPёРµ РiСрР»СѢСГР Р°Р±Ps Р°СѢС,РµСѢС-Р°Р»РёР»РёPSРёРµ С,РёСГРёС,
С,Р°С...С-РёР°СѢРrС-СЇ, РrС-Р°С,,PsСѢРµР· С,Р° СГРµСѢС†РµPIР° Р°СѢРёС,РjС-СЇ).

Р”PsРrР°С,РёPsPIC- PsР·PSP°РёРё РjPsР¶СрС,СѢ PIРёР»СѢС†Р°С,Рё
РjС-PsРiР»PsР±С-PSCрСѢС-СѢ (СѢР°Р±РrPsРjС-PsР»С-С-) С,Р° РiPsСГРёС,СѢСр PSPёСѢРёPsPICр
PSРµРrPsСГРёС,Р°С,PSC-СГРёС,СѢ. РiРёС%Ps Ср РiР°С†С-С”PSC,Р° СѢPsР·PIРёPIР°СѢС,СѢСГРёСЇ

PJ PīP°C†C-C" PSC,C-PI, C†PēC- PīC†PēPN₂PjP°C†C,C† P°PSC,PēPīC†PēC...PsC,PēPePē, PjPsP†Pμ C†PēPs·PIPēPIP°C,PēC†C† PīPsPrPsPIP†PμPSPSC† C-PSC,PμC†PIP°P»C† OPŷ.

PJ PeP»C-PSC-C#PSPsPjCf PrPsCfP»C-PrP¶PµPSPSC-, C¶PePµ PïC¶PsPIPsPrPëP»Pë PrP»C¶
PsC†C-PSPePë PïPsPrPsPIP¶PµPSPSC¶ C-PSC,PµC¶PIP°P»Cf QT, PïC¶Pë PïC¶PëPNëPsPjC-
PeP°C¶PëPïC¶P°P·PëPSCf PSPµ P±CfP»Ps PïPsPjC-C#PµPSPs P¶PsPrPSPsPiPs
PïPsPrPsPIP¶PµPSPSC¶ C-PSC,PµC¶PIP°P»Cf QT Cf PïPsC¶C-PIPS¶PSPSC- P· PïP»P°C†PµP±Ps
(PrPëPI. C¶PsP·PrC-P» B«PαP°C¶PjP°PePsPrPëPSP°PjC-PeP°B»). PJ PeP»C-PSC-C#PSPëC...
PrPsCfP»C-PrP¶PµPSPSC¶C... PïPsPIC-PrPsPjP»C¶P»PsCfCH P»PëCëPµ PïC¶Ps
PrPµPeC-P»CHPeP° PIPëPïP°PrPeC-PI PSPµP·PSP°C#PSPsPiPs PïPsPrPsPIP¶PµPSPSC¶
C-PSC,PµC¶PIP°P»Cf QT PïC¶Pë PïC¶PëPNëPsPjC- PeP°C¶PëPïC¶P°P·PëPSCf (PrPëPI.
C¶PsP·PrC-P» B«PµPsP±C-C#PSC- C¶PµP°PeC†C-C—B»). PÿPsPjCf PeP°C¶PëPïC¶P°P·PëPs
C,C¶PµP±P° PsP±PµC¶PµP¶PSPs P·P°CfC,PsCfPsPICfPIP°C,Pë PïP°C†C-C”PSC,P°Pj, Cf
C¶PePëC... PI P°PSP°PjPSPµP·C- C” CfPµC¶C†PµPIPs-CfCfPrPëPSPSPµ
P·P°C...PIPsC¶C¶PIP°PSPSC¶ P°P±Ps PïPsPrPsPIP¶PµPSPSC¶ C-PSC,PµC¶PIP°P»Cf QT PI
CfC-PjPµPNëPSPsPjCf P°PSP°PjPSPµP·C-, P° C,P°PePsP¶ PïP°C†C-C”PSC,P°Pj, C¶PeC-
P»C-PeCfPIP°P»PëCfC¶ PïC¶PµPïP°C¶P°C,P°PjPë, C%oPs PjPsP¶CfC,CH PïPsPrPsPIP¶PëC,Pë
C-PSC,PµC¶PIP°P» QT (PrPëPI. C¶PsP·PrC-P» B«PαP°C¶PjP°PePsPrPëPSP°PjC-PeP°B»).

P'PµPSPsP·PSP° C,C¶PsPjP±PsPµPjP±PsP»C-C¶ (P'PÿP·)

PµPsPIC-PrPsPjP»C¶P»PsCfCH PïC¶Ps PIPëPïP°PrPePë PIPëPSPëPePSPµPSPSC¶ P'PÿP· PïC¶Pë
P·P°CfC,PsCfCfPIP°PSPSC- P°PSC,PëPïCfPëC...PsC,PëC#PSPëC... P·P°CfPsP±C-PI.
PhCfPeC-P»CHPePë Cf PïP°C†C-C”PSC,C-PI, C¶PeC- PïC¶PëPNëPjP°CHC,CH
P°PSC,PëPïCfPëC...PsC,PëPePë, C#P°CfC,Ps PIPëPSPëPeP°CHC,CH PSP°P±CfC,C-
C#PëPSPSPëPePë C¶PëP·PëPeCf C¶PsP·PIPëC,PeCf P'PÿP·, PICfC- PjPsP¶P»PëPIC-
C#PëPSPSPëPePë PIPëPSPëPePSPµPSPSC¶ P'PÿP· CfP»C-Pr PIPëC¶PIPëC,Pë PïPµC¶PµPr C,P°
PïC-Pr C#P°Cf P»C-PeCfPIP°PSPSC¶ PeP°C¶PëPïC¶P°P·PëPSPsPj, P° C,P°PePsP¶ C,C¶PµP±P°
PïC¶PsPIPsPrPëC,Pë C—C...PSC¶ PïC¶PsC,,C-P»P°PeC,PëPeCf.

P“C-PïPµC¶PiP»C-PePµPjC-C¶ C,P° C†CfPeC¶PsPIPëPNë PrC-P°P±PµC.

PJ PïP°C†C-C”PSC,C-PI C-P· C†CfPeC¶PsPIPëPj PrC-P°P±PµC,PsPj P°P±Ps Cf
PïP°C†C-C”PSC,C-PI C-P· C#PëPSPSPëPeP°PjPë C¶PëP·PëPeCf C¶PsP·PIPëC,PeCf
C†CfPeC¶PsPIPsPiPs PrC-P°P±PµC,Cf (PSP°PïC¶PëPeP»P°Pr, PsP¶PëC¶C-PSPSC¶,
PSP°C¶PIPSC-CfC,CH PrC-P°P±PµC,Cf PI CfC-PjPµPNëPSPsPjCf P°PSP°PjPSPµP·C-), C¶PeC-
PïPsC#PëPSP°CHC,CH P»C-PeCfPIP°PSPSC¶ P°C,PëPïPsPIPëPjPë
P°PSC,PëPïCfPëC...PsC,PëPeP°PjPë, CfP»C-Pr PePsPSC,C¶PsP»C¶PIP°C,Pë C¶C-PIPS-
PiP»C¶PePsP·Pë PI CfPëC¶PsPIP°C,C†C-. PµC-Pr C#P°Cf PeP»C-PSC-C#PSPëC...
PrPsCfP»C-PrP¶PµPSC¶ PeP°C¶PëPïC¶P°P·PëPSCf PïPsPIC-PrPsPjP»C¶P»PsCfC¶ PïC¶Ps
PïPsP±C-C#PSC- C¶PµP°PeC†C-C— CfC,PsCfPsPIPS¶ C¶C-PIPS-PI PiP»C¶PePsP·Pë (PrPëPI.
C¶PsP·PrC-P» B«PαP°C¶PjP°PePsPrPëPSP°PjC-PeP°B»).

P—PjC-PSPë PjP°CfPë C,C-P»P°

PµC¶Pë PïC¶PëPNëPsPjC- PeP°C¶PëPïC¶P°P·PëPSCf CfPïPsCfC,PµC¶C-PiP°P»PsCfC¶
P·PSP°C#PSPµ P·P±C-P»CHCëPµPSPSC¶ PjP°CfPë C,C-P»P°. PµP°C†C-C”PSC,P°Pj CfP»C-Pr
C¶PµPiCfP»C¶C¶PSPs PePsPSC,C¶PsP»C¶PIP°C,Pë PjP°CfCf C,C-P»P° (PrPëPI. C¶PsP·PrC-P»
B«PµPsP±C-C#PSC- C¶PµP°PeC†C-C—B»).

PhPrPSPsC#P°CfPSPµ P»C-PeCfPIP°PSPSC¶ PïPsPjC-C¶PSPëPjPë C-PSPiC-P±C-C,PsC¶P°PjPë
CYP3A4

PhPrPSPsC#P°CfPSPµ P·P°CfC,PsCfCfPIP°PSPSC¶ PeP°C¶PëPïC¶P°P·PëPSCf P·
PïPsPjC-C¶PSPëPjPë C-PSPiC-P±C-C,PsC¶P°PjPë CYP3A4 PjPsP¶Pµ PïC¶PëP·PIPµCfC,Pë PrPs

P·P±C-P»CHC€PμPSPSCЦ P·P°PiP°P»CHPSPsC— PμPeCГPіPsP·PëC†C-C—
PeP°CГPëPіCГP°P·PëPSCr. P PμPePsPjPμPSPPrCfC”C,CHCГCЦ PjPsPSC-C,PsCГPëPSPi
C-PSPrPëPIC-PrCfP°P»CHPSPsC— CГPμP°PeC†C-C— C,P° PіPμCГPμPSPsCГPëPjPsCГC,C- C,P°,
CЦPeC%oPs PSPμPsP±C...C-PrPSPs, PrPsP·Cf PeP°CГPëPіCГP°P·PëPSCr CГP»C-Pr
(C,PëPjC±P°CГPsPIPs) P·PjPμPSC€PëC,Pë P· CГCГP°C...CfPIP°PSPSCЦPj
PіPsC,PμPSC†C-PNëPSPsPiPs P·P±C-P»CHC€PμPSPSCЦ PμPeCГPіPsP·PëC†C-C— (PrPëPI.
CГPsP·PrC-P» B«P·P·P°C”PjPsPrC-CЦ P· C-PSC€PëPjPë P»C-PeP°CГCГCHPePëPjPë
P·P°CГPsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C”PjPsPrC-PNëB»).

P”PsPіPsPjC-P¶PSC- CГPμC±PsPIPëPSPë

P PμP°PiC-P»P°, PeP°PіCГCfP»Pë C,PIPμCГPrC- PіPs 3 PjPi, 4,5 PjPi C,P° 6 PjPi, PjC-CГC,CЦC,CH
P±P°CГPIPSPëPe CГPіPμC†C-P°P»CHPSPëPNë C±PμCГPIPSPSPëPNë PђPŸ (P• 129), C%oPs
PjPsP¶Pμ CГPіCГPëC±PëPSCЦC,Pë P°P»PμCГPiC-C±PSC- CГPμP°PeC†C-C—.

*P—P°CГC,PsCГCзPIP°PSPSCЦ Cз PіPμCГC-PsPr PIP°PiC-C,PSPsCГC,C- P°P±Ps
PiPsPrCзPIP°PSPSCЦ PiCГCзPrPrCГ.*

P-C-PSPePë CГPμPіCГPsPrCfPeC,PëPIPSPsPiPs PIC-PeCf/ P¶C-PSPePë, CЦPeC-
PIPëPePsCГPëCГC,PsPICrCГC,CH PePsPSC,CГP°C†PμPіC†C-CГ

P-C-PSPeP°Pj CГPμPіCГPsPrCfPeC,PëPIPSPsPiPs PIC-PeCf PіPsC,CГC-P±PSPs CрPSPëPeP°C,Pë
PIP°PiC-C,PSPsCГC,C- PіC-Pr C±P°CГ PіCГPëPNëPsPjCр P»C-PeP°CГCГCHPePsPiPs
P·P°CГPsP±Cр P PμP°PiC-P»P°. PμP°C†C-C”PSC,PePë CГPμPіCГPsPrCfPeC,PëPIPSPsPiPs
PIC-PeCf PjP°CГC,CH PIPëPePsCГPëCГC,PsPICrPIP°C,Pë PIPëCГPsPePsPμC,,PμPeC,PëPIPS-
PjPμC,PsPrPë PePsPSC,CГP°C†PμPіC†C-C— PіC-Pr C±P°CГ P»C-PeCрPIP°PSPSCЦ C,P°
C%oPsPSP°PNëPjPμPSC€Pμ PіCГPsC,CЦPiPsPj 10 C,PëP¶PSC-PI PіC-CГP»CЦ PіCГPëPNëPsPjCр
PsCГC,P°PSPSCHPsC— PrPsP·Pë PіCГPμPіP°CГP°C,Cр P PμP°PiC-P»P°.

P’P°PiC-C,PSC-CГC,CH

P”P°PSC- C%oPsPrPs P·P°CГC,PsCГCрPIP°PSPSCЦ PeP°CГPëPіCГP°P·PëPSCr PIP°PiC-C,PSPëPj
P¶C-PSPeP°Pj PIC-PrCГCрC,PSC- P°P±Ps PsP±PjPμP¶PμPSC-.

P”PsCГP»C-PrP¶PμPSPSCЦ PSP° C,PIP°CГPëPSP°C... PіPsPeP°P·P°P»Pë
CГPμPіCГPsPrCfPeC,PëPIPSCr C,PsPeCГPëC±PSC-CГC,CH, PIPeP»CГC±PSPs P· PIP°PrP°PjPë
CГPsP·PIPëC,PeCf Cр C%oCрCГC-PI (PrPëPI. CГPsP·PrC-P» B«P”P°PSC-
PrPsPeP»C-PSC-C±PSPëC... PrPsCГP»C-PrP¶PμPSCГ P· P±PμP·PіPμPePëB»).

P—P°CГC,PsCГCрPIP°PSPSCЦ PіCГPμPіP°CГP°C,Cр P PμP°PiC-P»P° PSPμ
CГPμPePsPjPμPSPPrCfC”C,CHCГCЦ PіCГPsC,CЦPiPsPj PIP°PiC-C,PSPsCГC,C-, P° C,P°PePsP¶
P¶C-PSPeP°Pj CГPμPіCГPsPrCfPeC,PëPIPSPsPiPs PIC-PeCf, CЦPeC- PSPμ
PIPëPePsCГPëCГC,PsPICrCГC,CH PμC,,PμPeC,PëPIPSCr PePsPSC,CГP°C†PμPіC†C-CГ.
PμC-CГP»CЦ PіCГPëPіPëPSPμPSPSCЦ P»C-PeCрPIP°PSPSCЦ PeP°CГPëPіCГP°P·PëPSPsPj
C±PμCГPμP· PіPsPIC-P»CHPSPμ PIPëPIPμPrPμPSPSCЦ P°PeC,PëPIPSPëC...
PePsPjPіPsPSPμPSC,C-PI PjPμC,PsPrPë PePsPSC,CГP°C†PμPіC†C-C— PіPsC,CГC-P±PSPs
P·P°CГC,PsCГPsPICrPIP°C,Pë C%oPsPSP°PNëPjPμPSC€Pμ PіCГPsC,CЦPiPsPj 10 C,PëP¶PSC-PI.

PќPsPIPsPSP°CГPsPrP¶PμPSC-, PSP° CЦPePëC... PIPіP»PëPIP°P»Pë
P°PSC,PëPіCГPëC...PsC,PëPePë (PIPeP»CГC±PSPs P· PeP°CГPëPіCГP°P·PëPSPsPj) PіC-Pr C±P°CГ
C,CГPμC,CHPsPiPs C,CГPëPjPμCГC,CГCр PIP°PiC-C,PSPsCГC,C-, P·PSP°C...PsPrCЦC,CHCГCЦ

PI PiCḡCíPíC- CḡPëP·PëPeCí CḡPsP·PIPëC,PeCí C,P°PePëC... PíPsP±C-C‡PSPëC...
CḡPµP°PeC†C-PNḡ, CḡPe PµPeCíC,CḡP°PíC-CḡP°PjC-PrPSC- CíPëPjPíC,PsPjPë C,P°/P°P±Ps
CíPëPjPíC,PsPjPë PIC-PrPjC-PSPë, CḡPeC- PjPsP¶CíC,CH P±CíC,Pë CḡC-P·PSPsC—
C,CḡP¶PePsCíC,C- C,P° C,CḡPëPIP°P»PsCíC,C-. PµPsPIC-PrPsPjP»CḡP»PsCíCḡ PíCḡPs
P·P±CíPrP¶PµPSPSCḡ, PiC-PíPµCḡC,PsPSC-Cḡ, PiC-PíPsC,PsPSC-Cḡ, C,CḡPµPjPsCḡ,
CíPsPSP»PëPIC-CíC,CH, CḡPµCíPíC-CḡP°C,PsCḡPSPëPNḡ PrPëCíC,CḡPµCí-CíPëPSPPrCḡPsPj
C,P° PíPsCḡCíC€PµPSPSCḡ PIP¶PëPIP°PSPSCḡ C-P¶C-. PíC- CíCíPeP»P°PrPSPµPSPSCḡ
CḡC-P·PSPëP»PëCíCḡ P·P° C,CḡP¶PeC-CíC,CH; CḡPeC%Ps Cí PrPµCḡPePëC...
PIPëPíP°PrPeP°C... CíPëPjPíC,PsPjPë P·PSPëPeP°P»Pë CíP°PjC- CíPsP±PsCḡ, C,Ps PI
C-PSC€PëC... PIPëPíP°PrPeP°C... PSPsPIPsPSP°CḡPsPrP¶PµPSC- PíPsC,CḡPµP±CíPIP°P»Pë
P»C-PeCíPIP°PSPSCḡ Cí PIC-PrPrC-P»PµPSPSC- C-PSC,PµPSCíPëPIPsPsC— C,PµCḡP°PíC-C—
C,P° C,CḡPëPIP°P»PsC— PíPsCíPíC-C,P°P»C-P·P°C†C-C—. PýPsPjCí P·P° CíC,P°PSPsPj
PSPsPIPsPSP°CḡPsPrP¶PµPSPëC... PíPsC,CḡC-P±PSPs CḡPµC,PµP»CHPSPs
CíPíPsCíC,PµCḡC-PiP°C,Pë.

P°PsPrCíPIP°PSPSCḡ PiCḡCíPrPrCḡ

P°PsCíC- PSPµPIC-PrPsPjPs, C‡Pë PIPëPrC-P»CḡCḡC,CHCíCḡ PeP°CḡPëPíCḡP°P·PëPS C,P°
PNḡPsPiPs PsCíPSPsPIPsC- PjPµC,P°P±PsP»C-C,Pë P· PjPsP»PsPePsPj P»CḡPrPëPSPë.
PḡP°CḡPëPíCḡP°P·PëPS C,P° PNḡPsPiPs PjPµC,P°P±PsP»C-C,Pë PIPëPrC-P»CḡCḡC,CHCíCḡ P·
PjPsP»PsPePsPj C%CrCḡC-PI PíC-Pr C‡P°Cí P»P°PeC,P°C†C-C— (PrPëPI. CḡPsP·PrC-P»
B«P°P°PSC- PrPsPeP»C-PSC-C‡PSPëC... PrPsCíP»C-PrP¶PµPSCḡ P· P±PµP·PíPµPePëB»). PḡPµ
PjPsP¶PSP° PIPëPeP»CḡC‡P°C,Pë PIPíP»PëPICí PSP°
PSPsPIPsPSP°CḡPsPrP¶PµPSPëC.../PSPµPjPsPIP»CḡC,. PµC-Pr C‡P°Cí P»C-PeCíPIP°PSPSCḡ
PeP°CḡPëPíCḡP°P·PëPSPsPj PíPsC,CḡC-P±PSPs PiPµCḡPµCḡPIP°C,Pë PiPsPrCíPIP°PSPSCḡ
PiCḡCíPrPrCḡ.

PµPµCḡC,PëP»CHPSC-CíC,CH

P°PíP»PëPI PeP°CḡPëPíCḡP°P·PëPSCí PSP° C,,PµCḡC,PëP»CHPSC-CíC,CH P»CḡPrPëPSPë PSPµ
P±CíPI PIPëPIC‡PµPSPëPNḡ. Pj PrPsCíP»C-PrP¶PµPSPSCḡC... PSP° C%CrCḡP°C...
CíPíPsCíC,PµCḡC-PiP°P»PsCíCḡ P·PSPëP¶PµPSPSCḡ C,,PµCḡC,PëP»CHPSPsCíC,C- C,P°
PíPsPeP°P·PSPëPeC-PI P·P°PíP»C-PrPSPµPSPSCḡ Cí CíP°PjPsPe (PrPëPI. CḡPsP·PrC-P»
B«P°P°PSC- PrPsPeP»C-PSC-C‡PSPëC... PrPsCíP»C-PrP¶PµPSCḡ P· P±PµP·PíPµPePëB»).

*P—PrP°C,PSC-CíC,CH PIPíP»PëPIP°C,Pë PSP° C€PIPëPrPeC-CíC,CH CḡPµP°PeC†C-C— PíCḡPë
PePµCḡCáPIP°PSPSC- P°PIC,PsC,CḡP°PSCíPíPsCḡC,PsPj P°P±PsB C-PSC€PëPjPë
PjPµC...P°PSC-P·PjP°PjPë.*

PḡP°CḡPëPíCḡP°P·PëPS PjP°C” CíP»P°P±PePëPNḡ P°P±Ps PíPsPjC-CḡPSPëPNḡ PIPíP»PëPI PSP°
P·PrP°C,PSC-CíC,CH PíP°C†C-C”PSC,C-PI PePµCḡCíPIP°C,Pë P°PIC,PsC,CḡP°PSCíPíPsCḡC,PsPj
C,P° PíCḡP°C†CḡPIP°C,Pë P· C-PSC€PëPjPë PjPµC...P°PSC-P·PjP°PjPë. PµP°C†C-C”PSC,C-PI
PíPsC,CḡC-P±PSPs P·P°CíC,PµCḡPµPiC,Pë PIC-Pr CḡPsP±PsC,Pë P· PSPµP±PµP·PíPµC‡PSPëPjPë
PjPµC...P°PSC-P·PjP°PjPë, PIPeP»CḡC‡PSPs P· P°PIC,PsC,CḡP°PSCíPíPsCḡC,PsPj, PrPsPíPsPePë
PIPSPSPë PSPµ P±CíPrCíC,CH C†C-P»PePsPj PIPíPµPIPsPµPSC-, C%Ps
P»C-PeP°CḡCíCḡPePëPNḡ P·P°CíC-P± P PµP°PiC-P»P° PSPµ PjP°C” PSP° PSPëC...
PSPµPiP°C,PëPIPsPiPs PIPíP»PëPICí.

PŸPİPsCİC-P± P·P°CİC,PsCİCżPIP°PSPSCİ C,P° PrPsP·Pë.

P°PsP·CřPIP°PSPSCİ

P PµPePsPjPµPSPřPsPIP°PSP° PİPsC‡P°C,PePsPIP° PrPsP·P° PeP°CĤPëPİCĤP°P·PëPSCř CİC,P°PSPsPIPëC,CH 1,5 PjPi PsPrPëPS CĤP°P· PSP° PrPsP±Cř. P—PiPsPrPsPj PrPsP·Cř Cř CĤP°P·C— PİPsC,CĤPµP±Pë PjPsP¶PSP° PİPsPIC—P»CHPSPs PİC—PrPIPëC‰CřPIP°C,Pë PİPs 1,5 PjPi PrPs PjP°PeCİPëPjP°P»CHPSPsC— PrPsP·Pë 6 PjPi/PrPsP±Cř. PkP°PNëPSPëP¶C‡P° PµC„PµPeC,PëPIPSP° PrPsP·P° PjP°C” PİC—PrC,CĤPëPjCřPIP°C,PëCİCİ P·PiC—PrPSPs P· PeP»C—PSC—C‡PSPsCĤ PsC‡C—PSPePsCĤ P»C—PeP°CĤCİ. P§PµCĤPµP· PrPsPIPiPëPNë PİPµCĤC—PsPr PSP°PİC—PIPIPëPIPµPrPµPSPSCİ PeP°CĤPëPİCĤP°P·PëPSCř C,P° PNëPsPiPs P°PeC,PëPIPSPëC... PjPµC,P°P±PsP»C—C,C—PI P·PjC—PSPë PI PrPsP·CřPIP°PSPSC— PSPµ P±CřPrCřC,CH PİPsPIPSC—CİC,CĤ PIC—PrPsP±CĤP°P¶P°C,PëCİCİ PI PİP»P°P·PjC— PİCĤPsC,CİPiPsPj PeC—P»CHPePsC... C,PëP¶PSC—PI. P—P° CİC,P°PSPsPj PİP°C‡C—C”PSC,P° C,CĤPµP±P° CİPİPsCİC,PµCĤC—PİP°C,Pë CİC,PsCİPsPIPSs PİPsCİPIPë PİPsP±C—C‡PSPëC... CĤPµP°PeC‡C—PNë C,P° PIC—PrPİPsPIC—PrC— PSP° P»C—PeCřPIP°PSPSCİ PİCĤPsC,CİPiPsPj PeC—P»CHPePsC... C,PëP¶PSC—PI PİC—CİP»Cİ PİPsC‡P°C,PeCř PİCĤPëPNëPsPjCř PeP°CĤPëPİCĤP°P·PëPSCř C,P° PİC—CİP»Cİ PePsP¶PSPsC— P·PjC—PSPë PrPsP·CřPIP°PSPSCİ (PrPëPI. CĤPsP·PrC—P» B«PαP°CĤPjP°PePsPeC—PSPµC,PëPeP°B».).

PµPµCĤPµC...C—Pr P· C—PSCëPëC... P°PSC,PëPİCİPëC...PsC,PëPeC—PI PSP° PeP°CĤPëPİCĤP°P·PëPS

PµCĤPë PİPµCĤPµC...PsPrC— P· C—PSCëPëC... P°PSC,PëPİCİPëC...PsC,PëPeC—PI PSP° PeP°CĤPëPİCĤP°P·PëPS PİPsC,CĤC—P±PSPs PICĤP°C...PsPICřPIP°C,Pë PİPsCİC,CřPİPsPIPµ PİPµCĤPµC...CĤPµCİPSPµ C,PëC,CĤCřPIP°PSPSCİ P· PİPsCİC,CřPİPsPIPëPj PİCĤPëPİPëPSPµPSPSCİPj P·P°CİC,PsCİCřPIP°PSPSCİ PİPsPİPµCĤPµPrPSCĤPsC— C,PµCĤP°PİC—C— PİC—Pr C‡P°Cİ PİPsC‡P°C,PeCř PİCĤPëPNëPsPjCř PeP°CĤPëPİCĤP°P·PëPSCř.

PµPµCĤPµC...C—Pr P· PeP°CĤPëPİCĤP°P·PëPSCż PSP° C—PSCëPëPNë P°PSC,PëPİCİPëC...PsC,PëPe

PµCĤPë PİPµCĤPµC...PsPrC— P· PeP°CĤPëPİCĤP°P·PëPSCř PSP° C—PSCëPëPNë P°PSC,PëPİCİPëC...PsC,PëPe PİPsCİC,CřPİPsPIPsPİPs PİPµCĤPµC...CĤPµCİPSPsPİPs C,PëC,CĤCřPIP°PSPSCİ PSPµ PIC—PrP±CřPIP°C,PëPjPµC,CHCİCİ, C,PsPjCř PİCĤPëPNëPsPj PSPsPIPsPİPs P°PSC,PëPİCİPëC...PsC,PëPeP° PjPsP¶PSP° PİPsC‡PëPSP°C,Pë P· PNëPsPiPs PSP°PNëPSPëP¶C‡PsC— PrPsP·Pë PİC—Pr C‡P°Cİ PİCĤPëPİPëPSPµPSPSCİ PIPëPePsCĤPëCİC,P°PSPSCİ PeP°CĤPëPİCĤP°P·PëPSCř. PµPsC,CĤC—P±PSPs PICĤP°C...PsPICřPIP°C,Pë, C‰Ps PePsPSC‡PµPSC,CĤP°C‡C—Cİ PeP°CĤPëPİCĤP°P·PëPSCř C,P° PNëPsPiPs P°PeC,PëPIPSPëC... PjPµC,P°P±PsP»C—C,C—PI PI PİP»P°P·PjC— P·PjPµPSCëPëC,CHCİCİ PSP° 50 % PİCĤPëP±P»PëP·PSPs PİCĤPsC,CİPiPsPj 1 C,PëP¶PSCİ (PrPëPI. CĤPsP·PrC—P» B«PαP°CĤPjP°PePsPeC—PSPµC,PëPeP°B».).

PµCĤPsPİCżCİPe PİCĤPëPNëPsPjCż C,P°P±P»PµC,PsPe

PµCĤPë PİCĤPsPİCřCİPeCř PİCĤPëPNëPsPjCř C,P°P±P»PµC,PePë PİP°C‡C—C”PSC, PİPsPIPëPSPµPS PSPµPIP°PNëPSPs PİCĤPëPNëPSCİC,Pë PİCĤPsPİCřC‰PµPSCř C,P°P±P»PµC,PeCř. PhPrPSP°Pe CİPeC‰Ps CřP¶Pµ PjP°PNëP¶Pµ PSP°CİC,P°PI C‡P°Cİ PİCĤPëPNëPsPjCř PSP°CİC,CřPİPSPsC— C,P°P±P»PµC,PePë, PİCĤPsPİCřC‰PµPSCř C,P°P±P»PµC,PeCř PSPµ PIP°CĤC,Ps PİCĤPëPNëPjP°C,Pë, P° CİP»C—Pr PİCĤPëPNëPSCİC,Pë PSP°CİC,CřPİPSCř PrPsP·Cř P·PiC—PrPSPs P·C— P·PIPëC‡P°PNëPSPëPj PİCĤP°C„C—PePsPj. PkPµ CĤPµPePsPjPµPSPřCřC”C,CHCİCİ PİCĤPëPNëPjP°C,Pë PİPsPrPIC—PNëPSCř PrPsP·Cř, C‰PsP± PePsPjPİPµPSCİCřPIP°C,Pë PİCĤPsPİCřC‰PµPSCř PrPsP·Cř.

PhCf'PsP±P»PëPIC- PiCfCfPiPë PiP°C+C-C" PSC,C-PI

PuPsCfCzC€PµPSPSClI C,,CzPSPeC+C-C— PSPëCfPsPe

PµP°C+C-C" PSC,Pë P· PiPsCfCfC€PµPSPSClIj C,,CfPSPeC+C-C— PSPëCfPsPe P»PµPiPePsPiPs C±Pë Cf'PµCfPµPrPSCfPsPiPs Cf'C,CfPiPµPSClI C,CfP¶PePsCf'C,C- (PeP»C-CfPµPSCf' PeCfPµP°C,PëPSC-PSCf' (CrCl) ≥ 30 PjP»/C...PI C,P° < 89 PjP»/C...PI) PSPµ PiPsC,CfPµP±Cf'CfC,Cf P¶PsPrPSPëC... PePsCfPëPiCfPIP°PSCf PrPsP·Pë. P'PµP·PiPµC±PSC-Cf'C,Cf C,P° PµC,,PµPeC,PëPIPSC-Cf'C,Cf P·P°Cf'C,PsCfCfPIP°PSPSClI PeP°CfPëPiCfP°P·PëPSCf PrP»CfI PiP°C+C-C" PSC,C-PI C-P· C,CfP¶PePëPj PiPsCfCfC€PµPSPSClIj C,,CfPSPeC+C-C— PSPëCfPsPe (CrCl < 30 PjP»/C...PI) PSPµ PsC+C-PSCfPIP°P»PëCfCfI. PµP°C+C-C" PSC,P°Pj C-P· C,CfP¶PePëPj PiPsCfCfC€PµPSPSClIj C,,CfPSPeC+C-C— PSPëCfPsPe PSPµ CfPµPePsPjPµPSPrCfC"C,CfCfCfI PiCfPëPNëPsPj PeP°CfPëPiCfP°P·PëPSCf (PrPëPI. CfPµP·PrC-P» B«PαP°CfPjP°PePsPeC-PSPµC,PëPeP°B»).

PuPsCfCzC€PµPSPSClI C,,CzPSPeC+C-C— PiPµC±C-PSPePë

PµP°C+C-C" PSC,Pë P· PiPsCfCfC€PµPSPSClI C,,CfPSPeC+C-C— PiPµC±C-PSPePë P»PµPiPePsPiPs P°P±Ps Cf'PµCfPµPrPSCfPsPiPs Cf'C,CfPiPµPSClI C,CfP¶PePsCf'C,C- (5Bf"9 P·P° C€PeP°P»PsCf P§P°PNëP»PrP° Bf" PµBf™ Cf) PSPµ PiPsC,CfPµP±Cf'CfC,Cf P¶PsPrPSPëC... PePsCfPëPiCfPIP°PSCf PrPsP·Pë. P'PµP·PiPµC±PSC-Cf'C,Cf C,P° PµC,,PµPeC,PëPIPSC-Cf'C,Cf P·P°Cf'C,PsCfCfPIP°PSPSClI PeP°CfPëPiCfP°P·PëPSCf B PrP»CfI PiP°C+C-C" PSC,C-PI C-P· C,CfP¶PePëPj PiPsCfCfC€PµPSPSClIj C,,CfPSPeC+C-C— PiPµC±C-PSPePë (10Bf"15 P·P° C€PeP°P»PsCf P§P°PNëP»PrP° Bf" PµBf™ Cf) PSPµ PsC+C-PSCfPIP°P»PëCfCfI. PµP°C+C-C" PSC,P°Pj C-P· C,CfP¶PePëPj PiPsCfCfC€PµPSPSClIj C,,CfPSPeC+C-C— PiPµC±C-PSPePë PSPµ CfPµPePsPjPµPSPrCfC"C,CfCfCfI PiCfPëPNëPsPj PeP°CfPëPiCfP°P·PëPSCf (PrPëPI. CfPµP·PrC-P» B«PαP°CfPjP°PePsPeC-PSPµC,PëPeP°B»).

PuP°C+C-C" PSC,Pë P»C-C,PSCHfPsPiPs PIC-PeCz

P"PsCf'C,CfPiPSPëC... PrP°PSPëC... Cf'C,PsCf'PsPIPSPs P»C-PeCfPIP°PSPSClI PeP°CfPëPiCfP°P·PëPSPsPj PiP°C+C-C" PSC,C-PI P»C-C,PSCHfPsPiPs PIC-PeCf' (≥ 65 CfPµPeC-PI) PSPµPrPsCf'C,P°C,PSCHfPsB PrP»CfI PiPëCfIPIP»PµPSPSClI PIC-PrPjC-PSPSPsCf'C,PµPNë C—C...PSCHfPsC— PIC-PrPiPsPIC-PrC- PSP° P»C-PeCfPIP°PSPSClI PIC-Pr PIC-PrPiPsPIC-PrC- PiP°C+C-C" PSC,C-PI PjPsP»PsPrC€PsPiPs PIC-PeCf' (PrPëPI. CfPµP·PrC-P» B«PαP°CfPjP°PePsPeC-PSPµC,PëPeP°B»). PµC-PrP±C-Cf PrPsP·Pë PrP»CfI PiP°C+C-C" PSC,C-PI P»C-C,PSCHfPsPiPs PIC-PeCf' PjP°C" P±Cf'C,Pë P±C-P»CHfC€ PsP±PµCfPµP¶PSPëPj.

PŸPiPsCf'C-P± P·P°Cf'C,PsCfCfPIP°PSPSClI

P>C-PeP°CfCfCHfPePëPNë P·P°Cf'C-P± P PµP°PiC-P»P° P·P°Cf'C,PsCf'PsPICfPIP°C,Pë PiPµCfPµP»CHfPSPs 1 CfP°P· PSP° PrPsP±Cf PI PsPrPëPS C- C,PsPNë Cf'P°PjPëPNë C±P°Cf' PSPµP·P°P»PµP¶PSPs PIC-Pr PiP¶PëPIP°PSPSClI C—P¶C-.

PµCfPë P·P°Cf'C,PsCfCfPIP°PSPSC- PeP°CfPëPiCfP°P·PëPSCf Cf'P»C-Pr CfPSPëPeP°C,Pë PiP¶PëPIP°PSPSClI P°P»PePsPiPsP»Cf (PrPëPI. CfPµP·PrC-P» B«P'P·P°C"PjPsPrC-CfI P· C-PSC€PëPjPë P»C-PeP°CfCfCHfPePëPjPë P·P°Cf'PsP±P°PjPë C,P° C-PSC€C- PiPëPrPë PiP·P°C"PjPsPrC-PNëB»).

P"C-C,Pë.

P'PμP·PīPμPeCf C,P° PμC,,PμPeC,PēPIPSC-CfC,CH P·P°CfC,PsCfCfPIP°PSPSCf
PeP°CfPēPīCfP°P·PēPSCf PrP»Cf PrC-C,PμPNē (PIC-PePsPj PrPs 18 CfPsPeC-PI) PSPμ
PICfC,P°PSPsPIP»PμPSPs. PkPμPjP°C" PrP°PSPēC....

PμPμCfPμPrPsP·CzPIP°PSPSCf.

PŸPēPjPiC,PsPjPē

PμPsPIC-PrPsPjP»CfP»PsCfCf PīCfPs PIPēPīP°PrPePsPIPμ PiPsCfC,CfPμ
PīPμCfPμPrPsP·CfPIP°PSPSCf (48 PjPi/PrPsP±Cf) PI PsPrPSPsPiPs PīP°CfC-C"PSC,P°. PJ
CfCHPsPiPs PīP°CfC-C"PSC,P° P·bTTM CfIPIPēP»PēCfCf PsCfC,PsCfC,P°P· C,P°
CfPμPrP°C,PēPIPSPēPNē PμC,,PμPeC,. PŸC,P°PS PīP°CfC-C"PSC,P° PīPsPIPSC-CfC,CH
PIC-PrPSPsPIPēPICfCf PI C,PsPNē P¶Pμ PrPμPSCf.

P>C-PeCfPIP°PSPSCf PīCfPē PīPμCfPμPrPsP·CfPIP°PSPSC-

P>C-PeCfPIP°PSPSCf PīCfPē PīPμCfPμPrPsP·CfPIP°PSPSC- PjP°C" P±CfC,Pē
PīC-PrC,CfPēPjCfPIP°P»CHPSPμ, PIPeP»CHCfPSPs P· PīC-PrC,CfPēPjPePsCf PIC-P»CHPSPsC—
PīCfPsC...C-PrPSPsCfC,C- PrPēC...P°P»CHPSPēC... CēP»CfC...C-PI, PSP°CfPēCfPμPSPSCfPj
PePēCfPSPμPj C,P° PIPμPSC,PēP»CfCfC-C"Cf, P° C,P°PePsP¶ CfPēPjPiC,PsPjP°C,PēCfPSPμ.
PŸPīPsCfC,PμCfPμP¶PμPSPSCf P·P° CfPμCfCfPμPIPs-CfCfPrPēPSPSPsCf CfPēCfC,PμPjPsCf
PjP°C" CfPsP·PīPsCfPēPSP°C,PēCfCf PSPμPīP°PNēPSPs C,P° PIPeP»CHCfP°C,Pē
PμP»PμPeC,CfPsPeP°CfPrC-PsPīCfP°C,,C-CfPSPēPNē PjPsPSC-C,PsCfPēPSPi PrP»Cf
PIPēCfPIP»PμPSPSCf PjPsP¶P»PēPIPēC... P°CfPēC,PjC-PNē. PJ CfP°P·C-
PIPēPSPēPePSPμPSPSCf C,CfP¶PePēC... PμPeCfC,CfP°PīC-CfP°PjC-PrPSPēC...
CfPēPjPiC,PsPjC-PI CfP»C-Pr P·P°CfC,PsCfCfPIP°C,Pē P°PSC,PēC...PsP»C-PSPμCfPiC-CfPSC-
PīCfPμPīP°CfP°C,Pē. PhCfPeC-P»CHPePē PeP°CfPēPīCfP°P·PēPS CfPēP»CHPSPs
P·PībTTM CfP·CfC"C,CHCfCf P· P±C-P»PeP°PjPē PīP»P°P·PjPē, PīPμPjPsPrC-P°P»C-P· PSPμ
P±CfPrPμ B PμC,,PμPeC,PēPIPSPēPj PrP»Cf P>C-PeCfPIP°PSPSCf
PīPμCfPμPrPsP·CfPIP°PSPSCf. PμPēP»CHPSPēPNē PjPμPrPēCfPSPēPNē PSP°PīP»CfP Pr C,P°
PjPsPSC-C,PsCfPēPSPi PjP°CfC,CH C,CfPēPIP°C,Pē PrPsC,Pē, PrPsPePē CfC,P°PS
PīP°CfC-C"PSC,P° PSPμ PIC-PrPSPsPIPēC,CHCfCf.

PŸP°CfPēPīCfP°P·PēPS PSPμ PjP°C" CfPīPμCfPēC,,C-CfPSPsPiPs P°PSC,PēPrPsC,Cf.

PμPsP±C-CfPSC- CfPμP°PeCfC-C-.

PμPsP±C-CfPSPēPjPē CfPμP°PeCfC-CfPjPē, PīCfPs CfPeC- PSP°PNēCfP°CfC,C-CēPμ
PīPsPIC-PrPsPjP»CfP»PsCfCf PīCfPē P·P°CfC,PsCfCfPIP°PSPSC- PeP°CfPēPīCfP°P·PēPSCf PI
PrC-P°PīP°P·PsPSC- PrPsP· (1,5bTTM 6 PjPi), P±CfP»Pē P°PeP°C,PēP·C-Cf (19 %) C,P°
PīP°CfPeC-PSCfPsPSC-P·Pj (17,5 %). P'C-P»CHCēC-CfC,CH CfPμP°PeCfC-PNē P±CfP»Pē
P»PμPiPePsPiPs CfPē CfPμCfPμPrPSCfPsPiPs CfC,CfPīPμPSCf C,CfP¶PePsCfC,C-.

PŸP°P±P»PēCfPSPēPNē PīPμCfPμP»C-Pe PīPsP±C-CfPSPēC... CfPμP°PeCfC-PNē

PμPsP±C-CfPSC- P»C-PeP°CfCfCHPeC- CfPμP°PeCfC-C— (PμP>P) PSP° PsCfPSPsPIC-
PsP±bTTM C"PrPSP°PSPēC... PrP°PSPēC... P· PrPsCfP»C-PrP¶PμPSPSCf P»C-PeCfPIP°PSPSCf
CēPēP·PsC,,CfPμPSC-C— PeP°CfPēPīCfP°P·PēPSPsPj PīCfPμPrCfC,P°PIP»PμPSPs P·P°
CfPēCfC,PμPjP°PjPē PsCfPiP°PSC-PI C- P· PIPēPePsCfPēCfC,P°PSPSCfPj

$\text{P}\mu\text{PsP}\pm\text{C}-\text{C}\ddagger\text{PSC}-\text{C}\ddagger\text{P}\mu\text{P}^\circ\text{PeC}\ddagger\text{C}-\text{C}-\text{C}\ddagger\text{PsP}\cdot\text{PiPsPrC}-\text{P}\gg\mu\text{PSC}-\text{P}\cdot\text{P}^\circ\text{C}\ddagger\text{P}^\circ\text{C}\ddagger\text{C},\text{PsC},\text{PsC}\ddagger$
 $\text{PIP}\ddot{\text{P}}\text{PSP}\ddot{\text{P}}\text{PePSP}\mu\text{PSPSC}\ddagger\text{C},\text{P}^\circ\text{PeP}\ddot{\text{P}}\text{Pj}\text{C}\ddagger\text{P}\ddot{\text{P}}\text{PSPsPj}:\text{PrCrP}\P\mu\text{C}\ddagger\text{P}^\circ\text{C}\ddagger\text{C},\text{C}-\left(\geq 1/10\right);\text{C}\ddagger\text{P}^\circ\text{C}\ddagger\text{C},\text{C}-$
 $(\text{PIC}-\text{Pr}\geq 1/100\text{PrPs}<1/10);\text{PSP}\mu\text{C}\ddagger\text{P}^\circ\text{C}\ddagger\text{C},\text{C}-\left(\text{PIC}-\text{Pr}\geq 1/1\,000\text{PrPs}<1/100\right);$
 $\text{PiPsPsPrP}\ddot{\text{P}}\text{PSPsPeC}-\left(\text{PIC}-\text{Pr}\geq 1/10\,000\text{PrPs}<1/1\,000\right);\text{C}\ddagger\text{C}-\text{PrPeC}-\text{C}\ddagger\text{PSC}-\left(<1/10\,000\right);$
 $\text{C}\ddagger\text{P}^\circ\text{C}\ddagger\text{C},\text{PsC},\text{P}^\circ\text{PSP}\mu\text{PIC}-\text{PrPsPjP}^\circ\left(\text{PSP}\mu\text{PjPsP}\P\text{P}\gg\text{P}\ddot{\text{P}}\text{IPs}\text{PIP}\ddot{\text{P}}\cdot\text{PSP}^\circ\text{C}\ddagger\text{P}\ddot{\text{C}},\text{P}\ddot{\text{P}}\text{PSP}^\circ\right.$
 $\text{PsC}\ddagger\text{PSPsPIC}-\text{PSP}^\circ\text{C}\ddagger\text{PIPSP}\ddot{\text{C}}\dots\text{PrP}^\circ\text{PSP}\ddot{\text{C}}\dots\left.\right)\text{PjPePsP}\P\text{PSC}-\text{P}\mathbb{N}\text{PiC}\ddagger\text{CrPiC}-\text{P}\cdot\text{P}^\circ$
 $\text{C}\ddagger\text{P}^\circ\text{C}\ddagger\text{C},\text{PsC},\text{PsC}\ddagger\text{PIP}\ddot{\text{P}}\text{PSP}\ddot{\text{P}}\text{PePSP}\mu\text{PSPSC}\ddagger\text{PiPsP}\pm\text{C}-\text{C}\ddagger\text{PSC}-\text{C}\ddagger\text{P}\mu\text{P}^\circ\text{PeC}\ddagger\text{C}-\text{C}-$
 $\text{PiC}\ddagger\text{P}\mu\text{PrC}\ddagger\text{C},\text{P}^\circ\text{PIP}\gg\mu\text{PSC}-\text{PiPiPsC}\ddagger\text{C}\ddagger\text{PrPeCr}\text{P}\cdot\text{PSP}\ddot{\text{P}}\P\mu\text{PSPSC}\ddagger\text{C}-\text{C}\dots\text{PSC}\mathbb{H}\text{PsC}-$
 $\text{C}\ddagger\text{P}\mu\text{C}\ddagger\text{P}\mathbb{N}\text{PsP}\cdot\text{PSPsC}\ddagger\text{C},\text{C}-.$

[illegible]

¹ P PsP·P»P°PrPë CÍPSCr: P±PµP·CÍPSPSPSCÍ, P°PSPsPjP°P»CHBPSC- CÍPSPë, PePsCëPjP°CjPë, CjPSP·P»P°PrPë C†PëCjPeP°PrPSPsPiPs CjPëC,PjCr CÍPSCr, PrPëCÍPSPjPSC-CÍ, PiC-PiPµCjCÍPSPjPSC-CÍ, PiPsCjCrCëPµPSPSCÍ P·P°CÍPëPSP°PSPSCÍ, PiPsCjCrCëPµPSPSCÍ B PiPsCÍPµCjPµPr CÍPSCr, PSC-C†PSC- P¶P°C...Pë, CjPSP·P»P°PrPë CÍPSCr, CÍPSPjPSP°PjP±CrP»C-P·Pj, PiPsCjCrCëPµPSPSCÍ PiCjPSP±CrPrP¶PµPSPSCÍ.

² PhPeP°C,PëP·C-CÍ: P°PeP°C,PëP·C-CÍ, PiCÍPëC...PsPjPsC,PsCjPSP° PiC-PiPµCjP°PeC,PëPIPSC-CÍC,CH, P·P±CrPrP¶PµPSPSCÍ.

³ PµP°CjPeC-PSCÍPSPSC-P·Pj: P°PeC-PSPµP·C-CÍ, P±CjP°PrPëPeC-PSPµP·C-CÍ, P±CjP°PrPëC,,CjPµPSC-CÍ, CÍPëPjPiC,PsPj P·CrP±C†P°C,PsPiPs PePsP»PµCÍP°, PµPeCÍC,CjP°PiC-CjP°PjC-PrPSC- CjPSP·P»P°PrPë, PiPsCjCrCëPµPSPSCÍ C...PsPrPë, PiC-PiPsPeC-PSPµP·C-CÍ, CÍPeCrC,C-CÍC,CH PI CÍCrPiP»PsP±P°C..., C,CjPµPjPsCj, PjP°CÍPePsPiPsPrC-P±PSPµ PsP±P»PëC†C†CÍ, PjBj™ CÍP·PsPIP° CjPëPiC-PrPSC-CÍC,CH, CÍPePµP»PµC,PSPs-PjBj™ CÍP·PsPIP° CÍPeCrC,C-CÍC,CH, CjPëPiC-PrPSC-CÍC,CH PiPsC,PëP»PëC†PSPëC... PjBj™ CÍP·C-PI, PiP°CjPeC-PSCÍPSPSC-P·Pj.

⁴ P°PëCÍC,PsPSC-CÍ: P±P»PµC,,P°CjPSPCÍPiP°P·Pj, PrPëCÍC,PsPSC-CÍ, PjBj™ CÍP·PsPIPµ PSP°PiCjCrP¶PµPSPSCÍ, PsCjPSPjP°PSPPrPëP±CrP»CÍCjPSP° PrPëCÍC,PsPSC-CÍ, PeCjPëPIPsCëPëCÍ, C,CjPëP·Pj.

⁵ P†PSCëC- PµPeCÍC,CjP°PiC-CjP°PjC-PrPSC- C,P° CjCrC...PsPIC- CjPSP·P»P°PrPë: PiPsCjCrCëPµPSPSCÍ CjC-PIPsPSPiP°PiPë, P±CjCrPeCÍPëP·Pj, CÍP»PëPSPsC,PµC†P°, PrPëP·P°CjC,CjC-CÍ, PiPsCjCrCëPµPSPSCÍ C...PsPrPë, P°PSPsPjP°P»CHBPSPëPNë PiP»P°P±PµP»CÍCjPSPëPNë CjPµC,,P»PµPeCÍ, PiC-PiPsCjPµC,,P»PµPeCÍC-CÍ, CjPSP·P»P°PrPë CjCrC...C-PI, CÍPëPSPPrCjPSPj PSPµCÍPiPsPeC-PNëPSPëC... PSC-Pi, PiC-PiPµCjCÍP°P»C-PIP°C†C-CÍ, PiPsCjCrCëPµPSPSCÍ CjCrC...C-PI CÍP·PëPeP°.

⁶ P°PëCÍPeC-PSPµP·C-CÍ: C...PsCjPµPsP°C,PµC,PsP·, PrPëCÍPeC-PSPµP·C-CÍ, PiCjPëPjP°CÍPë, CÍPiP°P·Pj PiPsPiP»CÍPrCr, PiCjPsC,CjCrP·C-CÍ CÍP·PëPeP°.

PhPiPëCÍ PrPµCÍPePëC... PiPsP±C-C†PSPëC... CjPµP°PeC†C-PNë

PµPsPjCžC,PSC-PSPSCÍ PeCjPëCëC,P°P»PëPeP°/ PeP°C,P°CjP°PeC,P°

P PsP·PiPëC,PsPe PeP°C,P°CjP°PeC,Pë CÍPiPsCÍC,PµCjC-PiP°PICÍCÍ PiC-Pr C†P°CÍ PrPsPeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSCH PeP°CjPëPiCjP°P·PëPSCr (PrPëPI. CjPSP·PrC-P» B«P°P°PSC- PrPsPeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSCH P· P±PµP·PiPµPePëB»). PjPsPjCr P·P° C,,PsCjPjCrPIP°PSPSCÍPj PeP°C,P°CjP°PeC,Pë CÍPiPsCÍC,PµCjC-PiP°P»Pë P·P° PrPsPiPsPjPsPiPsCj PsPiP»CÍPrC-PI C-P· C%oC-P»PëPSPSPsCj P»P°PjPiPsCj, P° PiP°C†C-C°PSC,Pë, CÍPeC- PIP¶Pµ PjP°P»Pë PeP°C,P°CjP°PeC,Cr, P±CrP»Pë PIPëPeP»CjC†PµPSC- P· PrPsCÍP»C-PrP¶PµPSPSCÍ. PµC-Pr C†P°CÍ PeP»C-PSC-C†PSPsC— PiCjPSPiCjP°PjPë PrPsCÍP»C-PrP¶PµPSPSCÍ PrC-C— PeP°CjPëPiCjP°P·PëPSCr Cr PiP°C†C-C°PSC,C-PI P· CëPëP·PsC,,CjPµPSC-C°Cj PiPsPIC-PrPsPjP»CÍP»PsCÍCÍ PiCjPs PeC-P»CHPeP° PIPëPiP°PrPeC-PI PeP°C,P°CjP°PeC,Pë, C%oPs C...P°CjP°PeC,PµCjPëP·CrPIP°P»P°CÍCÍ PSPµP·PSP°C†PSPëPj PiPsPjCrC,PSC-PSPSCÍPj PeCjPëCëC,P°P»PëPeP° P±PµP· PiPsCjCrCëPµPSPSCÍ P·PsCjCr (13/3192; 0,4 %). P°PµCÍPeC- P· C†PëC... PiP°C†C-C°PSC,C-PI PjP°P»Pë C†PëPSPSPëPePë CjPëP·PëPeCr.

P'PëPïP°PrPePë P'PÿP•, PIPeP»C₇H₄±PSPs P· PIPëPïP°PrPeP°PjPë P»P_μPiP_μPSP_μPIPsC—
P_μPjP±PsP»C—C—C,P°C,C₇H₅PjP±PsP·Cr PiP»PëP±PsPePëC... PIP_μPS,
C₇F₁PiPsC₇F,C_μC₇H₄—PiP°P»PëC₇F₄Cl₄ PiC₇H₅Pë PiC₇H₅PëP_N±PsPjC—P°PSC,PëPiC₇F₄PëC...PsC,PëPeC—PI.

PJ PeP»C-PSC-C‡PSPsPjCr PrPsCf'P»C-PrP¶PµPSPSC- PrP»C¶ PsC†C-PSPePë
PiPsPrPsPIP¶PµPSPSC¶ C-PSC,PµC¶PIP°P»Cr QT PiC¶Pë PiC¶PëPNëPsPjC-
PeP°C¶PëPiC¶P°P·PëPSCr PSPµ P±Cr'P»Ps PiPsPjC-C‡PµPSPs P¶PsPrPSPsPiPs
PiPsPrPsPIP¶PµPSPSC¶ C-PSC,PµC¶PIP°P»Cr QT Cr PiPsC¶C-PIPSCLPSPSC- P· PiP»P°C†PµP±Ps

(PrPēPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPrPēPSP°PjC-PeP°B»). P' C-PSC€PēC...
 PeP»C-PSC-C‡PSPēC... PrPsCḡP»C-PrP¶PμPSPSCḡC... PīPsPIC-PrPsPjP»CḡP»PsCḡCH P»PēC€Pμ
 PīCḡPs PrPμPeC-P»CHPeP° PIPēPīP°PrPeC-PI PSPμP·PSP°C‡PSPsPiPs PīPsPrPsPIP¶PμPSPSCḡ
 C-PSC,PμCḡPIP°P»Cḡ QT PīCḡPē PīCḡPēPNēPsPjC- PeP°CḡPēPīCḡP°P·PēPSCḡ. PμC-Pr C‡P°Cḡ
 PrPsPIPiPsC,CḡPēPIP°P»PsPiPs PIC-PrPeCḡPēC,PsPiPs PīPμCḡC-PsPrCḡ P»C-PeCḡPIP°PSPSCḡ 3
 PīP°C‡C-C" PSC,Pē (0,4 %) PjP°P»Pē CḡPePsCḡPēPiPsPIP°PSPēPNē P·P° C„PsCḡPjCḡP»PsCḡ
 P'P°P·PμC,C,P° C-PSC,PμCḡPIP°P» QT > 500 PjCḡ, P° PsPrPēPS C-P·PSPēC... PjP°PI
 C-PSC,PμCḡPIP°P» QT P· PePsCḡPēPīCḡPIP°PSPSCḡPj PαCḡPēPrPμCḡPēC‡C-Cḡ > 500 PjCḡ.
 PμPsPrPsPIP¶PμPSPSCḡ PSP° > 60 PjCḡ CḡPePsCḡPēPiPsPIP°PSPsPiPs P·P° C„PsCḡPjCḡP»PsCḡ
 P'P°P·PμC,C,P° C-PSC,PμCḡPIP°P»Cḡ QT PIC-Pr PIPēC...C-PrPSPsPiPs CḡC-PIPSCḡ
 CḡPīPsCḡC,PμCḡC-PiP°P»PsCḡCḡ Cḡ 7 PīP°C‡C-C" PSC,C-PI (1 %), P° Cḡ 2 PīP°C‡C-C" PSC,C-PI
 (0,3 %) Bḡ" P· PePsCḡPēPīCḡPIP°PSPSCḡPj PαCḡPēPrPμCḡPēC‡C-Cḡ. Pj
 PrPsPIPiPsC,CḡPēPIP°P»PsPjCḡ PrPsCḡP»C-PrP¶PμPSPSC- PrP»Cḡ PīC-PrC,CḡPēPjP°PSPSCḡ
 PμC„PμPeC,Cḡ PīC-Pr C‡P°Cḡ PIC-PrPeCḡPēC,PsC— CḡC,P°PrC-C— PīPsPrPsPIP¶PμPSPSCḡ
 CḡPePsCḡPēPiPsPIP°PSPsPiPs P·P° C„PsCḡPjCḡP»PsCḡ P'P°P·PμC,C,P° C-PSC,PμCḡPIP°P»Cḡ QT
 PSP° > 60 PjCḡ PIC-Pr PIPēC...C-PrPSPsPiPs CḡC-PIPSCḡ CḡPīPsCḡC,PμCḡC-PiP°P»PsCḡCḡ Cḡ
 12 PīP°C‡C-C" PSC,C-PI (1,6 %), P° C-PSC,PμCḡPIP°P»Cḡ QT P· PePsCḡPēPīCḡPIP°PSPSCḡPj
 PαCḡPēPrPμCḡPēC‡C-Cḡ Bḡ" Cḡ 4 PīP°C‡C-C" PSC,C-PI (0,5 %). PμC-Pr C‡P°Cḡ
 PīPsPrPIC-PNēPSPs CḡP»C-PīPsPiPs PīPμCḡC-PsPrCḡ P»C-PeCḡPIP°PSPSCḡ
 PīPsPrPsPIP¶PμPSPSCḡ CḡPePsCḡPēPiPsPIP°PSPsPiPs P·P° C„PsCḡPjCḡP»PsCḡ P'P°P·PμC,C,P°
 C-PSC,PμCḡPIP°P»Cḡ QT PSP° > 60 PjCḡ PIC-Pr PIPēC...C-PrPSPsPiPs CḡC-PIPSCḡ
 CḡPīPsCḡC,PμCḡC-PiP°P»PsCḡCḡ Cḡ 3 PīP°C‡C-C" PSC,C-PI (3,1 %), CḡPeC-
 P»C-PeCḡPIP°P»PēCḡCḡ PeP°CḡPēPīCḡP°P·PēPSPsPj, C,P° Cḡ 2 PīP°C‡C-C" PSC,C-PI (2 %),
 CḡPeC- PīCḡPēPNēPjP°P»Pē PīP»P°C‡Pμ±Ps.

PμPsPIC-PrPsPjP»PμPSPSCḡ PīCḡPs PīC-PrPsP·CḡCHPIP°PSC- PīPsP±C-C‡PSC-
 CḡPμP°PeC‡C-C—

PμPsPIC-PrPsPjP»PμPSPSCḡ PīCḡPs PīPsP±C-C‡PSC- CḡPμP°PeC‡C-C— PīC-CḡP»Cḡ
 CḡPμC" CḡC,CḡP°C‡C-C— P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ PjP°C" PIP°P¶P»PēPIPμ
 P·PSP°C‡PμPSPSCḡ. PīPμ PrP°C" P·PjPsPīCḡ PīCḡPsPiPsPrPēC,Pē PjPsPSC-C,PsCḡPēPSPi
 CḡPīC-PIPIC-PrPSPsC€PμPSPSCḡ PePsCḡPēCḡC,CH/CḡPēP·PēPe PīCḡPē
 P·P°CḡC,PsCḡCḡPIP°PSPSC- C‡CHPsPiPs P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ.
 PμPμPrPēC‡PSPēPj C,P° C„P°CḡPjP°C‡PμPIC,PēC‡PSPēPj PīCḡP°C‡C-PIPSēPeP°Pj, P°
 C,P°PePsP¶ PīP°C‡C-C" PSC,P°Pj P°P±Ps C—...PSC-Pj P·P°PePsPSPSPēPj
 PīCḡPμPrCḡC,P°PIPSēPeP°Pj CḡP»C-Pr PīPsPIC-PrPsPjP»CḡC,Pē PīCḡPs CḡCḡC-
 PIPēPīP°PrPePē PīC-PrPsP·CḡCHPIP°PSPēC... PīPsP±C-C‡PSPēC... CḡPμP°PeC‡C-PNē C,P°
 PIC-PrCḡCḡC,PSPsCḡC,C- PμC„PμPeC,PēPIPSsCḡC,C- P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ
 C‡PμCḡPμP· P°PIC,PsPjP°C,PēP·PsPIP°PSCḡ C-PSC„PsCḡPjP°C‡C-PNēPSCḡ CḡPēCḡC,PμPjCḡ P·
 C„P°CḡPjP°PePsPSP°PiP»CḡPrCḡ P·P° PīPsCḡPēP»P°PSPSCḡPj: <https://aisf.dec.gov.ua>.

PḡPμCḡPjC-PS PīCḡPēPrP°C,PSPsCḡC,C-.

5 CḡPsPeC-PI.

PjPjPsPIPē P·P±PμCḡC-PiP°PSPSCḡ.

P—P±PμCḡC-PiP°C,Pē PI PsCḡPēPiC-PSP°P»CHPSC-PNē CḡPīP°PePsPIC‡C- PrP»Cḡ

$P \cdot P^{\circ} C \dots P \ddot{e} C \acute{I} C, C \acute{r} P I C - P r P I P \ddot{r} P \gg P \ddot{e} P I C \acute{r} C \acute{I} P I C - C, P \gg P^{\circ}.$

$P > C - P e P^{\circ} C \acute{I} C \acute{I} C \acute{I} C \acute{I} C \acute{I} C P e P \ddot{e} P N_{\circ} P \cdot P^{\circ} C \acute{I} C - P \pm P S P_{\mu} P I P \ddot{e} P j P^{\circ} P i P^{\circ} C'' C \acute{I} P \ddot{r} P_{\mu} C \dagger C - P^{\circ} P \gg C \acute{I} C P S P \ddot{e} C \dots$
 $C, P_{\mu} P j P i P_{\mu} C \acute{I} P^{\circ} C, C \acute{r} C \acute{I} C P S P \ddot{e} C \dots C \acute{r} P j P s P I P \cdot P \pm P_{\mu} C \acute{I} C - P i P^{\circ} P S P S C \acute{I}.$

$P - P \pm P_{\mu} C \acute{I} C - P i P^{\circ} C, P \ddot{e} P I P S P_{\mu} P r P s C \acute{I} C, C \acute{r} P \ddot{r} P S P s P j C \acute{r} P r P \gg C \acute{I} C P r C - C, P_{\mu} P N_{\circ} P j C - C \acute{I} C \dagger C -.$

$P j P \ddot{r} P^{\circ} P e P s P I P e P^{\circ}.$

$P_{\mu} P s 1,5 P j P i P^{\circ} P \pm P s P i P s 3 P j P i: P i P s 7 P e P^{\circ} P i C \acute{I} C \acute{r} P \gg C \acute{r} P \pm P \gg C - C \acute{I} C, P_{\mu} C \acute{I} C -;$ $P i P s 1 P^{\circ} P \pm P s 4$
 $P \pm P \gg C - C \acute{I} C, P_{\mu} C \acute{I} C P \ddot{e} P I P e P^{\circ} C \acute{I} C, P s P S P S C - P N_{\circ} C \acute{r} P \ddot{r} P^{\circ} P e P s P I C \dagger C -.$

$P_{\mu} P s 4,5 P j P i P^{\circ} P \pm P s P i P s 6 P j P i: P i P s 7 P e P^{\circ} P i C \acute{I} C \acute{r} P \gg C \acute{r} P \pm P \gg C - C \acute{I} C, P_{\mu} C \acute{I} C -;$ $P i P s 4$
 $P \pm P \gg C - C \acute{I} C, P_{\mu} C \acute{I} C P \ddot{e} P I P e P^{\circ} C \acute{I} C, P s P S P S C - P N_{\circ} C \acute{r} P \ddot{r} P^{\circ} P e P s P I C \dagger C -.$

$P_{\circ} P^{\circ} C, P_{\mu} P i P s C \acute{I} C - C \acute{I} C P I C - P r P i C \acute{r} C \acute{I} C P e C \acute{r}.$

$P - P^{\circ} C \acute{I} C P_{\mu} C \dagger P_{\mu} P i C, P s P j.$

$P' P \ddot{e} C \acute{I} C P s P \pm P S P \ddot{e} P e.$

$P' P \acute{h} P \acute{y} B \ll P'' P_{\mu} P r P_{\mu} P s P s P C - C \dots C, P_{\mu} C \acute{I} C B \gg, P j P i P s C \acute{I} C \% P \ddot{e} P S P^{\circ}.$

$P_{\circ} C - C \acute{I} C \dagger P_{\mu} P \cdot P S P^{\circ} C \dots P s P r P \P P_{\mu} P S P S C \acute{I} C P I P \ddot{e} C \acute{I} C P s P \pm P S P \ddot{e} P e P^{\circ} C, P^{\circ} P^{\circ} P r C \acute{I} C P_{\mu} C \acute{I} C P^{\circ}$
 $P j C - C \acute{I} C \dagger C \acute{I} C P i C \acute{I} C P s P I P^{\circ} P r P \P P_{\mu} P S P S C \acute{I} C P N_{\circ} P s P i P s P r C - C \acute{I} C P \gg C \acute{I} C P S P s C \acute{I} C, C -.$

$H-1103, P' C \acute{r} P r P^{\circ} P i P_{\mu} C \acute{e} C,, P I C \acute{r} P \gg. P'' P_{\mu} P j C \acute{I} C P_{\mu} C -, 19-21, P j P i P s C \acute{I} C \% P \ddot{e} P S P^{\circ}.$

B